

EX LIBRIS

GALILEO
FREUD
SOCRATES
DESCARTES
KAPPEAS
DARWIN
CHINESE
KRAEPELIN
DE JERINE
LEONARDO

ARISTOTEL

PROTAGORAS

LINNEUS

SMITH & ELY
JELLIFFE

JOHN BULLARD '05

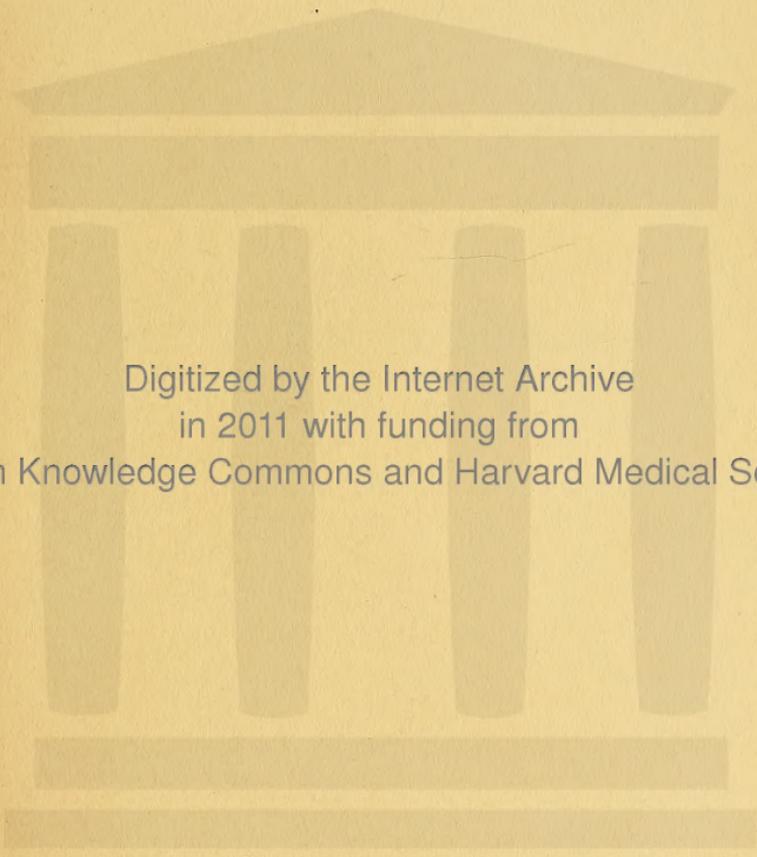
HARVARD
MEDICAL LIBRARY



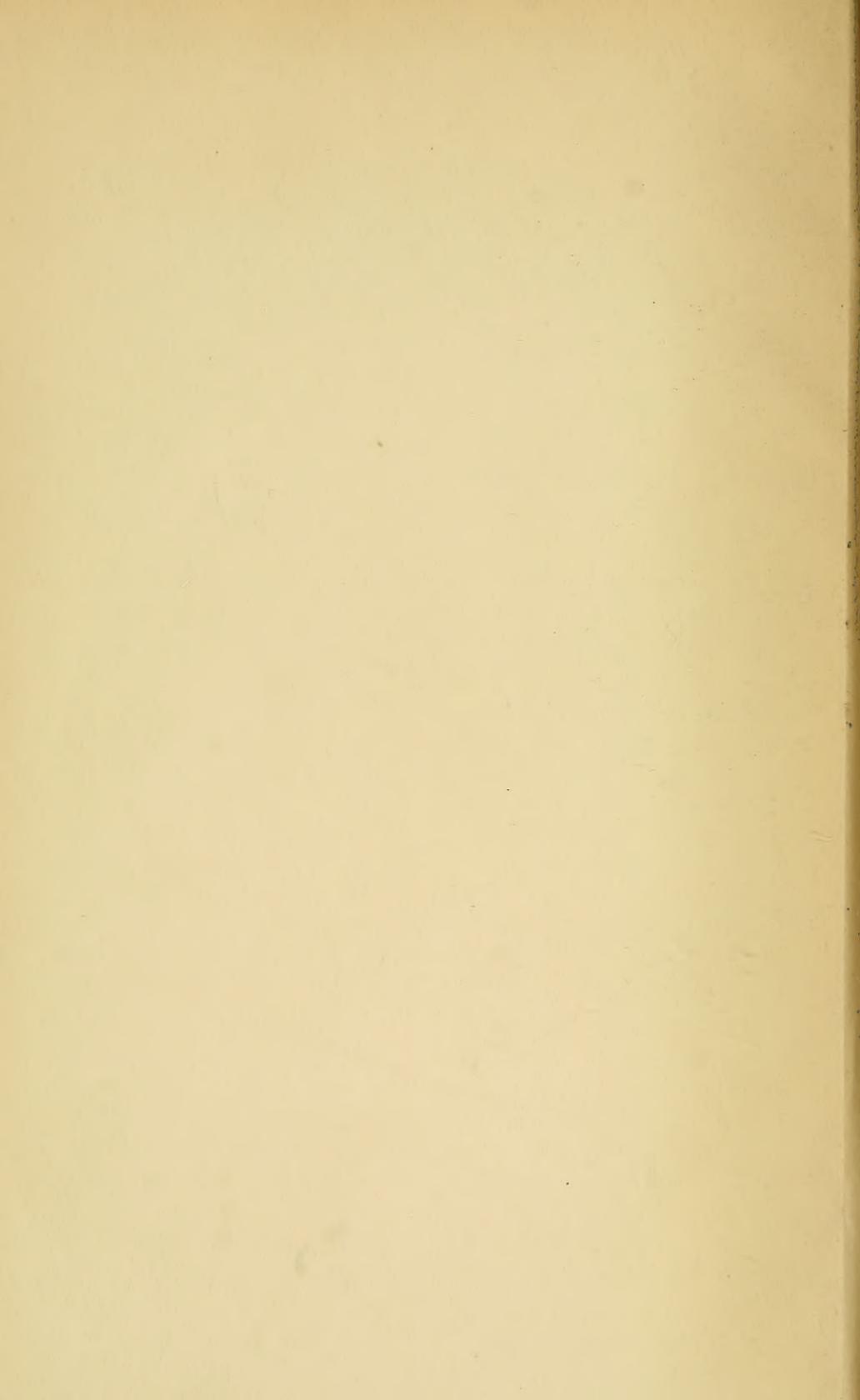
IN THE
Francis A. Countway
Library of Medicine
BOSTON

48888

211 175



Digitized by the Internet Archive
in 2011 with funding from
Open Knowledge Commons and Harvard Medical School



THE
FOOD FACTOR IN DISEASE

VOL. I.

'Quod est ante pedes nemo spectat : cœli scrutantur plagas.'—ENNIVS.

'When circumstantial proof is in its greatest perfection, that is, when it is most abundant in circumstances, it is much superior to positive proof.'—BURKE.

'False facts are highly injurious to the progress of science, for they often endure long; but false views, if supported by some evidence, do little harm, for everyone takes a salutary pleasure in proving their falseness; and when that is done, one path towards error is closed, and the road to truth is often at the same time opened.'—DARWIN.

'La tempérance et le travail sont les deux vrais médecins de l'homme.'
ROUSSEAU.

'Sanguis moderator nervorum.'—HIPPOCRATES.

'I am sick of diseases, I want to know origins and processes . . . the pathology of processes is the work of the future. . . . If we are to prevent disease it is to the beginning of the chain of accumulating stresses that we must look.'

CLIFFORD ALBUTT.

'I am prepared to maintain . . . that the practitioner is the man who very often plans the coach, and that the function of the worker in the laboratory is to drive in the bolts and put on the varnish. . . . To my mind the function of practice is to throw light on the functional and common ailments. . . . It is in these so-called trivial diseases, the common objects on the medical shore, that our danger comes of sinking into indifference—that is, unto death.'—GOODHART.

'What we need and wait for to-day in medicine is . . . some fundamental and far-reaching generalization in pathology and physiology which would vivify and vitalise some part at least of the mass of dead material facts which have been accumulated.'—CARTER.

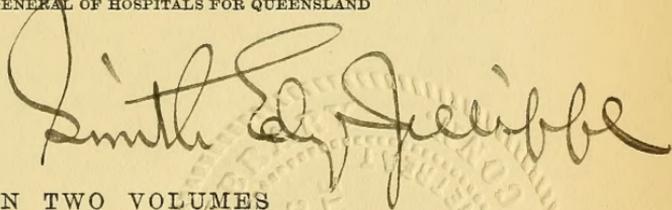
THE
FOOD FACTOR IN DISEASE

BEING AN INVESTIGATION INTO
THE HUMORAL CAUSATION, MEANING, MECHANISM, AND RATIONAL
TREATMENT, PREVENTIVE AND CURATIVE, OF THE
PAROXYSMAL NEUROSES (MIGRAINE, ASTHMA, ANGINA PECTORIS
EPILEPSY, ETC.), BILIOUS ATTACKS
GOUT, CATARRHAL AND OTHER AFFECTIONS
HIGH BLOOD-PRESSURE, CIRCULATORY, RENAL AND
OTHER DEGENERATIONS

BY

FRANCIS HARE, M.D.

LATE CONSULTING PHYSICIAN TO THE BRISBANE GENERAL HOSPITAL
VISITING PHYSICIAN TO THE DIAMANTINA HOSPITAL FOR CHRONIC DISEASES, BRISBANE
INSPECTOR-GENERAL OF HOSPITALS FOR QUEENSLAND

A large, stylized handwritten signature in dark ink, appearing to read "Smith E. Scribble". The signature is written in a cursive, flowing style and is positioned over a faint circular library stamp.

IN TWO VOLUMES

VOL. I.

LONGMANS, GREEN, AND CO.

39 PATERNOSTER ROW, LONDON
NEW YORK AND BOMBAY

1905

5M
H274F
v.1



PREFACE

IN the first half of the nineteenth century Buckle wrote the following indictment of the physical philosophers of the day :

I cannot but regard as the worst intellectual symptom of this great country, what I must venture to call the imperfect education of physical philosophers. . . . It cannot be concealed that they display an inordinate respect for experiments, an undue love of minute detail and a disposition to overrate the inventors of new instruments and the discoverers of new, but often insignificant, facts. Their predecessors of the seventeenth century, by using hypotheses more boldly, and by indulging their imagination more frequently, did certainly effect greater things, in comparison with the then state of knowledge, than our contemporaries with much superior resources have been able to achieve. The magnificent generalizations of Newton and Harvey could never have been compiled in an age absorbed in one unvarying round of experiments and observations. We are in that predicament that our facts have outstripped our knowledge and are now encumbering its march. The publications of our scientific institutions and of our scientific authors overflow with minute and countless details which perplex the judgment and which no memory can retain. In vain do we demand that they should be generalized and reduced into order. Instead of that, the heap continues to swell. We want ideas and we get more facts. We hear constantly of what Nature is doing, but we rarely hear of what man is thinking. Owing to the indefatigable industry of this and the preceding century, we are in possession of a huge and incoherent mass of observations which have been stored up with great care, but which, until they are connected by some presiding idea, will be utterly useless. The most efficient way of turning them to account would be to give more scope to the imagination and incorporate the spirit of poetry with the spirit of science. By this means our philosophers would double their resources instead of working, as now, maimed and with only half their nature. They fear the imagination on account of its tendency to form hasty theories. But surely all

our faculties are needed in the pursuit of truth, and we cannot be justified in discrediting any part of the human mind. And I can hardly doubt that one of the reasons why we in England made such wonderful discoveries during the seventeenth century was because that century was also the great age of English poetry.

Since the above was written, science generally has of course made enormous advances. But, with regard to the science of medicine—at any rate medicine as distinguished from surgery—I would ask: Is Buckle's indictment altogether undeserved at the present day? I have long held the opinion that it is not, and I have been greatly fortified in this view by reading the recent masterly addresses of Goodhart¹ and Carter.²

It seems to me that the pendulum has swung from inadequately aided deduction over to inadequately aided induction. The former undoubtedly led to disaster; but it seems no less true that the latter is now unduly hampering progress. The method of election lies somewhere between these two extremes. Induction, though an excellent collector, is but an indifferent organizer. It tends to make us specialists only. Our eyes are fixed upon the near foreground: we miss the pathological horizon. Our investigations are minutely analytical: we train ourselves to observe mere shades of difference in the symptom groups we term diseases. Hence classification becomes at once decreasingly comprehensive and increasingly artificial: pathological antagonisms become accentuated, pathological affinities blurred: we drift farther from common factors and from the supremely important question of primary causation.

In this work I have attempted to take a deductive view of disease—to approach the solution of pathological problems from the side of physiology. Manifestly, in order to bridge the interval between these two branches of human biology, hypotheses are necessary. Many have been formed. Some of these seem firmly substantiated by fact: in others, the basis of fact is slender; while a few are unsupported by fact. But none, so far as I myself can see, are inconsistent with fact. Nevertheless, it is inevitable that some will be found to be so by others of keener

¹ *Brit. Med. Journal*, November 3, 1900.

² *Lancet*, December 21, 1901.

insight. And I can only hope that such errors, when brought to light, will prove of detail only and not material to the main argument ; which, after all, depends, I am inclined to think, less upon the accuracy of any individual fact, than upon the number of long established, but hitherto inco-ordinated and therefore meaningless, facts which it seems capable of mutually correlating and thereby more or less fully explaining—than, in other words, upon a certain ‘continuity of essence,’ a general coherency and consistency. Now if it is true, as has been claimed, that ‘a perfect consistency can be nothing but an absolute truth,’ then perhaps it may be suggested that a degree of consistency points in the direction of truth.

Though they led to disaster in the past, it cannot be contended that imaginative methods are now capable of serious injury to medical science. As Darwin says, ‘False facts are highly injurious to the progress of science, for they often endure long, but false views, if supported by some evidence, do little harm, for everyone takes a salutary pleasure in proving their falseness, and when that is done, one path towards error is closed, and the road to truth is often at the same time opened.’¹ The mass of carefully recorded and thoroughly authenticated medical facts is now so enormous, that any fundamentally fallacious hypothesis is hopelessly foredoomed to founder amongst them. To doubt the inevitability of such consummation were indeed but little less than insult to the medical profession in this twentieth century.

It is customary for one who is advancing a novel theory to draw largely for illustration and confirmatory evidence upon his own experience. This would have been possible in the present instance : but I have considered it inexpedient. The existence of a dominant idea in the mind of an observer tends inevitably, even in perfect honesty, to some colouration of fact. But no taint of suspicion can cling to observations already recorded in medical literature—observations collected in illustration of different and divergent conceptions. Accordingly, in the selec-

¹ *Descent of Man*, 1899, p. 606.

tion of evidence, I have in nearly all cases given preference to the observations of others, adducing those of my own only where gaps existed. This filling in of gaps has perhaps added to the continuity of the argument, but I can hardly regard it as having been indispensable. For, were all my own observations struck out, the number of those which would remain seem to me sufficient to establish the main thesis of this work.

In order that the recorded observations of others should exert their full force, I have in general quoted verbatim. This has had the disadvantage of adding to the bulk of the work, already too great; but it has had some compensating advantages. It has enabled me to exhibit the work in its true character, namely, as in the main a mere generalization of a group of hitherto more or less disconnected facts and clinical observations; and to prefer an inadequate appreciation of the immense number of conscientious clinical observations recorded in medical literature, especially during the nineteenth century. Some of these, it is to be feared, have almost sunk out of sight during recent years. It is unfortunate that I have been forced to give many quotations at second, or even third, hand; but this was inevitable, since most of the work was written in a country destitute of reference libraries.

The various chapters in the work are by no means of even value. In most, the arguments seem to me to be illustrated by a sufficiency of accredited and pertinent clinical facts. But one or two chapters are largely speculative: this applies especially to Chapter XVII (Glycosuria, Consumption and Cancer), which has been introduced more for the sake of preserving continuity of the argument, than in the hope of establishing the views contained therein: indeed, I have myself grave doubts as to the tenability of some of these views. The chapter is, however, non-essential to the main purpose of the work, and may accordingly be omitted without loss by the general reader.

I fear I have at times lapsed into the use of teleological terms; but this has been merely for facility of expression and through poverty of language. And whenever 'designed adaptation to

a predestined end' seems to be implied, it will, I feel sure, be found that the facts or principles in question are explicable on the general theory of natural selection.

It may be that some will blame me for premature publication, and I am conscious that the charge will not be wholly undeserved from a scientific standpoint. But I feel that further delay could only have been made on purely selfish grounds. For the generalization contained in this work stands somewhat apart from other generalizations, in that it leads, not indirectly, but directly, to successful practice: the main theory can be tested daily by every practitioner of medicine. Consequently, one who would be tardy in publication would have to be content to stand aside and allow to pass unrelieved before his eyes an amount of preventable, if not always curable, human suffering which is incalculable: of this I have been painfully and increasingly conscious of late.

It remains for me to acknowledge my deep sense of obligation to my friends Drs. A. Jefferis Turner and Claude S. Hawkes, from both of whom I have had most valuable advice and assistance, not to mention much illustrative clinical material.

ROYAL COLONIAL INSTITUTE,
NORTHUMBERLAND AVENUE, LONDON.

CONTENTS

OF

THE FIRST VOLUME

INTRODUCTION	PAGE 1
------------------------	-----------

CHAPTER I

§§ 1-36

Metabolism—Nitrogenous metabolism: nitrogenous equilibrium: nitrogenous katabolism and excretion: nitrogenous anabolism and accretion: improbability of a nitrogenous accumulation in the blood—Carbonaceous metabolism: carbonaceous katabolism and excretion: carbonaceous anabolism and accretion: probability of a carbonaceous accumulation in the blood—The steam-engine analogy—The problem of a physiological diet: deductive investigation: inductive investigation: harmonization of the results of deductive and inductive investigation—Summary	14
---	----

CHAPTER II

§§ 37-61

Carbon income: carbonization of the blood, or the digestion and absorption of carbonaceous material—Oral digestion: conservative influence of oral disease: secondary effects of oral disease—Gastric digestion: conservative influence of gastric dyspepsia: secondary effects of gastric dyspepsia—Intestinal digestion and dyspepsia—Evidence that carbonization of the blood is a vital action and depends on the supply of proteid—Summary	36
---	----

CHAPTER III

§§ 62-98

Regulation of the carbon income—The glycogenic function of the liver—Physiological distension of the liver by glycogen—Pathological distension: acute: subacute or recurrent: chronic—Effects on the portal circulation: diarrhoea: haemorrhoids: inter-relations of diarrhoea and haemorrhoids—Relations between glycogenic distension and the carbon contents of the blood—Possible late results of glycogenic distension—The missing glycogenic factor in medicine—Summary	55
---	----

CHAPTER IV

§§ 99-118

PAGE

Carbon expenditure, or decarbonization of the blood: katabolism—Combustion a vital capacity of the nitrogenous tissues and a process of decarbonization—Variations in the rate of combustion: inherent individual variations: nutritional variations: variations depending on the supply of oxygen: variations in accordance with the demand for force and heat production: variations in accordance with the necessity for decarbonization, or variations determined by the supply of fuel—Rhythmical fluctuations in combustion: daily fluctuations: fluctuations associated with menstruation and utero-gestation: seasonal fluctuations—Clinical evidence that the temperature of the body may be regulated by decrease of heat production—Secondary results of strained combustion—Combustion inadequate for decarbonization—Summary	86
---	----

CHAPTER V

§§ 119-153

Carbon expenditure or decarbonization of the blood (<i>cont.</i>): anabolism—Utero-gestation and lactation—Secretion formation—Formation and deposition of muscle glycogen—Fat-formation: the functional factor, an active or vital capacity of the nitrogenous tissues: the supply factor, a due amount of carbonaceous material in the general blood-stream available for fat-formation: a process of decarbonization: carbon equilibrium at various levels: limitations to the decarbonizing influence of fat-formation—Combustion and fat-formation correlated—Obesity—Leanness—Summary	102
---	-----

CHAPTER VI

§§ 154-185

Carbon expenditure or decarbonization of the blood (<i>cont.</i>): haemorrhage a means of decarbonization through direct loss—The meaning of menstruation: possible objection to the adopted theory—Symptoms of menstruation—Amenorrhoea: amenorrhoea due to absence of carbonaceous surplus (supply): amenorrhoea due to imperfect discharging capacity (function): amenorrhoea of anaemia—Puberty and climacteric—Katabolic, anabolic, and haemorrhagic decarbonization correlated—Summary	128
--	-----

CHAPTER VII

§§ 186-252

Hyperpyraemia—Physiological variations in the carbon or fuel contents of the blood: pyraemic variations—The blood in starvation— <i>A priori</i> probability of hyperpyraemia—The food factor in hyperpyraemia: deficient nitrogenous intake: excessive carbonaceous intake—Functional factors in hyperpyraemia: a powerful digestive and absorptive capacity:	
--	--

	PAGE
deficient hepatic regulation : deficient katabolic decarbonization or combustion : deficient anabolic decarbonization, especially fat-formation : deficient haemorrhagic decarbonization or menstruation : mental strain and psychical factors—The principles of treatment of hyperpyraemia : treatment of hyperpyraemia through increased expenditure : treatment of hyperpyraemia through restriction of income : the two dietetic methods, that by reduction of the proteid, and that by reduction of the carbonaceous, intake, compared—Diatheses—Summary . . .	151

CHAPTER VIII

§§ 253–283

Pathological acarbonization—Bilious attacks—The paroxysmal neuroses : migraine or sick-headache : gastralgia : major epilepsy : asthma : catarrhal croup : angina pectoris : acute mania—Haemorrhage—Diarrhoea and lymphorrhoea—Glycosuria—Pyrexia : phthisis : acute gout : cyclic vomiting—Pathological anabolism—Summary	185
---	-----

CHAPTER IX

§§ 284–349

Recurrent hyperpyraemia ; or hyperpyraemia interrupted by recurrent pathological acarbonizing processes depending on hyperpyraemia : the paroxysmal neuroses—Theories of the paroxysmal neuroses : primary neurosal theory or theory of accumulation and discharge of nerve-force : toxic and uric-acid theories : hyperpyraemic theory—Evidence in support of the hyperpyraemic theory : food : external temperature : physical exercise : oxygen inhalation : daily fluctuations in the carbon contents of the blood : monthly fluctuations : utero-gestation and lactation : fat-formation : plumbism : pyrexia : haemorrhage : diarrhoea and lymphorrhoea : glycosuria : cancer : self-curative and mutually curative influence of the paroxysmal neuroses : dietetic treatment by reduction of proteid : dietetic treatment by reduction of the carbonaceous intake : a salt-free diet—Summary of evidence and conclusions	206
---	-----

CHAPTER X

§§ 350–415

Mechanism of the paroxysmal neuroses : priority of vaso-motor action—Migraine : vaso-constriction : vaso-dilation : cardiac compensation : mechanism of the pain : clinical evidence confirmatory of the vaso-motor theory : some objections to the vaso-motor theory : relation of migraine to rigor : summary of pathology of headache, migrainous and other—Asthma : vaso-constriction : vaso-dilation : cardiac compensation : clinical evidence confirmatory of the vaso-motor theory : summary of pathology of asthmatic dyspnoea—Angina pectoris : vaso-motor theory : confirmatory clinical evidence : angina and malaria : angina caused by flatulent distension of the stomach : summary of pathology of angina pectoris	273
--	-----

CHAPTER XI

§§ 416-465

	PAGE
Mechanism of the paroxysmal neuroses (<i>cont.</i>)—Epilepsy: theory of idiopathic epilepsy: evidence of initial rise of blood-pressure, vaso-motor and other: evidence of modification of the heart-beat: brain anaemia the proximate factor of some convulsions: convulsions due to causes other than cerebral anaemia: relation of convulsions to rigor, malarial and other: summary of pathology of epileptic convulsions—The connexion between vaso-motor action and glycogenic distension of the liver—Physiological model of the paroxysmal neuroses: mechanism of menstruation: confirmatory clinical observations: the full meaning of menstruation	330

CHAPTER XII

§§ 466-509

Some less common paroxysmal neuroses—Periodic or recurrent gastralgia: its dependence on hyperpyraemia: mechanism—Some neuralgias: priority of vaso-motor action: evidence of hyperpyraemia: malarial neuralgia—Raynaud's disease: a vaso-motor neurosis: its dependence in some cases on hyperpyraemia—Recurrent oculo-motor and other paralyses—Recurrent temporary amblyopia: malarial cases—Hydrops articulo-rum intermittens—Paroxysmal vertigo—Atypical affections—Mechanism of the paroxysmal neuroses collocated and correlated . . .	376
---	-----

CHAPTER XIII

§§ 510-581

The theory of pathological prepotency as applied to the paroxysmal neuroses—Factors in the paroxysmal neuroses other than humoral: secondary or functional factors: exalted irritability of the vaso-motor system: some extrinsic factors: heredity: acquired intrinsic factors: the 'memory of the body': nasal mucosa: eye-strain—Results of prolonged recurrence of the paroxysmal neuroses: humoral results or results as regards supply: functional results—Conditions which may be left on the stoppage, through means other than acarbonization, of the efficiently acarbonizing paroxysmal neuroses: substitutive physiological acarbonization: substitutive pathological acarbonization: unrelieved hyperpyraemia—General principles of treatment of the paroxysmal neuroses: physiologically prepotent cases: pathologically prepotent cases—Summary . . .	411
INDEX TO AUTHORITIES	469
INDEX OF SUBJECTS	479

ERRATUM

Page 22, line 1 from bottom of page, for 'largely' read 'mainly.'

THE FOOD FACTOR IN DISEASE

INTRODUCTION

THE argument contained in this work proceeds from the consideration of physiological metabolic processes to the elucidation of processes which we are accustomed to regard as pathological: it is, therefore, in the main deductive, not inductive. Such an inquiry is of necessity severely hampered by the existing poverty of exact chemical knowledge of normal metabolism. But there is no reason for regarding it as hopeless. For, by a bolder use of the imagination than is usually considered scientific from an inductive standpoint, it is possible to frame provisional hypotheses, which may be brought thereafter to the test of clinical experience. Many such hypotheses were tested in this way, and, being found inconsistent with established clinical facts, were abandoned.

Although we are accustomed to speak of deduction and induction as distinct and separate methods of inquiry, yet in practice the two are almost invariably used in combination, or rather alternately. The investigations herein pursued are no exception to this rule. Though I have for the most part tried to follow deductive lines, yet induction sometimes takes precedence; and, indeed, my starting-point was a clinical observation which long remained unexplained.

In the year 1889, I happened to prescribe for a travelling acquaintance. This gentleman was a resident of tropical China: he was in good general health, but for some years had been increasing considerably in weight: he was about forty

years of age and weighed between fifteen and sixteen stone. The treatment prescribed was directed against the increasing corpulence: it consisted in a diet scale which largely excluded fats, carbohydrates, and saccharine alcoholic drinks, throwing the onus of nutrition in the main upon proteids. I lost sight of this patient until 1891, when I met him in the North of Scotland. He then informed me that he had ever since practically adhered to the plan of diet I had prescribed, not on account of the obesity, for he had fallen in weight to between eleven and twelve stone, but because he had quite ceased to suffer from periodic headaches. I then elicited for the first time that he had suffered from violent headaches since early boyhood: that the attacks had recurred at intervals of a month, three weeks, or a fortnight; and that, having tried many physicians and numerous drugs without relief, he had ceased to seek advice on their account. His description of the attacks, from which he used to suffer, left me in no doubt that they were typically migrainous; but, so imbued was I at that time with the teaching that migraine was a primary—usually an hereditary—disorder of the brain, that I reflected little on the case. I regarded the cessation of the headaches as a coincidence, or as resulting, in a sort of general way, from change of climate and habits. It was not until an almost identical result occurred in a second case, that I began to suspect a direct causal relation between the food supply and this particular variety of ‘primary neurosis.’

In the second case, the patient had suffered for many years from typical hemicrania, commencing with visual symptoms and ending in bilious vomiting: the attacks recurred with great regularity every fortnight. He had abandoned hope of getting rid of his ‘bilious attacks’: indeed, he regarded them as salutary; but he wished to have his weight reduced. He was dieted accordingly as in the previous case. In three or four months, he had attained the desired reduction in weight: he then returned to his usual diet. *The attacks of migraine ceased absolutely from the day on which he commenced dietetic treatment: they returned within a fortnight after the cessation of treatment, and they continued to recur thenceforward with their old regularity.* No other alteration in his habits had been made: although he took but little exercise at any time, his general health remained excellent, as it had always been.

Such results appeared inexplicable, except on the hypothesis that migraine, in these cases at least, was a food disease. It seemed as if something, derived from the ordinary food supply, remained unassimilated by the tissues and accumulated in the blood, inducing, at regular intervals, a kind of salutary explosion. And, since the alteration in diet, which conferred immunity from the attacks, consisted of an increase of the nitrogenous, with a decrease of the carbonaceous, intake, it seemed reasonable to ascribe to the latter the source of the accumulation.

This idea, however, was manifestly out of harmony with accepted views as to the destination of the carbonaceous portion of the food in the organism. The carbonaceous portion of the food consists of the fats, carbohydrates, and two-thirds of the proteid: the nitrogenous portion, on the other hand, is nearly all found in the remaining third of the proteid. Now it seems to be always assumed that the former either undergoes rapid oxidation by the tissues, or is rapidly assimilated by them and laid down mainly in the form of fat; and that it is something derived from the latter which alone is capable of accumulating in the blood.

There remained the possibility that these commonly accepted views were incorrect; and the possibility of such a fundamental error having crept in was supported by several considerations. In particular, it was admitted that the known carbonaceous contents of normal blood (sugar, fat, glycogen, etc.) were liable to wide physiological variations: there was nothing to show that other carbonaceous compounds were not normally present; and it was felt that the amount of work done upon the chemistry of the plasma was insufficient to justify a position of absolute negation with regard to the possibility of carbonaceous material accumulating in the blood to a pathological degree.

Accordingly, it was determined to reconsider the whole position *ab initio*, and to adopt provisionally the hypothesis that carbonaceous material might, in certain circumstances, accumulate in the blood to an ultra-physiological degree, such accumulation constituting a primary cause of pathological action. To the blood-state supposed to eventuate, the term 'hyperpyraemia' (Gr. *pureia*=fuel) was applied. The term implies a condition in which the contained fuel or carbonaceous

matter, whatever its exact chemical composition, is in excess of the capacity of the organism for physiological disposal, whether by katabolism (combustion or oxidation) or by anabolism and storage (fat-formation, etc.). Conformably with this use of the term hyperpyraemia, we may speak of the physiological condition of the blood, in which the contained fuel or carbonaceous matter is capable of purely physiological disposal, as one of 'pyraemia'; and, in accordance with the view that the fuel, or carbonaceous matter in the blood, may fluctuate within physiological limits, we may speak of high and low degrees, or grades, of pyraemia.

Were it excusable to mention this crude, and possibly premature, attempt at a medical generalisation in the same breath with the greatest scientific generalisation of the nineteenth century, the argument for hyperpyraemia might be compared, in some respects, with Darwin's argument for the theory of natural selection. Darwin's scientific imagination led him early in his career to conceive his great theory. Provisional at first, the theory of natural selection soon ceased to be so, for it was found to correlate and explain an enormous number of accredited, but isolated and unexplained, biological observations. Further, the truth of the theory was confirmed by the fact that the theory pointed out the way to a further series of observations, altogether new.

The theory of hyperpyraemia, as already said, was suggested by a few therapeutic observations. It was at first purely provisional; but it rapidly ceased to be so when seriously entertained; for it was found to correlate and explain a large number of isolated clinical observations, otherwise inexplicable, or, at any rate, unexplained. Further, it was found (1) to indicate beforehand the direction in which such observations were to be sought, and (2) to discover what seem to me¹ to be an altogether new series of observations. An example or two will serve to make this clear.

¹ I have determined to refrain from claiming priority with regard to any of the observations in this work. It is true many of the contained observations seem to me, and, I doubt not, will seem to others, entirely new; yet the prolonged use in medicine of the almost exclusively inductive method has resulted in the collection of such a mass of clinical observations, that a large number of these are now forgotten: this is especially true of such as have hitherto led to the establishment of no principle. The more one looks into the literature of the past, the more one becomes convinced of this, so that it seems over bold to claim any observation as new.

1. If migraine depends upon hyperpyraemia, and is, as will be argued, a conservative 'explosion' adapted to clear the blood from the carbonaceous accumulation, it follows that conditions, whether physiological or pathological, which are hostile to hyperpyraemia, will be capable of relieving or dispersing migraine paroxysms. It will be argued that physical exercise and abstinence from food tend to reduce, or disperse, hyperpyraemia; and, on searching through Edward Liveing's classic work on 'Megrim and Sick-headache,' many examples of the salutary influence of both conditions upon recurring migraine paroxysms are to be found. Again, migraine and asthma have long been known to be capable of alternation, or mutual substitution, in the same individual. The obvious inference is that asthma also depends upon hyperpyraemia. If so, asthma, equally with migraine, should be relievable, or dispersable, by physical exercise and abstinence from food; and, on searching through Hyde Salter's classic work 'On Asthma,' numerous instances of the salutary influence of both conditions upon this affection are to be found.

2. Hyperpyraemia, we shall see, is of necessity incompatible with pyrexia of any severity or duration. Hence both asthma and migraine should remain in abeyance during pyrexia. On searching through medical literature, plenty of cases may be found in which asthma ceased during pyrexia. Hitherto I have failed to find the same recorded of migraine; but anyone can satisfy himself that the cessation of migraine during pyrexia is almost invariable. However, whether the latter is a new observation or not, what I am especially anxious to point out, is that, so far as I am concerned, the inverse relations of both migraine and asthma to pyrexia, were in the first place pure deductions from the theory of hyperpyraemia, which deductions led up later to the discovery of the facts. One more illustration. If asthma depends upon hyperpyraemia, then the supervention of obesity should be capable of relieving asthma. This deduction prompted search for such a result—a search which ended in the discovery of Berkhart's three cases (§ 323). And so with the majority of observations, some apparently new, many obviously old, deduction preceded and observation succeeded. It is this consideration, more than any other, which has served to convince me of the fundamental truth of the theory of hyperpyraemia.

The argument for hyperpyraemia is therefore cumulative : it depends for its strength, both upon the number of well-accredited clinical and experimental facts which it explains, and upon the number of apparently new observations, all capable of independent proof, which it has facilitated. These facts and observations, taken together, are extremely numerous ; and probably not a tithe of them are included in this work.

In that it will convey some idea of the scope of the work, it may be advantageous to refer here to a few of the more familiar physiological and pathological problems which the theory of hyperpyraemia seems capable of solving.

1. It will hardly be disputed that there is an old-standing and widespread, though vague, impression, both within and without the medical profession, that dyspeptic conditions are in a sense conservative, in that persons, so affected, are relatively less liable than others to become the victims of certain other and graver diseases : it is, at any rate, freely admitted that some constitutional diseases, such for example as gout, are commonly acquired by the aid of a sound stomach (Ewart). Under the theory of hyperpyraemia, these conceptions become definite and explicit.

2. Physical exercise is widely recognised as an almost essential factor in physiological health : its influence in preventing, and even dispersing, a host of minor ailments, such as dyspepsia, biliousness, bilious attacks, headaches, and nervousnesses, is unquestioned ; and many authors have pointed out that, under its influence, formal attacks of migraine, asthma, epilepsy, gout, etc., may be greatly modified, if not altogether abolished. I do not think any satisfactory explanation of the therapeutic influence of physical exercise has been offered ; but if, as is maintained in this work, hyperpyraemia enters as a factor into all the above-mentioned departures from health, then a simple and complete explanation is to hand : exercise operates by dispersing hyperpyraemia through greatly increasing the combustion of carbon and the consequent output of carbonic acid.

3. It is generally admitted that extreme leanness, unless it has been attained deliberately as in training, is incompatible with perfect health ; and that increasing deposit of fat goes hand in hand with convalescence from disease and with

improving health. It has also been observed that the development of obesity has, in some cases, replaced a long-standing recurrent neurosis or other recurrent affection, such as gout. No explanation of any of these facts has been offered, but they are all readily explicable on the theory of hyperpyraemia. For, in the process of fat-formation, carbonaceous material is withdrawn from the blood, thus relieving hyperpyraemia, upon which many forms of depraved health, recurrent neurosis, gout, etc., can be shown by independent evidence to depend: the process of fat-formation thus becomes an actual factor in, rather than a mere index of, the improvement in general health.

The temperaments of the lean and fat are in general antagonistic. Lean persons tend to be physically active and energetic, if not fidgety and irritable: fat persons tend to be physically inactive and placid, if not lazy and indifferent. We commonly assume that the temperament determines the state of nutrition—that inactivity leads to corpulence, restlessness to the opposite. The theory of hyperpyraemia does not exclude this sequence of cause and effect; but it suggests that, in some cases, the sequence is reversed—that many lean persons, being deficient in the capacity to form fat, are constrained, in order to avert hyperpyraemia, to depend upon constant exercise, a necessity not experienced by persons of an obese tendency.

4. The meaning of menstruation has yet to be elucidated. Under the theory of hyperpyraemia and all that it involves, menstruation depends upon a tendency to continuous accumulation of carbonaceous material in the blood. This accumulation results from a retardation of combustion—a reduction of the specific coefficient of heat production—introduced at puberty by the evolution of ovarian activity: it is demanded by the preponderatingly anabolic functions of the mature female: it is devoted to the anabolism of the offspring; or, in the absence of conception, it is discharged at regularly recurring intervals during the menstrual process.

This conception of the causation and meaning of menstruation explains the occurrence of vicarious menstruation: the antagonism, complete or incomplete, between menstruation on the one hand, and, on the other, pregnancy, lactation, hard physical exercise, exposure to cold climates, obesity, fever, diabetes, haemorrhage, and other conditions: the 'normal' symptoms of menstruation: the variations in the excretion of

carbonic acid, urea and uric acid, which have been observed at puberty, each menstrual period, and the menopause: the well-known tendency for the attacks of many paroxysmal disorders, such as migraine, asthma, epilepsy and gout, together with numerous minor ailments, to group themselves around each menstrual epoch: the accentuation of all such disorders which supervenes on the suppression of the flow; and the special tendency for many of them to commence at the period of puberty, to be increased in severity at the menopause, and to disappear thereafter.

5. The salutary influence of pregnancy. It is an old observation that some women enjoy perfect health only during pregnancy. This is readily understood when we come to realise (1) that, during pregnancy, hyperpyraemia is less probable than at other times; and (2) that a very large number of common ailments, as well as many more or less formal paroxysmal affections, have hyperpyraemia for an essential factor. Cases are recorded in which long-standing recurrent migraine, asthma, epilepsy, and even mania, have remained in complete abeyance during pregnancy.

6. Nearly all sufferers believe that recurrent bilious attacks and paroxysmal affections, such as migraine, asthma, epilepsy, and gout, are in a sense salutary, in that each attack is apt to be succeeded by a period of considerably improved general health and comfort. So widely recognised was the salutary influence of an acute gouty paroxysm at the commencement of the nineteenth century, that deliberate endeavours were not infrequently made to precipitate attacks. Conformable with these facts, is the observation that, in many cases the attacks of these paroxysmal disorders tend to be severe in proportion to their infrequency, and conversely.

All the observations, contained in the above paragraph, are explicable on the theory of hyperpyraemia, but not, I think, upon any other. The affections, referred to, depend upon hyperpyraemia and are themselves adapted to disperse this blood-state: though pathological, they are conservative but not necessarily salutary.

7. The phenomena termed 'alternation of the neuroses,' 'neurosals transformations or metamorphoses,' have attracted much attention and speculation. Recurrent paroxysmal disorders, such as migraine, asthma, epilepsy, gastralgia, paroxysmal

mania, and many other less definite nervous affections, have been observed to be susceptible of mutual replacement in the same individual at different periods of his life. Such alternations have been explained on the theory of accumulation and discharge of nerve energy: it has been supposed that nerve energy accumulates and that the paroxysmal affections, referred to, are manifestations of the discharge of this accumulated nerve energy. This explanation might appear sufficient, were it not for the fact that the 'alternation of neuroses' is but a portion of a much longer series of alternations: almost any of the above conspicuously nervous disorders may be replaced by very numerous processes, such as gout and pyrexia, affections in which the nervous element is inconspicuous and seemingly of secondary importance. This far longer series of alternations is explicable only on the theory of hyperpyraemia. This theory retains the ideas of accumulation and discharge, but not as applied to nerve energy: instead, it applies these ideas to the fuel, or carbonaceous material, which is the source of all energy, nervous and other, but which is as yet unconverted into energy of any kind: further, it locates the accumulation in the blood and regards the recurrent paroxysmal affections in question as conservative manœuvres, adapted to relieve the blood of its accumulated load.

8. The attacks of the paroxysmal affections, we are considering, exhibit a remarkable preference for the small hours of the morning. Asthma, epilepsy, angina pectoris, gastralgia, gout, and other allied affections, are all especially prone to arise between midnight and about five in the morning. This is a fact which has been long observed, but for which, so far as I am aware, no definite tenable explanation has ever been offered.

On the theory that these affections depend upon hyperpyraemia, their special predilection for these hours is susceptible of a simple explanation. For, other things equal or approximately so, carbonaceous accumulation will tend to vary inversely with the rate of combustion and the output of carbonic acid; and it is during the small hours that the rate of combustion and the output of carbonic acid sink to the minimum.

9. Many paroxysmal affections, whether prominently nervous, such as migraine, or other, such as gout, have been treated with more or less success by plans of diet which are seemingly opposed to each other in nature and effect.

Haig strongly recommends for migraine a diet in which the proteid intake is largely reduced and drawn in the main from milk and cheese: he lays no stress upon the necessity of restricting the purely carbonaceous intake. Plans somewhat similar are commonly accepted as the best for gout. On the other hand, both migraine and gout may be treated by the Salisbury diet which consists almost exclusively of lean meat and hot water: in this plan, the purely carbonaceous intake is almost abolished, the proteid intake considerably increased.

Either plan has been attended with more or less success; and this upon a superficial view is difficult to explain. But it will not, I think, be by any means impossible to show that both these apparently divergent methods join in one common tendency—namely, a tendency to the reduction of hyperpyraemia.

10. A condition of unrelieved, or inadequately relieved, hyperpyraemia fully explains the almost interminable list of symptoms variously ascribed to lithaemia, the gouty, arthritic or herpetic diathesis, larvaceous, irregular, abarticular, suppressed or concealed gout, arthritism, uricacidaemia, etc. For it will be pointed out that all conditions, dietetic, hygienic, therapeutic, physiological or pathological—amongst the last notably acute articular gout—which are capable theoretically of dispersing the hypothetic state of hyperpyraemia, have been observed, in different cases, to abolish, temporarily at least, the whole train of morbid manifestations referred to.

11. Finally, the theory of hyperpyraemia seems to shed a new light upon the retention and excretion of uric acid, and upon the pathological potentialities of this compound, limiting these potentialities, for the most part, to true articular gout, the morbid affections dependent on uro-lithiasis and calculus, and certain forms of renal degeneration.

The problems and observations in the above eleven paragraphs are but a few of the large number which seem to me explicable on the theory of hyperpyraemia. I have selected them because of their importance and because they are probably amongst those which are most familiar to students of contemporary medicine. To attempt anything further would be out of place at the present stage of this work.

But, besides offering a rational explanation of numerous medical problems and observations, the theory of hyperpyraemia

seems to form a fundamental bond of union, hitherto missing, between many of the theories of individual diseases, which have been best received by the medical profession, and which have stood the test of time—it seems to stand behind and complement, not in any way to contravene, many of the less comprehensive generalizations, already accepted or favourably regarded. Thus it will be found to be almost wholly consistent with, and perhaps to lend additional confirmation to, the following :—

The theory that the energy of muscular action is supplied by the carbonaceous portions of the food ; and that function, whether katabolic or anabolic, is dominated by the nitrogenous supply : both Bernard's and Pavy's views as to the glycogenic function of the liver in so far as these views are not mutually antagonistic : Marey's law of the inverse relation between blood-pressure and pulse-rate : Möllendorff's theory of the mechanism of migraine : the vaso-motor theories of the mechanism of asthma as set forth by Sir Andrew Clark and others : Moxon's theory, and vaso-motor theories generally, of the mechanism of an epileptic fit : Nothnagel's theory of functional angina pectoris : Raynaud's theory of local syncope : the influence of hereditary or acquired pathological habit in perpetuating the recurrence of paroxysmal nervous disorders : Garrod's theory of gout, and Roberts's quadriurate theory : the humoral (usually termed toxic) conception of insanity, of many functional nervous disorders, and of many dermatoses : George Johnson's theory of the stop-cock action of the arterioles as applied to high blood-pressure, renal cirrhosis, etc. : Cohnheim's theory as to the meaning of the high blood-pressure in degenerative diseases of the kidney ; and many more.

Finally, and to my mind most important of all, because fundamental, the theory of hyperpyraemia constitutes a tangible basis for the conception of the conservative principle of disease—of the *vis medicatrix naturæ*—which has been held by practically all philosophic physicians from Hippocrates downwards : it implies, indeed, a considerable extension of this conservative principle.

The theory of hyperpyraemia is consistent with, and explanatory and confirmatory of, a smaller conception, subordinate to, but constituting an integral portion of, the larger conception of the conservative principle of disease : this

subordinate conception, held by Jonathan Hutchinson, Harry Campbell and others, is to the effect that physiological and pathological action differ from each other in degree, rather than in kind, and graduate by insensible gradations into each other. It will be admitted that physiological action is fully, and on all occasions, conservative in nature; and we shall, I think, come to believe, from a study of the theory of hyperpyraemia, that pathological action is, for the most part, but an exaggeration or modification of physiological action, equally 'purposive,' though less accurately adaptive, and therefore less economical, more damaging, and perhaps as a rule less successful.

A short capitulation of the argument of the work will be convenient and may serve to reduce the necessity for repetition. Chapter I is an attempt to deal with what is known of the physiological uses and actions of food in so far as concerns the subject of this work. Herein it is argued that the nitrogenous and carbonaceous portions of the food differ essentially in their functions and are, indeed, in many respects diametrically opposed to each other: that the former represents in great part the steel of the human engine, both that of which it is constructed and that which is required for repair: that the latter is strictly a fuel. Further, *à priori* reasons are given for thinking that the former is less likely to accumulate in the blood than the latter. Chapters II and III deal with the income of carbon to the blood and with the regulation of this income by physiological, and to some extent by pathological, methods. In Chapters IV, V and VI, are discussed the physiological methods of expenditure by the blood of carbonaceous material—decarbonization¹ of the blood. Chapter VII is an argument, mainly *à priori*, in support of the view that, in certain circumstances, the carbon expenditure of the blood may fall below its income, so that there occurs in this fluid an accumulation of carbonaceous material to a pathological degree: this is the blood-state to which the term 'hyperpyraemia' is applied.

The whole of the rest of the work may be regarded as an

¹ The term decarbonization has been applied to the excretion of carbonic acid from the blood through the lungs. In this work, it is used throughout in a different sense, namely, to include the processes whereby the blood is relieved from the unoxidized carbonaceous material constantly being supplied from the products of digestion.

à posteriori argument in favour of the existence of hyperpyraemia. Chapter VIII discusses, *irrespective of their causation*, the chief pathological methods whereby the amount of carbonaceous material in the blood may be reduced, whether by reduction of income, by increase of expenditure or by both. Chapters IX, XIV, and XVI, treat of recurrent pathological processes which have the same effect, but which depend upon hyperpyraemia and which, therefore, may be regarded as especially adapted to disperse this blood-state: these processes include many of the so-called paroxysmal neuroses, gout and some catarrhal, pyrexial and haemorrhagic affections. Chapter XVII deals with some continuous pathological processes having, presumably, a like influence on the blood: some of these processes seem to depend on hyperpyraemia, or on some of the factors of hyperpyraemia. In Chapters X, XI, and XII the mechanism of some of the paroxysmal neuroses is discussed. In Chapter XIII factors in their causation, other than hyperpyraemia. Chapter XV deals with the relation between the carbon contents of the blood, or pyraemia, and uric acid. Chapter XVIII concerns classification. Chapters XIX to XXIII, inclusive, deal with the clinical manifestations of unrelieved hyperpyraemia: Chapter XXIV with degeneration, an ultimate result of hyperpyraemia. Chapter XXV is recapitulatory and contains some general conclusions; and in Chapter XXVI, the general principles of treatment are discussed. The Appendix consists of a selection of illustrative cases.

CHAPTER I*

§§ 1—36

Metabolism — Nitrogenous metabolism : nitrogenous equilibrium : nitrogenous katabolism and excretion : nitrogenous anabolism and accretion : improbability of a nitrogenous accumulation in the blood—Carbonaceous metabolism : carbonaceous katabolism and excretion : carbonaceous anabolism and accretion : probability of a carbonaceous accumulation in the blood—The steam engine analogy—The problem of a physiological diet : deductive investigation : inductive investigation : harmonization of the results of deductive and inductive investigation—Summary.

§ 1. An enquiry into the possibility of an accumulation of carbonaceous material in the blood, whereby there arises the humoral condition which has been termed hyperpyraemia, may be conveniently commenced with a brief survey of what is known or conjectured as to the metabolism of the chief food-stuffs, namely, proteids, carbohydrates and fats. All three contain carbon in varying proportions : proteid alone contains nitrogen. The carbohydrates and fats, though differing widely in their mode of digestion and absorption and in their subsequent course through the circulation, present so much similarity in metabolism, that we may frequently speak of them as one, under the term *carbonaceous food-stuffs*. Following the usual custom, the digestive changes of food-stuffs will be excluded from the scope of the expression metabolism (Schäfer) :¹ metabolism will include only those changes which occur subsequent to absorption.

§ 2. Metabolism comprises two fundamentally distinct processes, namely, anabolism or assimilation, and katabolism or dissimilation : these, though distinct, may be concurrent in the one cell. Whether, however, the fresh food-material on reaching the cell is invariably in the first place built up into the substance of the cell, or whether, under certain conditions,

* Copyright, 1905, by F. E. Hare, in the United States of America.

¹ *Text-book of Physiology*, Schäfer, vol. i. p. 868.

the fresh food-material may be split by the agency of the cell, but outside its proper substance or bioplasm—whether, in short, anabolism of food-stuffs invariably precedes their katabolism—seems at present not fully determined. It is probable that, in the case of the proteid food-stuffs, such antecedent anabolism may occur; but 'it¹ is not probable that the non-proteid materials (fat, carbohydrate, gelatin) of the food become, after assimilation, built up into bioplasm, and, although they are undoubtedly taken into cell protoplasm, they can hardly be regarded as forming constituent parts of the molecules of its bioplasm. In this sense, therefore, they are outside, although in contact with, the bioplasm of the tissues' (Schäfer). In summing up upon these questions, Schäfer² says:—'The phenomenon of contact changes is . . . too universal to be denied. Since this is so, the most reasonable view to be taken of the matter appears to be one which supposes that metabolism may occur both as a splitting up and oxidation of the molecules of living tissue or bioplasm, and as a splitting up and oxidation both of unorganized proteid and of non-proteid materials outside, but in contact with, the molecules of bioplasm. Such a view . . . is consistent with all the known facts, and is . . . readily applicable to the phenomena, both of animal and vegetable metabolism.' What is, however, certain is that, in probably all cases, the metabolic changes, whether anabolic or katabolic, in the apported food-material, whether proteid or non-proteid, occur through the active agency of the cell or of its bioplasm. This fact is of essential importance from the standpoint of the theory of hyperpyraemia.

NITROGENOUS METABOLISM

§ 3. It is a fundamental biological fact that all structures, manifesting energy of any kind (muscles, nerves, gland cells, floating cells, seminal and ovarian cells, etc.), are nitrogenous. The same is true of the non-cellular digestive fluids, which prepare the food for absorption into the blood. This constancy of nitrogen implies the necessity of nitrogen wherever function has to be performed (Parkes).

But the performance of function involves nitrogenous waste

¹ *Text-book of Physiology*, Schäfer, vol. i. p. 898.

² *Ib.* pp. 898, 899.

from destruction of tissue proteid. This is clearly seen during inanition. Schäfer¹ says:—‘The amount of urea in the urine, during a fasting period of not too long duration, is probably a definite measure of the necessary destruction of tissue proteid which goes on within the body. . . . Such destruction occurs in spite of the fact that there is still plenty of non-nitrogenous material (fat) able to be drawn upon.’

This essential continuous waste of nitrogen can only be replaced by proteid food—in other words, the anabolism of bioplasm is possible only from nitrogen supplied in the form of proteid. Though other food-stuffs such as gelatin contain nitrogen, yet they are unable to replace proteid in this respect. Consequently, the satisfactory performance of function depends upon the supply of proteid. Parkes² says:—‘If the nitrogen be cut off from the body, the various functions languish. . . . If it is wished to increase the manifestations of the energies of the various organs, more nitrogen must be supplied’; and it must be supplied, as just stated, in the form of proteid. The above generalized statement is true within certain limits, whether the functions concerned consist mainly of anabolism or of katabolism.

§ 4. NITROGENOUS EQUILIBRIUM.—Since, as we have seen, the continued katabolism of tissue proteid is essential to the performance of function and therefore to life, it follows that continued anabolism of tissue proteid is no less essential. When the processes of proteid katabolism and proteid anabolism are evenly balanced, and when, consequently, the output of urea is practically equivalent to the intake of proteid, the body is said to be in nitrogenous equilibrium.

The proteid intake, necessary for the maintenance of this equilibrium, varies with a number of circumstances. If, during total deprivation of food, an amount of proteid, exactly equal to the loss of tissue proteid as estimated by the urea excretion, is given, the loss of tissue proteid is restricted, but not abolished. ‘The whole³ of the nitrogen of the added proteid appears in the urine as urea, and in addition there is a certain amount, although not as much as during complete starvation, of tissue nitrogen still present in the urine. In order to keep up nitro-

¹ *Text-book of Physiology*, vol. i. pp. 888, 889.

² *Practical Hygiene*, 1891, p. 242.

³ *Text-book of Physiology*, vol. i. p. 891, Schäfer.

genous equilibrium, Voit found that it was necessary to give two and a half times as much proteid as the animal had metabolized during fasting. This result . . . is due to the fact that the ingestion of proteid food directly excites the tissues to increased metabolic activity so that tissue proteid itself still becomes split up . . . Non-proteid substances do not produce this effect. On the contrary, the giving of gelatin, carbohydrates and fat has . . . a sparing effect upon proteid metabolism and tends to diminish the amount of tissue proteid which is becoming broken down' (Schäfer). Nitrogenous equilibrium can be produced with a far smaller amount of proteid, provided that, for the amount removed, an adequate quantity of any of these food-stuffs is added to the diet.

'If¹ to a starving animal, instead of what would appear to be just a sufficient amount of proteid, an excess be given, a point is at length reached at which the building up process exceeds the breaking down, and the tissues, and therefore the body generally, gain in weight. This increase in body weight, due to the laying on of tissue, proceeds to a certain point with any constant amount of added proteid, until a balance between the N laid on and the N lost is struck, when a condition of N-equilibrium is again obtained. A further increase of proteid food will now again produce an increase of tissue and of body weight, until again a condition of N-equilibrium is established. And this may apparently be carried up to the limit of the power of digestion of the animal for proteid food, so that ultimately fifteen times as much proteid may be metabolized as in the condition of inanition. On the other hand, diminution of the amount of proteid food tends in the same way to gradually establish N-equilibrium on a lower level, and with a diminished body weight; the animal losing flesh until such equilibrium becomes established, and then maintaining itself, provided the N ingested be constant, at a constant but lower level of N-equilibrium. In short "N-equilibrium is possible with the most different amounts of proteid in the food"' (Schäfer).

§ 5. NITROGENOUS KATABOLISM AND EXCRETION.—The view is commonly accepted that proteid consists of two parts, namely (1) a nitrogenous part, which is discharged in the form of urea; and (2) a non-nitrogenous or carbonaceous (fatty or carbohydrate) part, which may be utilized as fuel by the

¹ *Text-book of Physiology*, Schäfer, vol. i. pp. 891, 892.

tissues, or stored therein—which may, in short, behave like the carbonaceous food-stuffs¹ (Foster). Now there is reason to think that the primary katabolism or splitting of proteid into these two parts is *quite unconnected with the process of oxidation*. For, as Schäfer points out on the authority of Voit, ‘in² a dog fed with proteid, the urea was found by Feder to make its appearance in the urine within fourteen hours after feeding, whereas the removal of the remainder of the proteid molecule in the form of carbon dioxide and water did not occur for twenty-four hours after, so that the splitting of the proteid molecule must have occurred at one time and its complete oxidation at another.’ Further, were nitrogenous katabolism an oxidative process in ordinary circumstances, we should expect that muscular exercise would materially increase nitrogenous excretion; and this, as we shall see, is not the case, except perhaps when the carbonaceous portion of the diet is of insufficient caloric value,³ and in prolonged starvation when the tissue stores of purely carbonaceous material have been exhausted⁴ (Schäfer).

Except in the case of the loss of nitrogenous material which occurs with the menstrual flow, nitrogenous katabolism precedes and *determines* nitrogenous excretion. This applies to urea which constitutes by far the greater part of the waste nitrogen of the body, and which, as Voit has shown,⁵ is excreted in direct proportion to the amount of proteid ingested.⁶

Stewart⁷ says:—‘Within the limits of nitrogenous equilibrium, which is the normal state of the healthy adult, the body lives up to its income of nitrogen: it lays by nothing for the future. In the actual pinch of starvation, the organism becomes suddenly economical. When a plentiful supply of proteid is presented to the starving tissues, they pass at once from extreme frugality to luxury: some flesh may be put on for a short time, some nitrogen may be stored up; but the tissues soon pitch their wants to the new scale of supply and spend their proteid income as freely as they receive it.’ Hence we may infer that *nitrogenous katabolism, and therefore nitro-*

¹ *Text-book of Physiology*, Foster, 1895, pp. 789, 801, 811.

² *Text-book of Physiology*, p. 894.

³ *Ib.* vol. i. pp. 913, 914.

⁴ *Ib.* p. 889.

⁵ *Ib.* Schäfer, vol. i. p. 892.

⁶ The excretion of uric acid will be considered at a later stage of this work (Chapter XV).

⁷ *Manual of Physiology*, 1899, p. 457.

genous excretion, is largely determined by supply. This may be regarded as the first great law of nitrogenous katabolism and excretion.

§ 6. A second law of nitrogenous katabolism and excretion is that, in ordinary circumstances, they are 'nearly¹ independent of muscular work, that is to say, the quantity of nitrogen excreted by a man on a given diet, is practically the same whether he rests or works' (Stewart). Foster says:² 'We have no evidence of any nitrogenous waste at all as the result of a contraction' [of muscle]; 'and indeed . . . the study of the waste products of the body as a whole, leads us to believe that the energy of the work done by the muscles of the body comes from the potential energy of the carbon compounds and not of the nitrogen compounds at all.' Professor J. Bauer says:³—'It has been proved, chiefly through the researches of Voit, that the consumption or metabolism of albumen in the body is not raised in the least by the most laborious efforts; it is the non-nitrogenous materials only whose consumption is increased by activity. This fact is in no way opposed to the matter of experience, that the body requires a more liberal supply of albumen during hard labour; it rather tends to counteract false conclusions from these results of experience and to make the connexion clear. There can of course be no doubt that a labourer requires for the performance of a hard task powerfully developed and well-nourished muscles—that is, a large proportion of albuminous tissue in the body, for the maintenance of which a corresponding amount of albuminous food is necessary, as all experience of intense bodily activity goes to show.'

§ 7. We may, I think, formulate a third law to the effect that, in ordinary circumstances—that is, so long as there is available a sufficiency of purely carbonaceous material,—nitrogenous katabolism and excretion are independent of external temperature. Parkes⁴ says of the influence of high air temperature:—'The urea is lessened as shown by experiments in hot seasons at home and during voyages (Dr. Forbes Watson and Dr. Becher).' But he adds:⁵—'It is probable that this is simply from lessened food.' Similarly, it might fairly be

¹ *Manual of Physiology*, Stewart, 1899, p. 457.

² *Text-book of Physiology*, 1895, p. 103.

³ *Ziemssen's Hand-book of General Therapeutics*, 1885, vol. i. p. 154.

⁴ *Practical Hygiene*, 1891, p. 402. ⁵ *Ib.*

presumed that any increase of urea excretion under cold weather results from increased food. In both cases, the food variations would refer to nitrogenous, especially proteid, food.

§ 8. The general conclusions, to be drawn from a consideration of these three laws of nitrogenous katabolism and excretion, would be (1) that, except in the special circumstances of a deficiency of purely carbonaceous material, the organism does not draw to any extent upon proteid to supply energy, whether as force or heat; and (2) that, with the same limitations, nitrogenous katabolism and excretion are mainly determined by supply.

§ 9. NITROGENOUS ANABOLISM AND ACCRETION.—Just as nitrogenous katabolism for the most part precedes and determines nitrogenous excretion, so nitrogenous anabolism is a necessary condition of nitrogenous accretion. Under increased nitrogenous anabolism, there is a disturbance of nitrogenous equilibrium in a direction opposed to what occurs under increased nitrogenous katabolism, that is, the nitrogenous output falls below the nitrogenous intake.

Increased nitrogenous anabolism and accretion occur under the following, amongst other, conditions:—

1. During the period of physiological growth of the organism, whether, (1) as a parasite in utero, (2) as an ecto-parasite during lactation, or (3) subsequently, as an independent being. While it is certain *à priori* that, under these conditions, the output of nitrogen is below the intake, the fact has been demonstrated experimentally in the case of utero-gestation. Thus Reprev¹ has shown, from metabolic experiments on rabbits and dogs, that 'during pregnancy the organism absorbs more from the food and rejects less than during periods of sexual rest.' The katabolism 'of nitrogen decreases and less is excreted in the urine. Nitrogen is stored up in the body. In other words, the processes of assimilation are intensified, while those of excretion are diminished. Less urea and phosphates are excreted during pregnancy than under normal conditions. The amount diminishes as pregnancy advances.'

2. During the development in size of an individual tissue from increased use, for example, muscle from increased exercise, as in the case of cardiac hypertrophy from increased peripheral resistance. We have already seen that it is impossible, in

¹ *Digest of Metabolism Experiments*, Atwater and Langworthy, p. 344.

ordinary circumstances, by increasing muscular contraction to increase nitrogenous katabolism and excretion ; but the evidence, that it is easy, by this means, to increase nitrogenous anabolism and accretion, seems to me irrefutable.

3. In repair, during recovery from loss of tissue proteid, whether such loss has arisen from deficient proteid income, as in starvation or partial starvation ; or whether it has occurred through the pathologically exaggerated nitrogenous katabolism of pyrexia or possibly other morbid conditions (§ 104).

4. To some extent, as we have seen (§ 4), as a consequence of the ingestion of proteid in excess of the amount necessary for the maintenance of nitrogenous equilibrium.

§ 10. On taking a comprehensive survey of the above-mentioned conditions under which nitrogenous anabolism and accretion are increased as regards nitrogenous katabolism and excretion, we can hardly fail to be impressed by the idea that the metabolic variation is for the most part determined by the *demand* for new tissue. In the first two examples, the demand is manifestly created by a superadded or an increased physiological function. In the third, the demand results from an abnormal or pathological expenditure of the nitrogenous capital of the body. In the fourth only, is there any question as to the dominant influence of demand : in this case it would appear at first sight as if *supply* were the determining factor. But, even here, we cannot I think finally exclude the influence of an increase of function. We have seen that an increase of proteid stimulates the tissues to increased katabolism ; and it is open for us to assume that such increased antecedent katabolism in the presence of a plentiful supply, is the real determining factor of the succeeding increased anabolism and accretion.

But, be that as it may, we shall have to admit that in the great majority of cases, while a due supply of fresh proteid is essential, nitrogenous anabolism and accretion are not determined by the supply, but by the demand for fresh tissue, whether this has been created by an additional or increased function or by an exaggerated waste.

§ 11. IMPROBABILITY OF A NITROGENOUS ACCUMULATION IN THE BLOOD.—We have arrived at the conclusions that nitrogenous katabolism and excretion depend mainly on supply, nitrogenous anabolism and accretion, mainly on demand. Now it seems to me that these laws of nitrogenous metabolism—if

they may be so designated—afford a strong *à priori* argument against the probability of an accumulation of nitrogenous material occurring in the blood. For it would seem, on the one hand, that the organism experiences no difficulty in getting rid of superfluous nitrogen, but that, on the other, something of a struggle is involved in the retention of such nitrogen as is essential. Hence nitrogen, which fails to be anabolised and accreted, is discharged by an *automatic* mechanism.

These remarks apply only to the metabolism of proteid and to the excretion of urea. The metabolism of nucleo-proteid and the excretion of uric acid, will be referred to at a later stage of this work.

CARBONACEOUS METABOLISM

§ 12. The subject of carbonaceous metabolism will be considered in some detail in Chapters III to VI inclusive. Meanwhile, it will be convenient to refer to some of its leading features in order to contrast them with nitrogenous metabolism.

Carbonaceous metabolism presents an almost complete contrast to nitrogenous metabolism. The purely carbonaceous food-stuffs cannot be said to be essential to the organism, since proteid is a complete food and will alone continue to support life indefinitely. Again, unlike proteid, the purely carbonaceous food-stuffs have no power to increase the metabolic activity of the tissues; on the contrary, fat and carbohydrates, as we have seen, have a sparing effect upon proteid katabolism and tend to diminish the amount of tissue proteid which is being broken down. Further, it goes without saying that the purely carbonaceous food-stuffs have a sparing effect upon the katabolism of the fixed carbonaceous tissues.

§ 13. CARBONACEOUS KATABOLISM AND EXCRETION.—Unlike the primary katabolism of proteid, carbonaceous katabolism consists essentially of a process of slow combustion or oxidation: as a result, oxygen is absorbed and carbonic acid given out.

Except in the case of the loss of carbonaceous material which occurs with the menstrual flow, carbonaceous katabolism precedes and determines carbonaceous excretion. In this, the katabolism and excretion of carbon and nitrogen agree. But, as we have seen, nitrogenous katabolism is largely determined by nitrogenous supply. This does not hold of carbonaceous

katabolism. Stewart¹ points out that 'although the consumption of fat is to a certain extent increased with the supply of fat or fat-producing food, there is by no means the same prompt adjustment of expenditure to income in the case of carbon, as in the case of nitrogen.' In other words, carbonaceous katabolism and excretion do not depend, except within certain narrow limits, upon carbonaceous supply. This may be regarded as a first law of carbonaceous katabolism and excretion.

§ 14. Again, in contrast with nitrogenous katabolism and excretion, is a second law of carbonaceous katabolism and excretion, namely, that they are largely dependent on physical exercise. Foster² says:—'One hour's hard labour will increase fivefold the quantity of carbonic acid given off within the hour.' Parkes³ gives the observations of Pettenkofer and Voit on this point in the following table.

TABLE I.

Weight of man experimented upon 60 kilos. = 132 lb. avoird.	Absorption of Oxygen in grammes	Elimination in grammes of		
		Carbon Dioxide	Water	Urea
Rest day	708·9	911·5	828·0	37·2
Work day	954·5	1,284·2	2,042·1	37·0
Excess on work day (with exception of urea)	245·6	372·7	1,214·1	-0·2

'In other words, during the working day . . . 5,751 grains or 13·15 ounces of carbon dioxide in excess were evolved. Expressing this as carbon, an excess of 1,568 grains or 3·58 ounces, were eliminated on the work day. There was an excess of oxidation of carbon equal to 41 per cent., and it must be remembered that the so-called "work day" included a period of rest: the work was done only during the working hours, and was not excessive' (Parkes).

§ 15. In further contrast with nitrogenous katabolism and excretion, is a third law of carbonaceous katabolism and excretion, namely, that they vary widely with the external temperature. Foster says: ⁴—'within a lower and higher limit, cold increases and heat diminishes the bodily metabolism,

¹ *Manual of Physiology*, 1899, p. 461.

² *Text-book of Physiology*, 1895, p. 844.

³ Parkes' *Practical Hygiene*, 1891, p. 370.

⁴ *Text-book of Physiology*, 1895, p. 853.

as shown by the increased or diminished consumption of oxygen and production of carbonic acid as the temperature falls or rises.’

§ 16. But there is a fourth law of carbonaceous katabolism and excretion—and herein carbonaceous and nitrogenous katabolism and excretion are found to be in agreement—namely that they depend largely upon the nitrogenous—that is the proteid—supply. Foster¹ points out that proteid food augments the whole metabolism of the body, hurrying on the destruction, not only of proteid, but of carbon, food: in other words, proteid increases the excretion of carbonic acid, as well as the excretion of urea. This is in accordance with the accepted view, that all katabolic changes in apported food material occur through the active agency, and constitute functions, of the nitrogenous bioplasm (§ 2); and that function generally is increased with the supply of proteid. The power of proteid to increase the katabolism and excretion of the purely carbonaceous food-stuffs, is of extreme importance from the standpoint of the theory of hyperpyraemia.

§ 17. The general conclusions to be drawn from a consideration of these four laws of carbonaceous katabolism and excretion, would be (1) that, in ordinary circumstances, the organism is accustomed to draw upon the purely carbonaceous food-stuffs, fats and carbohydrates, to supply energy, whether as force or heat; and (2) that carbonaceous katabolism and excretion are mainly determined by the exercise of function.

§ 18. CARBONACEOUS ANABOLISM AND ACCRETION.—Just as carbonaceous katabolism for the most part precedes and determines carbonaceous excretion, so carbonaceous anabolism is, with some possible exceptions to be afterwards considered (§ 126), a necessary condition of carbonaceous accretion.

Carbonaceous anabolism and accretion concern mainly fat-formation. Later (§§ 125 to 135) I shall argue that fat-formation depends fundamentally upon two factors, namely (1) a margin of carbonaceous material in the blood over and above the amount which is being utilized as fuel; and (2) a vital or active construction capacity on the part of the bioplasm of some of the nitrogenous tissues, which construction capacity depends, as do all functions, upon the supply of proteid in the food (§ 127).

¹ *Text-book of Physiology*, 1895, p. 884.

Now the capacity to construct fat is always present *in some degree* in a physiological condition of the organism. Hence, in ordinary circumstances, fat formation will be determined by the margin of carbonaceous material in the blood, that is, by the supply. In general terms, then, we may conclude that carbonaceous anabolism and accretion do not depend upon demand, but upon supply.

§ 19. PROBABILITY OF A CARBONACEOUS ACCUMULATION IN THE BLOOD.—We have arrived at the conclusions that carbonaceous katabolism and excretion do not depend (except slightly) upon supply, but upon the exercise of function ; and that carbonaceous anabolism and accretion do not depend upon demand, but upon supply and upon a vital construction capacity on the part of some of the nitrogenous tissues. Now it seems to me that these laws of carbonaceous metabolism—if they may be so designated—afford a strong *à priori* argument in favour of the probability of an accumulation of carbonaceous material occurring in the blood in some circumstances. For, on the one hand, the exercise of the functions, force-production and heat-production, which mainly determine carbonaceous katabolism and excretion, is largely dependent on conditions, such as physical exercise and exposure to cold, which are more or less voluntary or accidental ; and, on the other hand, the capacity for fat-construction may, as we shall see (§ 237), be conspicuously inadequate. Hence carbonaceous material, which is superfluous through a retardation of combustion from deficient physical exercise or from hot weather, will not of necessity fully undergo anabolism and accretion ; neither will carbonaceous material, which fails to be anabolised and accreted, be of necessity discharged, as in the case of superfluous nitrogenous material, by an automatic mechanism. It would seem, indeed, that, in the case of nitrogen, accretion alone demands something of a struggle on the part of the organism, whereas in the case of carbon, something of a struggle is demanded by both excretion and accretion.

These views are not in accordance with current medical thought. We are accustomed to argue as if fat-formation were on all occasions adequate to the requirements of the organism—as if carbonaceous material in the blood, in excess of the fuel requirements of the tissues, were, *ipso facto*, stored extravascularly as fat, and also to some extent as glycogen. This

optimistic assumption has arisen, as seems to me, through our laying insufficient stress upon the constructive capacity of the tissues in fat-formation; and its disproval is one of the main objects of this work.

THE STEAM ENGINE ANALOGY

§ 20. The preceding conclusions were originally largely suggested by the old analogy between the human organism and the steam engine. This, as Robert Hutchinson¹ says, 'is a rather threadbare and not altogether accurate analogy, but it is perhaps the best that can be found. The building material of food' (proteid) 'corresponds to the metal of which the engine is constructed, the energy producers' (the non-nitrogenous, or purely carbonaceous, food-stuffs) 'to the fuel which is used to heat the boiler. Where the body differs from the engine is that it is able to use part of the material of its construction' (the carbonaceous part of the proteid) 'for fuel also.'

We are often warned that it is easy to push the analogy of the steam engine too far: it is seldom suggested that it is possible to err in the opposite direction. And yet it may be that, hitherto, an over-timidty, arising through a too conscientious adherence to the severely inductive method of investigation, has unduly restricted us in the use of analogical methods in general and of the steam engine analogy in particular.

For this analogy seems to me much more complete than is commonly claimed. In both the steam, and the human, engine, there is in general a practical equilibrium of building material: in neither, is there carried any store of such material beyond what is in daily use: accretion in either occurs only when such is in actual demand. In the steam engine, the waste of building material is determined in the main by friction—at least it depends upon function and is not directly dependent on combustion or oxidation. In the human engine also, it depends upon function and, with an apparent exception, is not directly dependent on combustion or oxidation. This apparent exception occurs when, in consequence of a deficiency of its accustomed fuel, the organism exercises its capacity for burning its building material. On the other hand, fuel in

¹ *Food and Dietetics*, 1900, p. 2.

both cases is apt to be stored in advance: its expenditure in both is strictly proportionate to the energy developed, whether as force or heat; and accretion may occur in the absence of any immediate demand—it is apt to occur, indeed, in inverse proportion to the immediate demand.

There is a further resemblance which, to my mind, is of extreme importance in practical medicine. It will be admitted that a well-constructed, large and therefore heavy, engine has a capacity for combustion, and therefore for the development of energy, which is not possessed by a smaller one—that the possible energy is largely proportionate to the amount of building material. The same is true of the human organism: the capacity for combustion, and therefore for the development of energy, is largely proportionate to the amount of anabolised proteid or bioplasm; and it is possible, as we have seen, to increase this anabolised proteid by increasing, under proper conditions, the supply of proteid in the food. Such conditions commonly include the creation of the demand for fresh tissue through the exercise of function, as, for example, systematic muscular contractions (§ 9). But, as we have seen (§ 16), the mere increase of proteid intake, though it may not result in an increase of anabolised proteid, increases the rate of combustion.

THE PROBLEM OF A PHYSIOLOGICAL DIET

§ 21. Our knowledge of physiological metabolism, meagre as it is, is sufficient to suggest that considerable variations in the quantity and constitution of the diet should be made in accordance with the variations in external conditions and work, inseparable from modern civilized life. In an attempt to solve the problem of a physiological diet, we may proceed in either of two fundamentally different ways. We may proceed by deduction from what we know of physiological metabolism; and we may proceed by induction from observations of the food customs of mankind in various environments.

§ 22. DEDUCTIVE INVESTIGATION.—Since exposure to cold largely increases the expenditure of carbon in response to the increased demand for heat-production, we should infer that, under conditions, such as the approach of winter or a change of residence from a low to a high latitude, we ought to

increase considerably the carbonaceous or fuel intake. And, since physical exercise largely increases the expenditure of carbon in response to the increased demand for force-production, we should infer that, under conditions such as a change from a sedentary to a laborious occupation, a similar addition to the food should be made. *À fortiori*, under conditions involving an increased demand for both heat and force production such as a change from a sedentary occupation in a low latitude to a laborious occupation in a high latitude, it is clear that the addition to the carbonaceous or fuel intake would be urgent.

§ 23. The converse of the above would necessarily follow. Under conditions, involving diminished exposure to cold or diminished physical exercise, we should infer the propriety of a considerable diminution of the carbonaceous or fuel intake; and, *à fortiori*, under conditions involving a diminution of both sources of expenditure. Conformably, Robert Hutchinson says: '—Compared with the diet of muscular labour . . . the diet for mental work should be small. The reduction should probably affect the carbohydrates and fats more than proteid, for it is the two former . . . which tend to be specially made use of as muscle foods. . . . Hence it is, that it is far easier for a man who is performing bodily labour to be a vegetarian, than for one who is engaged in mental work.'

§ 24. The variations in the nitrogenous or proteid intake, which should on physiological grounds be made in accordance with variations of external conditions or personal habits, are less clear. In the steam engine, the *capacity for combustion* will depend, *inter alia*, upon the size and strength of the furnace; and, if these qualities are to be assured, the supply of building material must not be stinted. So it is, perhaps, with the human engine. The capacity for combustion will depend, *inter alia*, upon the bulk and nutrition of the nitrogenous tissues, especially the muscles; and to assure these qualities, a due supply of proteid is essential. Hence it may be argued that, in an environment or with personal habits which entail rapid combustion, an ample supply of proteid is demanded. But manifestly such supply will not be proportionate to the combustion as in the case of a fuel supply.

§ 25. But there is another side to the question. External

¹ *Food and the Principles of Dietetics*, 1900, p. 43.

heat involves a diminished demand for heat-production and, consequently, a diminished combustion. But the development of energy, whether as heat or force, is not the only *object* of combustion. Combustion is also adapted, as we shall see later (§ 107 to 109), to clear the blood of superfluous carbonaceous material. Hence it may be argued that the diminished combustion, which results from the diminished demand for heat-production due to external heat, may lead, in some cases, to a deleterious accumulation of carbonaceous material in the blood; and that this tendency is best met by an increased supply of proteid which, as we have seen, has the power of stimulating the nitrogenous tissues to increased combustion (§ 16).

§ 26. So also in the case of the diminished combustion which results from the diminished demand for force-production due to sedentary habits. It may be argued that, here also, there is demanded the stimulating influence of an increased proteid supply upon the oxidizing nitrogenous tissues in order to compensate for the absence of physical exercise. In conformity with this, is, I think, an observation of Clifford Allbutt. This author says:—‘I am always assured by brain workers, and I share the prejudice, that for them also a somewhat liberal diet is required.’¹

It must be admitted that the theoretical indications for varying the proteid supply are complex, if not conflicting. On the whole, it would seem that, while a certain minimum is essential, the variations, demanded in accordance with variations of environment and personal habits, are much less than in the case of the purely carbonaceous food-stuffs.

The objections to the deductive method of investigating the problem of a physiological diet, consist in the seeming lack of complete harmony which exists between the conclusions so arrived at, on the one hand, and observation of the food customs of mankind and the experience of the medical profession on the other. This subject will be returned to presently.

§ 27. INDUCTIVE INVESTIGATION.—Sir William Roberts² says:—‘The science of dietetics must, I apprehend, be mainly based and built up on an observation and a study of the practices and customs of mankind in regard to their food,

¹ *System of Medicine*, vol. v. p. 845.

² *Digestion and Diet*, 1891, pp. 96, 97.

rather than upon *à priori* data supplied by physiology. In the case of the lower animals, we assume that each creature selects from the nutrient materials within its reach those articles which are most suited to its well-being and are best fitted to promote its success in the struggle for existence, and that it is guided in this selection by an almost unerring instinct. This, like other instincts, is now explained by biologists as consisting essentially in an inherited experience, which has been gradually accumulated through a long line of ancestors, and is transmitted by heredity to the descendants. Accordingly, when we see an animal feeding on a particular kind of food, we conclude without hesitation that that food is, of all the nutrient materials accessible to it, the best adapted for the special wants of its economy. But we know that man, in regard to his bodily functions, is subject to the same laws as those which govern the life of the lower animals. And we cannot doubt that in the formation of his dietetic habits, man is guided by the same kind of instincts as those which guide the rest of the animal creation in the choice of their food.

‘The generalised food-customs of mankind are therefore not to be viewed as random practices adopted to please the palate or to gratify an idle or vicious appetite. These customs must be regarded as the outcome of profound instincts, which correspond to important wants of the human economy. They are the fruit of a colossal experience, accumulated by countless millions of men through successive generations. They have the same weight and significance as other kindred facts of natural history, and are fitted to yield to observation and study, lessons of the highest scientific and practical value.’

§ 28. I have given this long quotation partly because of the eminence of the writer and of the weight which his teachings undoubtedly carry, but chiefly because the widespread adoption of such exclusively inductive views is, in my opinion, very largely responsible for the confusion which admittedly prevails at the present day in the science of dietetics. The optimistic assumption that the food customs of the *civilized* races of mankind are almost of necessity physiological, seems to me unfortunate, as well as untenable. It is unfortunate because it practically precludes food as a primary factor of disease, and thus closes the door at the out-

set upon investigation in this direction. By excluding *supply*, it throws into undue prominence disorder of *function*, whether hereditary, congenital, or acquired in many incidental ways, as the original starting-point of pathological action: this source of fallacy seems to permeate modern pathology, but is, I think, especially conspicuous in disorders of the digestive system. The optimistic assumption, just referred to, is untenable because it depends upon the further assumption that civilized man and the lower animals are subject *in equal degrees* to the law of natural selection—an assumption the truth of which cannot, in my opinion, be maintained.

§ 29. Harry Campbell¹ points out that 'the essential purpose of instinct and reason is to regulate the environment of the individual, to surround him by such conditions as are best suited to his existence': that 'man and brutes stand out in bold contrast in that reason is the chief means of the one, instinct of the other'; and further that instinct, though 'the most perfect possible guide,' is fully operative only in the presence of a stable environment.

Now it is admitted that, in the course of ages, owing to the stability of their environment, animals have developed an almost unerring instinct with regard to the selection of their food. The same is true doubtless of primitive man, and probably also to a less extent of contemporary human races whose environment has undergone little alteration through long periods. It is probable for example that the primitive Asiatic² 'took to rice eating not from desire but from the scarcity of animal food' (Hueppe); and that, through the operation of the law of natural selection, the modern Asiatic now lives upon an approximately physiological diet.

It cannot, I think, be upheld that instinct, operating through natural selection, has exercised a preponderating influence on the formation of the *present food customs of Western civilized man*. Instinct, as already stated, is fully operative only under a stable environment; and civilization implies an ever-changing environment. Further, the growth of reason, in itself an essential cause of the unstable environment, tends to blur the precision of instinct. Hence civilized man has come to depend largely, if not mainly, on the former.

¹ *Causation of Disease*, Chap. II.

² Prof. Ferdinand Hueppe in *Brit. Med. Journal*, 1901, March 2.

But reason, though doubtless far better adapted to a changing environment, is, as argued by Harry Campbell,¹ 'a far less perfect guide than instinct' under a stable environment. For 'in order that reason shall on all occasions give a correct result, two things are necessary: man must be acquainted with every natural law, and he must be gifted with perfect reasoning power.' Now, whatever may happen in the future, it is certain that such conditions are unattainable now. Consequently, we might perhaps regard the present in the light of an 'evolutionary interregnum'—an interregnum succeeding the despotic reign of instinct and preceding that of reason in its full development.

Hence it must, I think, be admitted that, into our present civilized food customs, there have entered many factors in addition to the operation of natural selection. Amongst these, we shall have to include greatly increased accessibility to a variety of food-stuffs through advancing knowledge in the science and art of manufacture and through increased facilities of transport, cultivated tastes, sentimentalism, fashion and many more. If this is true, then we *may* have in our present food customs a primary factor of disease possessing vast potentialities.

Conformably, we shall find that practically all the affections which are ascribed in this work to hyperpyraemia are more or less peculiar to civilized, especially to highly civilized, man: that they are comparatively absent from man in a savage state; and that they are unknown in the lower animals, except perhaps in such domesticated varieties as have come largely under the civilized human environment. Hence we shall have to regard hyperpyraemia as largely a result of civilization or of the evolutionary interregnum implied in the development of civilization. Moebius has said:—'The tendency to headache is a part of the degeneration which is inseparable from civilization.' Now headaches—at any rate, recurrent sick-headaches—are amongst the commonest of all the manifestations of hyperpyraemia; and if we might use the term 'degeneration' to cover conditions which depend upon inadequately rapid adaptation to the ever-changing environment of civilization, then the view held by Moebius would include the view preferred in this work.

¹ *Causation of Disease*, pp. 192 *et seq.*

§ 30. HARMONIZATION OF THE RESULTS OF DEDUCTIVE AND INDUCTIVE INVESTIGATION. — The conclusions already reached by deduction from physiology are supported to some extent by observation of the food customs of mankind. Thus in the Arctic Zone the Esquimaux live largely upon fat, the most concentrated form of purely carbonaceous, or fuel, food. Nor are there wanting examples of races inhabiting hot climates—the aborigines of Northern Australia, the Indians of parts of South America—who live largely upon flesh, the main source of proteid. And Schäfer¹ states that ‘it has been observed by Tiegel that the Japanese rickshaw runners consume rice in large quantities and at frequent intervals during their periods of work, whereas on off days, they live mainly on a flesh diet.’

§ 31. Consistent with these observations is the experience of a minority of the profession (of which I am one) that proteid is practically as essential in a hot climate and under sedentary conditions of life as in the opposite circumstances; but that, under both external heat and diminished physical exercise, the purely carbonaceous food-stuffs should be largely reduced; and conversely.

§ 32. On the other hand, the above physiologically deduced conclusions are seemingly in conflict with other observations. Many Asiatic races, such as the natives of India, Java, parts of China and the South Sea Islands, take comparatively little proteid and live very largely on carbohydrates, such as rice, sago and fruit.

§ 33. Consistent with, perhaps largely based upon, the latter series of observations, is, I think, the opinion of the majority of the medical profession upon dietetics. It is held that, under increased heat, meat should be largely eschewed, the carbohydrates somewhat increased; and that meat, except in small amount, is an improper food for those whose occupation is sedentary. The last is a deep-rooted and old-standing conviction, dating from long before the time when Liebig formulated his theory (now exploded)² ‘that the functional activity of the nitrogenous tissues involved a proportionate waste of the structural elements of those tissues, and necessitated a corresponding consumption of nitrogenous material to replace

¹ *Text-book of Physiology*, vol. i. p. 915.

² *Food in Health and Disease*, I. B. Yeo, 1897, p. 12.

that loss' (Yeo). Indeed the influence of this conviction may be traced in the Old Testament. Further, it seems to be the general view that one class of the purely carbonaceous or purely fuel foods, namely the carbohydrates, is, except in the presence of certain clearly defined diseases (glycosuria, diabetes), a suitable and practically harmless nutriment in all circumstances.

§ 34. Now it will be argued throughout this work that the views of the aforementioned minority of the medical profession are correct and that the conclusions deducible from physiology *are* applicable in the majority of cases to practice, both hygienic and therapeutic. Hereupon, the following crucial questions arise. If the views of the majority are incorrect, (1) how is it that the purely carbonaceous or fuel intake, which must often be excessive from the standpoint of physiological metabolism, is not a frequent primary cause of disease? and (2) how is it—and the fact of this objection may be admitted beforehand—that the purely carbonaceous or fuel intake can be increased—as in the substitution of a vegetarian or modified vegetarian, for an ordinary mixed, diet—under conditions, which theoretically demand a reduction, with, in some cases, absolute benefit?

§ 35. The answer to these questions largely constitutes the purpose of this work. Meanwhile, it may be stated in anticipation, (1) that a relatively excessive intake of carbonaceous material *is* one of the most fertile of the causes of disease, the diseases so arising being, for the most part, those whose fundamental pathology or meaning has hitherto baffled investigation; and (2) that an increase of the purely carbonaceous or fuel intake does not *of necessity* involve any increased intrusion of such material into the blood; often the contrary, indeed, since, as will be argued, the digestion and absorption of carbonaceous material depends largely upon the nitrogenous or proteid intake (§§ 55 to 60). In short, it will be argued that the views of the aforesaid majority are necessarily incorrect only from the standpoint of metabolism, using this term in its restricted sense (§ 1); and that these views frequently become correct when the processes of digestion and absorption are included within the scope of the term.

SUMMARY

§ 36. In this chapter, I have endeavoured to contrast with each other some of the fundamental laws of nitrogenous and carbonaceous metabolism; and to show thereby, and from the analogy of the steam engine, that any excess of nitrogenous material in the blood tends to be automatically excreted, but that a carbonaceous excess tends, in some circumstances, to accumulate in the blood.

CHAPTER II*

§§ 37—61

Carbon income: carbonization of the blood, or the digestion and absorption of carbonaceous material—Oral digestion: conservative influence of oral disease: secondary effects of oral disease—Gastric digestion: conservative influence of gastric dyspepsia: secondary effects of gastric dyspepsia—Intestinal digestion and dyspepsia.—Evidence that carbonization of the blood is a vital action and depends on the supply of proteid—Summary.

§ 37. It will be convenient to consider next the processes by which the blood is supplied with fuel or carbonaceous material. These comprise the numerous processes whereby the raw carbonaceous material, contained in the proteid, fats and carbohydrates of the food, is first suitably modified and then transported from the surface of the alimentary mucous membrane into the blood—in short, digestion and absorption, processes which we shall often find it convenient to speak of conjointly as ‘carbonization.’ Digestion occurs in the organs of primary digestion, the mouth, stomach and intestinal canal: absorption occurs to some extent in all three, but mainly in the last. Both processes, though they include various kinds of mechanical and chemical action, are manifestations of vital energy—they are vital functions; and ‘since every structure of the body, in which any form of energy is manifested . . . is nitrogenous,’ the due performance of these functions will demand, *inter alia*, a due supply of proteid in the food. Hence the primary essentials for the due performance of the complex function of carbonization, as carried on in ordinary circumstances,¹ will concern supply and function: (1) a due supply of carbonaceous material; and (2) a due functional capacity on the part of the organs and tissues concerned, this depending largely upon the supply of proteid.

* Copyright, 1905, by F. E. Hare, in the United States of America.

¹ I am not considering here the carbonization of the blood which occurs during starvation: that is an essentially different process and will be referred to later (§§ 187 to 189).

ORAL DIGESTION

§ 38. The digestive functions of the mouth are mainly mechanical: the only food-stuffs which are chemically altered are the starches: these are converted into soluble sugar. Although 'the action of the human saliva is very energetic, indeed, almost instantaneous'¹ (Bauer), yet the starches will have to be intimately mixed, and remain a certain minimum time in contact, with the saliva. For efficiency of oral digestion, therefore, as for efficiency of the whole complex process of carbonization, the primary essentials will concern supply and function.

1. The amount and character of the food presented. The food should be in such a form that thorough mastication and insalivation are necessary before swallowing is possible: biscuits, rusks, breadcrust, etc., would be ideal forms.

2. The functional capacity of the organs and fluids of oral digestion. The teeth, mucous membranes and glands will have to be in good order: this will imply due nutrition by a due supply of proteid. The saliva must be chemically active: for this, it must be alkaline in reaction; and, since it is a nitrogenous fluid, probably it will be dependent upon the proteid supply for its constant reinforcement.

It is probable, therefore, that the amount of proteid in the daily diet exercises no inconsiderable influence upon the digestion of carbohydrate material in the mouth, and less directly, upon its subsequent absorption.

§ 39. CONSERVATIVE INFLUENCE OF ORAL DISEASE.—In the commoner forms of mouth disease, such as dental caries, gingivitis and pyorrhoea alveolaris, mastication is necessarily imperfect and the saliva is not infrequently acid. Hence there will be a failure of salivary digestion, and by so much probably, a failure of subsequent absorption. And if, as is argued in this work, a long series of morbid affections of the general system depend primarily upon hyperpyraemia, then we shall be entitled to regard many of the functional and structural disorders of the oral cavity as at least incidentally conservative in their influence. Conformably, Sir Henry Thompson thinks that most people eat their way to the grave with their teeth; and many of the older physicians laid great

¹ Prof. J. Bauer in Ziemssen's *Handbook of General Therapeutics*, vol. i. p. 100.

stress upon the condition of the teeth as signs of the 'arthritic diathesis,' a constitutional state which, I shall argue later (§§ 858 to 865), is synonymous with hyperpyraemia. Laycock,¹ speaking of the characteristic features of this diathesis, refers to 'teeth massive, well-enamelled, regular, even undecayed in advanced life' (J. M. Fothergill).

The great increase of dental caries and other inflammatory conditions of the mouth during recent years, is beyond dispute: as to the cause of such increase there has been much speculation but little agreement. Here, as in other departments of pathology, the dominant prejudice against animal food has been conspicuous: excessive consumption of meat, together with an assumed hereditary tendency to degeneration, has been claimed as the essential factor. But recently, there has been a revolt against this teaching: Dr. J. Sim Wallace argues that the modern finely pulverized carbohydrate food-stuffs are the directly responsible agents; and in this he is supported by a report of a 'Decay of Teeth Committee.' The report,² referred to, says:—'Comparing the condition of the mouth after a meal of flesh and after some form of carbohydrates, in the one case the mouth is comparatively clean, a few fibres perhaps remaining between the teeth, which may be easily removed: in the other case, the interstices between the teeth and the fissures of the teeth are packed with soft masses of fermentable material, difficult, and in fact impossible, to remove entirely, and thus presenting all the conditions most favourable for the production of lactic acid.'

The following seems a reasonable view of the etiology of dental caries. Carbohydrate retention leading to fermentation and acidity of the secretions and contents of the mouth: erosion of the protecting enamel; and decay of dentine through bacteria thus admitted to the body of the teeth. And it is more than probable, as ably argued by Harry Campbell,³ that pyorrhoea alveolaris has a similar origin in soft carbohydrate food.

Here it will probably be objected that the Hindoos, who are in the main starch eaters, possess as a rule, large, healthy, strong, and exceptionally well-developed teeth. It is apt to be overlooked, however, that, with this race, careful and regular

¹ *Gout in its Protean Aspects*, J. M. Fothergill, 1883, p. 36.

² Quoted in the *British Medical Journal*, August 11, 1900.

³ 'Observations on Mastication,' *Lancet*, July 25, 1903, pp. 219, 220.

cleansing of the teeth is imposed as a part of their religious ritual; and it is easy to see that decay may be prevented by a careful and systematic toilet of the mouth in spite of injurious food customs. Hindoo vegetarianism, such as it is (for it is by no means exclusive), is in all probability a result of environment; and it is conceivable that the rigid enjoinder of mouth cleanliness has, in their case, its origin in the remote past in an experience of its dominant necessity under the food conditions of the country.

§ 40. A better index of the influence of food may be obtained from an examination of the teeth of races who take no special care in their preservation. Dr. W. A. Alden¹ of Montana, U.S.A., says:—‘I have examined in the last 21 years hundreds of these (Crow) Indians, and have yet to find one with pyorrhoea alveolaris. I have found it in negroes and in the mound builders, but not so in the Crow Indian tribe, as the Crows were almost exclusively flesh eaters, their diet being buffalo, elk, mountain sheep, deer and antelope. I present a model which I have obtained from Iron Bull, Crow Chief, at the age of 70 years.’ The illustration of the model referred to shows that every tooth in both jaws is present: that they are all perfect in size and shape; and that no trace of decay is anywhere visible. The aborigines of Australia, excluding the degenerate specimens who live on the confines of the towns, are mainly flesh eaters and are remarkable for the excellence of their teeth; and the same is true, to a less extent, of the white bushmen of the plains.

One fact alone seems almost fatal to the view that meat is the cause of the modern increase in dental disease. In Queensland at least, especially in its tropical portion, women suffer more frequently and more severely than men, from dental caries. For some years, I examined systematically the mouths of patients, and I do not hesitate to say that in women disease commences earlier, progresses more rapidly, and attains a higher grade of destruction, than in men. The number of young girls in North Queensland wearing complete sets of artificial teeth is startling. It is unnecessary to point out that the tendency of the tropics is to spoil the appetite for animal food and to increase the taste for starches, sugars and

¹ *Items of Interest: A Monthly Magazine of Dental Art, Science and Literature*, April 1900.

fruits; and that women are notoriously more influenced in this direction than are men.

§ 41. We may then assume that the modern increase of dental and mouth disease is in some way connected with the modern excessive use of soft carbohydrate food-stuffs; and there can be little doubt that, if carbonaceous excess is a common food fault, it is in the main a carbohydrate excess. Shall I then be accused of straining the imaginative privileges I am claiming throughout this work, if I suggest that dental and oral disease, incurred under these conditions, are protests against improper and excessive supply?

§ 42. SECONDARY EFFECTS OF ORAL DISEASE.—As in other departments, so here, local disorganization, whether we choose to regard it as conservative or not, leads ultimately to disorganization affecting remoter parts; and we may trace a series of pathological processes from the starting-point of dental and oral disease. The influence of imperfect mastication upon gastric digestion and general nutrition will be admitted by all. Recently, William Hunter¹ has called attention in a series of articles to 'oral sepsis as a cause of septic gastritis, toxic neuritis and other septic conditions.' And, in the 'Lancet' for August 22, 1903, a case of sapraemia, due to pyorrhoea alveolaris simulating typhoid fever, is described by Dr. J. W. Carr and Mr. E. W. Roughton.

GASTRIC DIGESTION

§ 43. The next step in carbonization of the blood is gastric digestion. Here again efficiency will depend upon function and supply.

1. The functional capacity of the organ, of its glands and of their secretion, will depend, *inter alia*, upon nutrition by a due supply of proteid food.

2. The supply of material for gastric digestion concerns chiefly proteid, which is the food-stuff mainly digested in the stomach. The amount will be of importance: it is easily conceivable that the functional capacity of the organ may be strained by excess of work, performed even under favourable conditions. The character of the proteid will be of the highest importance: it will have to be soft in consistence and sufficiently

¹ *Medical Review*, viii. No. 27, p. 733.

subdivided. A soft finely divided mince, made from the lean of meat, as free as possible from fat, etc., would be, on theoretical grounds, an ideal food for gastric digestion; and practically, I know of none more readily digested. Saliva having no action upon proteid, mastication will be less necessary than in the case of starch foods; but it will not be altogether superfluous, since, as pointed out by Harry Campbell,¹ mastication acts reflexly upon the stomach and promotes the flow of gastric juice. The conditions under which the proteid is presented to the organ are of the greatest importance: they concern mainly the consistency and state of subdivision of the proteid and the presence, or otherwise, of other food-stuffs in the organ at the same time. Other things being equal, the most perfect gastric digestion will occur when all material, other than proteid, is excluded.

Arguing from physiology, then, starch should be given in such a form as necessarily to undergo digestion in the mouth; and proteid should be submitted to the gastric juice unhampered, as far as possible, by the admixture of food-stuffs which have been undigested in the mouth, and which are indigestible in the stomach.

§ 44. These physiological ideals will not be found to agree with common practice. The proteid of an average meal is presented as a solid, often a very tough solid, requiring toilsome mastication to fit it for a passage through the gullet; and our practice as regards starch foods appears to be to hasten by all possible means their passage through the mouth, where they should be in great part at least digested, and to prolong their stay in the stomach, where their digestion is impossible. The every-day dinner of the Englishman must be regarded as highly unphysiological. Meat, insufficiently divided, is swallowed with imperfectly insalivated potatoes. As proteid digestion is commencing, the gastric juice is liable to be suddenly diluted to the point of impotence by a drench of beer or other liquid. Later, a mass of soft undigested—and, as far as the stomach is concerned, indigestible—starch, such as rice, is spread over, and mingled with, the proteid, which is still only in the early stages of peptonization.

We are often advised to restrict the fluid taken during a meal on account of the danger of diluting the gastric juice, but

¹ 'Observations on Mastication,' *Lancet*, July 11, 1903, p. 85.

the caution is rarely extended to slop-food in general: yet here it would seem to be even more necessary. The dilution by water is temporary: the fluid excess is rapidly passed on and absorbed, and digestion proceeds as before. But a starchy pulp is retained and hampers digestion, not only by diluting the gastric juice, but by coating the meat fibres and preventing due penetration by the digestive fluid. While thus prolonging proteid digestion, the retention of starch, useless at best, leads to abnormal fermentation, to the production of irritating organic acids,¹ and to the evolution of quantities of gas—in short, to the phenomena of acid and flatulent dyspepsia.

§ 45. It is an opprobrium of medicine that theory and practice are often in conflict—that medicine is, in other words, an inexact science. The charge can hardly be denied, but I venture to submit that we are too ready to plead guilty and to ignore the instances in which theory and practice can be placed in perfect harmony. This would seem to be true, at least, of gastric dyspepsia; for I do not hesitate to say that, were we to deduce our practice in this most common disorder from physiological principles (say from Foster's 'Text-book of Physiology'), we should in many even old-standing cases obtain rapid success. In these physiological principles, I would suggest the inclusion of the following:—1. That good digestion implies quick digestion, and bad digestion, slow digestion. 2. That the commonest cause of slow digestion is the admixture in the stomach of unaltered starch with the proteid that is undergoing, or is about to undergo, solution by the gastric juice. 3. That proteid alone, if mechanically suitable, is rapidly digested in the stomach. 4. That starch foods should be largely digested in the mouth.²

§ 46. We are accustomed to lay much stress upon idiosyncrasy, especially with regard to the digestibility of various articles of diet. There can be no doubt that true idiosyncrasies

¹ Professor J. Bauer says: 'Since the investigations of C. Schmidt there can be no doubt that when lactic, butyric, or acetic acids are found in the stomach, they are always to be viewed as products of the decomposition of the carbohydrates of the food.'

² These sentences were written in 1898. Since then I have often been on the point of excising them: the contained truisms seemed too obvious to be other than an impertinence in a work addressed to the medical profession. Yet as late as August 1903, no less an authority than Harry Campbell finds it necessary to point out that starch foods 'should be given not, as is the custom, as liquid or pap, but in a form compelling vigorous mastication.'—'Observations on Mastication,' *Lancet*, August 8, 1903, p. 376.

exist, and such should be treated with due deference. But are they anything like as frequent as we are wont to assume? I very much doubt it. Many alleged idiosyncrasies, on examination and clinical experiment, are apt to resolve themselves into some grossly unphysiological relation between the food and the digestive organs—between *supply and function*. Patients, nearly always women, inform me almost daily that they are unable to digest meat. This statement, in nearly all cases, amounts to this: that meat, perhaps overcooked or badly cooked, imperfectly masticated and mixed with, or immediately followed by, a quantity of soft carbohydrate, upon which the saliva has had no time to exert any action at all, is followed by flatulence, pain and distension, whereas the omission of the meat from such a meal leads to much less discomfort. This is, of course, easy to understand. But it seems to me that it constitutes evidence of physiological, rather than unphysiological, function on the part of the stomach. And I have yet to find an instance in which a hungry stomach, unaffected with gross organic changes, is unable to digest, without morbid symptoms of any kind, meat in proper amount, properly prepared and properly presented, that is, unmixed with food-stuffs unsuited for gastric digestion.

§ 47. It seems to me that to excessive consumption of starch foods must be ascribed the extreme frequency of dyspeptic conditions. Clifford Allbutt says:—‘There is no superstition more tenacious of life than that which prescribes carbohydrates to all dyspeptics as so “digestible”; and into weak stomachs ready to dilate, is thrown a mass of such a dish as rice pudding—a bulky food, imperfectly insalivated and peculiarly apt to fall into decomposition with the disengagement of volumes of carbonic acid.’ Harry Campbell¹ also animadverts strongly upon the many serious disadvantages of the modern tendency towards ‘soft and pappy’ food-stuffs in the dietary of both children and adults. He says: ²—‘In this age of abundant starch and imperfect mastication the stomach and intestines are flooded with undigested starch, this giving rise to many evils.’

§ 48. Will it not then be justifiable to regard the prevalence of gastric dyspepsia as a protest against the commonest

¹ ‘Observations on Mastication,’ *Lancet*, July 18, 1903, p. 152.

² *Brit. Med. Journal*, April 11, 1903, p. 855.

form of carbonaceous excess, namely, excess in soft carbohydrates? Such a view amounts to little more than that gastric dyspepsia results in most cases from improper food (supply) and that it is not, primarily at least, due to mechanical or chemical defect on the part of the organ (function). And it is not far removed from the view of Sir Henry Thompson, who says indigestion is mostly not a disease, but an admonition.¹ 'It is the language of the stomach, and is mostly an unknown tongue to those who are addressed.'

§ 49. CONSERVATIVE INFLUENCE OF GASTRIC DYSPEPSIA.—It will be admitted that the general tendency of dyspepsia is to restrict appetite and to limit absorption; and if, as will be argued later, many common affections depend primarily upon hyperpyraemia, then it will have to be admitted that dyspepsia may play the part of a conservative process. Certain physicians throughout the history of medicine, not to mention a considerable section of the intelligent public, have held the view that dyspepsia acts as a safeguard against greater evils. Usually, the view is restricted to the case of gout, one of the few remaining strongholds of the humoralists. Fothergill says: ²—'In plethoric gout dyspepsia is out of the question. Often, if the patient could only be rendered dyspeptic, it would be the best thing that could happen to him; for dyspepsia would relieve him from the consequences of too much good living ("I have been a dyspeptic for fifty years," said an old clergyman. "Thank God for it!") All his brothers had died of gout).' Gout, which, I shall argue later, depends upon hyperpyraemia, is stated by Ewart to be 'commonly acquired with the aid of a sound stomach.' We know that it is chiefly the wealthy classes who suffer from gout. Their food is of good quality: long experience in the art of cooking has led to its preparation in such a way, that immediate peptic discomfort is evaded; it is calculated, too, to tempt the palate. Consequently dyspepsia—at any rate primary dyspepsia, the variety at present under consideration—is rare: excess absorption, common. The stomach is cheated (so to speak) into passing much that it might reject, were it presented in a cruder form. As regards alcohol, it is widely recognised, that the particular variety of intemperance which makes for gout is not irregular heavy

¹ *Lancet*, November 30, 1901.

² *Gout in its Protean Aspects*, J. M. Fothergill, 1883, p. 111.

drinking bouts, but the systematic wine bibbing which is customary amongst good livers—exactly that form of drinking, indeed, which is unlikely to upset digestion and unlikely to interfere with absorption. And the general tendency of high culinary art is to override and defeat the instinctive avoidance of excess, which is allowed full play under a coarse and monotonous dietary.

In the case of disorders other than gout, the conservative influence of dyspepsia has been very commonly ignored; and this has led to much confusion in etiology. Most of the disorders and diseases to be ascribed later to hyperpyraemia have, at different times and by various authorities, been ascribed to dyspepsia. I may here refer to asthma, migraine and some forms of skin disease. Some have regarded the dyspepsia, acting reflexly through the nervous system, as the exciting factor of the associated affection: others have regarded the dyspepsia as leading to the formation of deleterious chemical substances (toxins, etc.), which, after absorption, constitute the real underlying factor in the disease; nor are we called upon to deny the possibility of either of these modes of origin.

§ 50. We may, however, reconsider the whole question from a different point of view. We may take the stand that we have failed to grasp sufficiently the conservative principle of dyspepsia and have come, therefore, to restrict the influence of food in the etiology of disease to its influence in causing dyspepsia: because many disorders are preceded, or accompanied, by dyspepsia, we have assumed that the dyspepsia is causative. And the frequent observation that many of the disorders in question are associated with no subjective or objective sign of dyspepsia seems to have led us still further astray. It has forced us to fall back upon one or other of the only two possibilities which seem to remain, (1) that dyspepsia may be existent, but latent; or (2) that many affections, identical clinically, own, at different times and in different persons, fundamentally different etiologies.

The prevailing uncertainty as to the relative etiological positions of food, dyspepsia and associated diseases is voiced in the following passage from the work of a well-known author on dietetics. After referring to the usually prescribed dietetic treatment of certain forms of skin disease, the writer says:¹—

¹ *Food in Health and Disease*, 1897, p. 511 *et seq.*

‘In other words these dietetic directions amount to this: if dyspepsia accompanies these disorders, the dyspepsia must be treated by the usual dietetic measures.’ From a somewhat similar point of view, another author says of gout,¹ ‘the best dietary is in truth that which is most suitable for the dyspeptic.’ It may be that this is usually true, but if so, it is true because a simple diet, which precludes excess, is hostile to both gout and dyspepsia: not because gout depends upon dyspepsia.

In the view here taken, we admit that commonly dyspepsia precedes or accompanies many other diseases, but we explain the association by ascribing the two to a common factor, an excessive carbonaceous intake. We regard the dyspepsia as a protest against the excessive supply and as an attempt on the part of the digestive organs to prevent further intrusion of the excess into the system. The ensuing or accompanying disorder (migraine, asthma, gout, etc.), we regard as an index of the failure of these conservative measures—as events arising in spite, and not in consequence, of the dyspepsia. In short, we admit that the efforts of the organism to deal with adverse conditions are successful only within certain limits.

§ 51. This view will, I believe, be found to bring into line a greater number of clinical observations than any view hitherto propounded. It will simplify our ideas of etiology; and it will explain a fact which does not seem often to have been observed, but which I am convinced is true, namely, that migraine, asthma, and many similarly induced affections, though possibly less frequent, are, other things being equal, *distinctly more severe, if not more intractable, in those who possess hearty appetites and vigorous digestions, than in poor eaters and dyspeptics.* J. Comby, in an article on arthritism in children, enumerates, and ascribes to this assumed diathetic condition, most of the affections which are ascribed in this work to hyperpyraemia. He says:²—‘It has been suggested that most of the children suffering from symptoms enumerated are dyspeptic. On the other hand, some of the most typical gouty manifestations in children occur in those who have no dyspeptic symptom.’ I am aware that

¹ *Treatise on Gout*, Duckworth, 1890, p. 366.

² *Medical Review*, May 1902, p. 273. Synopsis of article in *Archives de Médecine des Enfants*, January and February, 1902.

the contrary has been stated. Graeme M. Hammond¹ says of migraine:—‘All severe cases without exception are chronic dyspeptics.’ I can only say that my own experience and that of numerous medical men, whom I have consulted on this point, are directly opposed to this statement; and I cannot doubt that the total absence of all digestive troubles, in many of the severer cases of the disorders in question, has done much to perpetuate the ‘primarily neurosal’ fallacy (§ 286).

§ 52. The conservative influence of dyspepsia, when once the idea is entertained, becomes a conspicuous clinical fact: it may be seen in the alternations exhibited between dyspepsia and the affections we are ascribing to hyperpyraemia. Dr. Hawkes tells me of a man of sixty-four who consulted him for dyspepsia. He had suffered from his school days up to the age of fifty-three from ‘bilious headaches’ recurring once a fortnight or even once a week. About the age of fifty-three he began to suffer severely from carious teeth and pyorrhoea: as a consequence he contracted the habit of bolting his food: this soon resulted in severe dyspepsia which became chronic and has persisted ever since. He *volunteered* the statement that, since the commencement of dyspeptic symptoms, he has never had a bilious headache.

Hyde Salter relates cases in which dyspepsia and asthma alternated, the one condition displacing and replacing the other. In one,² a little girl was subject for years to vomiting after every meal: later, the vomiting ceased, and immediately spasmodic asthma appeared: later still, the vomiting reappeared, and again the asthma ceased. ‘In this way they alternated, the vomiting always coming on when the asthma was better.’ In another,³ a girl of eighteen, on the death of a sister, to whom she was much attached, suddenly ceased almost entirely to suffer from long recurrent attacks of spasmodic asthma, but in place of them she became subject ‘to attacks of dyspepsia, frequently causing her as much suffering and inconvenience as her previous asthma.’ In my own experience, I have met with cases in which recurrent bilious attacks, and even formal migraine, alternated with constant, or frequently recurring, dyspepsia: in one, regular periodic sick headaches of some years’ duration remained in complete abeyance for about eight

¹ *Medical Annual*, 1902, p. 426.

² *On Asthma*, 1868, pp. 256, 257.

³ *Ib.* p. 258.

months, during which time severe dyspepsia followed almost every meal. It may be—indeed, it seems most probable—that, in many such cases, the dyspepsia is not primary and directly due to the food, but secondary and dependent, as we shall see later (§§ 77, 81), upon glycogenic distension of the liver; but even so, these cases are still examples of the conservative influence of dyspeptic conditions.

The view here adopted will have an important bearing on the treatment of the dyspepsia in these cases. Treatment addressed solely to the suppression of the discomfort attending the gastric disorder may possibly turn out to be injurious in proportion to its success; and treatment which, by means of artificial digestive ferments or other agents, increases the absorption which the gastric revolt is adapted to diminish, will certainly be so. Therapeutic interference will have to be limited strictly to the removal of the common cause.

§ 53. SECONDARY EFFECTS OF GASTRIC DYSPEPSIA.—Though we may fully subscribe to the view that gastric dyspepsia is often a protest against improper or excessive food and conservative against the results of excessive absorption (*e.g.* hyperpyraemia), yet we must admit that long recurrent and unheeded protests, here as elsewhere, tend to local stress and disorganization; and that such local damage may constitute the starting-point of a series of secondary disorders and diseases affecting the system generally. Nor shall we be called upon to modify these views if we find that some of these secondary pathological conditions are more serious or more fatal than those which, presumably, the gastric protest is adapted to avert; for the conservative measures of the organism are not restricted to such as are economical in their operation (§§ 921 to 924).

A few of the pathological conditions, which may take their starting-point from gastric dyspepsia, may here be referred to. Reflex disturbances, such as some forms of headache: catarrhal conditions of the mucous membrane: gross structural changes, such as glandular and other degenerations, dilatation, possibly ulcer: various forms of malnutrition; and probably some anaemias. We may freely admit the possibility that dyspepsia may lead to the formation of abnormal or toxic compounds which after absorption may exercise deleterious influences upon the economy; but this will not preclude us from ascrib-

ing a long list of well-known nervous and other disorders such as migraine, asthma, epilepsy, angina and many more, to hyperpyraemia.

INTESTINAL DIGESTION AND DYSPEPSIA

§ 54. We know that the process of digestion continues after the contents of the stomach have escaped from the pylorus. The chyme is now brought under the influence of the bile, the pancreatic and intestinal juices, and its various constituents modified still further to fit them for absorption by the blood-vessels and lacteals. In all probability, the digestive processes occurring in the intestinal canal are at least equally important with those occurring higher in the alimentary tract; and it is certain that absorption occurs here to a far greater extent than heretofore.

Intestinal digestion, however, is much more complicated and much more obscure than digestion in the mouth and stomach; and the same is naturally true of intestinal dyspepsia. But we may, I think, apply to it the same general principles as to primary digestion elsewhere.

The efficiency of the process will depend upon (1) supply, and (2) function. 1. The supplied material comprises the more or less digested contents of the stomach: the suitability of these for intestinal digestion and absorption will depend largely upon the efficiency of digestion in the oral and gastric cavities, and indirectly therefore upon all the factors which govern these latter, such as proteid supply, etc. 2. The functional capacity of the intestinal canal concerns its mechanical, chemical and physiological actions: these will depend no doubt upon a multitude of factors, but, *inter alia*, upon nitrogenous nutrition, and therefore upon a due supply of proteid.

Consequently, that part of the process of carbonization of the blood, which consists of digestion and absorption in the intestinal canal of carbonaceous material (for it is only the carbonaceous material which now concerns us), will depend in no small degree upon the supply of proteid in the food. We shall expect therefore to be able, in some cases, to increase carbonization by increasing the supply of proteid, in others to decrease carbonization by decreasing the supply of proteid.

EVIDENCE THAT CARBONIZATION OF THE BLOOD IS
A VITAL ACTION AND DEPENDS ON THE SUPPLY
OF PROTEID

§ 55. The *à priori* arguments, advanced in favour of the view that carbonization of the blood is a vital action and is conditioned by the supply of proteid in the food, are well supported by experimental and other data. It is well known, as Foster¹ points out, that 'when an animal is fed simply on non-nitrogenous food, death soon takes place; the food rapidly ceases to be digested, and starvation ensues.' The cessation of digestion is not, of course, immediate: otherwise no meal from which proteid is excluded would be of any nutritive value whatever. For a time after the complete withdrawal of proteid, the efficiency of the digestive mechanism, solid and fluid, is maintained, doubtless at the expense of the nitrogen of the body derived from previous proteid intake. But the subsequent failure is rapidly progressive. The above experiment shows that fresh proteid intake is essential to the continued carbonization of the blood; it does not, however, give any idea of the minimum amount of fresh proteid which is essential. But it is fair to infer that carbonization would increase with the supply of proteid up to a certain point.

§ 56. Under an ordinary mixed diet, the carbonaceous contents of the alimentary canal include the carbohydrates, the carbonaceous portion of the proteids, and the fats. The two former pass probably by the portal blood-vessels to the liver, where some of the carbohydrates at least are in part temporarily stored as glycogen. Now it is admitted that 'of² the three great classes of food-stuffs, the carbohydrates stand out prominently as the substances which, taken as food, lead to an accumulation of glycogen in the liver' (Foster). But 'a³ quantity of carbohydrate mixed with a certain proportion of proteid gives rise to a larger amount of glycogen in the liver than the same quantity of carbohydrate by itself' (Foster). And it is reasonable to explain this experimentally demonstrated fact by ascribing to the added proteid some power to assist in the digestion and absorption of the carbohydrate. But if this

¹ *Text-book of Physiology*, 1895, p. 833.

² *Ib.* M. Foster, 1895, p. 751.

³ *Ib.* p. 751.

is true, then the carbonization of the blood by carbohydrates will be dependent largely upon the proteid supply.

§ 57. Against this conclusion, it might perhaps be argued that, since many persons consume but a very small amount of proteid, carbohydrate should often appear undigested in the faeces; and it is asserted that 'in¹ health the carbohydrate food that is eaten does not appear in the faeces.' But Herter² points out that 'the fact that there is no soluble carbohydrate material in the faeces does not enable us to infer that it is all absorbed and utilized. Even in health there is always some waste of energy and potential from the fermentation of the carbohydrates'; and it is natural to believe that a retardation of digestion and absorption, brought about by a reduction of the proteid intake, would be fraught with an exaggeration of such fermentative processes and by a consequent increased loss of energy and potential. Further, the statement that carbohydrates do not appear in the faeces is not exclusively true. As Herter says,³ 'a frequent peculiarity of patients who are receiving an excess of starchy carbohydrate is that the faeces show the effect of this excess by the presence of undigested starch.'

§ 58. There is ample evidence to show that the digestion and absorption of fats (the carbonization of the blood by fats) depends, in great part, upon the supply of fresh proteid in the food. It will be admitted that the secretion of the bile is largely dependent on the supply of proteid. 'H. Nasse⁴ . . saw . . a great increase of the secretion of bile, when with fat nitrogenous foods were also given. Ritter found that, in a dog fed only on potatoes, or on potatoes and fat only, the amount of bile daily excreted fell very low.' And 'Bidder⁵ and Schmidt . . noticed that, upon an exclusive diet of fat, the secretion of bile at once fell to the level of that in an animal from whom all food was withdrawn.' Less conspicuously, the same occurs in the human subject. Those who have experimented clinically with various diets know that, under a diet markedly deficient in proteid, bile is deficient from the motions, which are large, pale and usually dry; and that, on the other hand, under a diet of nearly pure proteid, as for

¹ *Chemical Pathology*, Herter, p. 41. ² *Ib.* p. 41. ³ *Ib.* 1902, p. 49.

⁴ Quoted by J. Milner Fothergill, *Indigestion and Biliousness*, vol. i. p. 170, 1883.

⁵ *Ib.*

example the Salisbury diet, bile is in excess in the motions, which are small, dark and usually moist. In the first case, the amplitude of the evacuations may be taken to indicate deficient absorption: in the second, the opposite condition, to indicate the contrary. The excessive bile formation in the second case may explain a fact which I have often observed, namely, that, under a lean meat diet, even in the presence of constipation, the dose of any aperient required to cause purgation is much less than under other dietaries.

From all this it might be—indeed it often has been—inferred that the bile is manufactured out of the proteid of the food, rather than out of the fats and carbohydrates. But this is no necessary inference. We know that bile formation is a function of the hepatic cells and that these, like all functionally active tissues, are nitrogenous. Hence we have the right to infer that the cessation of bile secretion, which follows withdrawal of proteid, is due, in great part at least, to a *failure of function*, rather than to a *failure of supply*; and we may hold this view without denying that the constituents of bile are in part derived from the proteid ingesta.

But, be that as it may, there is no question that the absorption of fat is largely dependent on the supply of bile to the intestinal canal. Bidder and Schmidt demonstrated this experimentally. ‘A¹ dog, which in its normal condition absorbed on an average seven grains of fat for every two pounds of its weight, absorbed only three grains, or even as little as one grain, after the bile was prevented entering the intestines in consequence of a ligature being applied to the gall-duct.’ These observers found also ‘that² while the chyle in the thoracic duct of a healthy dog contains thirty-two parts of fat per thousand, that in the thoracic duct of a dog with a ligatured gall-duct contains only two parts per thousand.’ In man, the influence of the bile in promoting the absorption of fats may be inferred from observations on the faeces. Herter³ says:—

Normally the faeces contain a considerable proportion of fat; but, in cases of jaundice, this proportion tends to increase.

Hence it is clear that the ingestion of proteid, through dominating bile formation, dominates also in great part the carbonization of the blood by fats.

¹ *Treatise on Diseases of the Liver*, George Harley, 1883, p. 87.

² *Ib.* p. 87.

³ *Chemical Pathology*, 1902, p. 57.

§ 59. Finally, what is true of carbonization by carbohydrates and fats is in all probability true of carbonization by proteids—that is to say, the digestion and absorption of proteids depends upon nitrogenous nutrition, and this upon the proteid intake. And what is true of the digestion and absorption which is effected, directly or indirectly, through the action of the saliva, gastric juice, and bile, is doubtless true of the digestion and absorption which follows the action of the pancreatic and intestinal juices.

§ 60. The actual process of digestion may be in the main chemical; but the manufacture of the chemically active juices is a vital action. Hence digestion, as we have seen, depends primarily upon due nutrition by proteid. Of absorption, the same is true. B. Moore says: ¹—‘It was for many years believed that the absorption of the products of digestion from the alimentary canal was governed by exactly the same physical laws as determine the passage of a solution through an inert membrane, but the accumulation of experimental evidence has rendered such a belief no longer tenable. It is now known that the cells which line the alimentary canal take an active part, not only in absorbing the materials prepared for them by the action of the digestive secretions, but in modifying these products in various ways during the process.’ Thus absorption, as well as digestion, depends upon an active or vital capacity of the nitrogenous cells; and it is open for us to regard every step in the complex process of carbonization as dependent, more or less directly, upon nitrogenous nutrition and, therefore, upon the supply of proteid in the food.

SUMMARY.

§ 61. In this chapter, I have attempted to show that the carbonization of the blood—the supplying of the blood with unoxidized carbonaceous material, or fuel—is a complex chemico-vital function of the nitrogenous tissues of the digestive organs, and that it depends, *inter alia*, upon a due supply of proteid in the food: that some functional disorders, for example, dyspepsia, and even some structural diseases, for example, dental caries, may sometimes be regarded as conservative against hyperpyraemia, inasmuch as they tend to restrict

¹ *Text-book of Physiology*, Schäfer, 1898, vol. i. p. 431.

the carbonization of the blood: that many general diseases do not, as so often assumed, depend upon dyspepsia, but own with it a common factor in an excess of carbonaceous food; and that some functional disorders and structural diseases, though immediately conservative, often form the starting-points of secondary pathological processes.

CHAPTER III

§§ 62-98

Regulation of the carbon income—The glycogenic function of the liver—Physiological distension of the liver by glycogen—Pathological distension: acute, sub-acute or recurrent: chronic—Effects on the portal circulation: diarrhoea: haemorrhoids: inter-relations of diarrhoea and haemorrhoids—Relations between glycogenic distension and the carbon contents of the blood—Possible late results of glycogenic distension—The missing glycogenic factor in medicine—Summary.

THE GLYCOGENIC FUNCTION OF THE LIVER

§ 62. It is probable that most, if not all, of the nutrient material, derived from proteid and carbohydrate digestion in the alimentary canal, passes into the radicles of the portal vein and so is carried to the liver. Therein the carbohydrates are, in great part, reconverted from soluble sugar into insoluble glycogen and stored within the hepatic cells; and it is probable that some portion of the proteid also is normally stored as glycogen. In the liver, the glycogen is again gradually converted into sugar, and this enters the general circulation through the hepatic vein to be utilized by the tissues as fuel. Such at least is the theory of Claude Bernard—a theory which seems to have held its own against all rivals.

The dehydration of sugar, whereby glycogen is formed and stored, is regarded as a vital capacity or function of the hepatic cells (Foster);¹ and we may, perhaps, assume that, during life, the hepatic cells exert a more or less continuous inhibitory action, preventing the too rapid reversion of glycogen into sugar. This assumption seems justifiable, since, very rapidly after death, when function of all kinds has ceased, all the liver glycogen is reconverted into sugar, unless this action is prevented by rapidly freezing the organ or by throwing it into boiling water immediately after the animal is killed.² Were it

¹ *Text-book of Physiology*, Foster, 1895, pp. 756, 757.

² *Ib.* p. 749.

true, as is sometimes argued, that the reconversion of liver glycogen into sugar constitutes a function of the hepatic cells, we should, I think, be obliged to assume that this function is greatly increased in power by systemic death.

§ 63. Now it is probable that the vital capacity of the liver cells for glycogen formation is no exception to the general rule, which holds of the vital capacities of all nitrogenous tissues, namely, that they vary in power with the individual, with the supply of proteid, and with other conditions. Pavy, speaking of this dehydrating capacity of the liver cells, which he regards as the normal safeguard against diabetes, says: '—Every grade of diversity exists between the healthy state and the state belonging to the severest form of diabetes.'

§ 64. Under Bernard's theory, the liver seems to be regarded as a storehouse, adapted to guard against a deficiency, and to insure a constant supply, of fuel during the intervals of digestion. But it is open for us to view things from a slightly different standpoint. We may regard the glycogenic function of the liver in the light of a dam, whereby the flow of liquid fuel, arriving from the alimentary canal, is held back and prevented from suddenly flooding the general circulation. Of course, storage and detention here are one, but it may well be that the capacity to detain is of higher import to the organism than the capacity to store, since in modern civilized life, at least, there will usually be other reserves of fuel (fat) on hand, and fresh supplies are practically always accessible. This view differs from the more ordinary view merely by laying less stress upon the danger of deficiency than upon the danger of excess; but it enables us to regard the glycogenic function of the liver as a physiological barrier against the intrusion into the general circulation of an excess of one form of carbonaceous matter. It is consistent too in the main with the conception formed by Pavy,² who says:—'The liver . . . instead of actually throwing sugar into, or allowing it to pass into, the general circulation, in reality checks the progress of carbohydrate matter onwards. It prevents the fluctuating condition, as regards sugar belonging to the portal blood, from travelling on and being transmitted to the blood of the general circulation': in short, it is a safeguard against hyperglycaemia and glycosuria.

It is true, Pavy does not believe that the hepatic glycogen

¹ *Physiology of the Carbohydrates*, 1894, p. 227.

² *Ib.* Pavy, 1894, p. 224.

is reconverted into sugar and passed on into the general circulation, and herein he differs radically from Bernard: he considers the glycogenic function of the liver a sugar-destroying function. But it is unnecessary to go so far as this in order to be consistent in holding the view that the liver is a natural safeguard against diabetes. We know that sugar in the systemic circulation above a certain percentage appears in the urine in estimable quantities; and we may believe that the dehydration of the portal sugar into hepatic glycogen is a conservative device, adapted to regulate, not to destroy, the supply of sugar to the general circulation. We cannot with Pavy refuse to believe that the tissues of the body utilize sugar as fuel, thereby destroying it; and this on several grounds. For example, a moderate degree of glycosuria may often be dispersed by physical exercise without any restriction of the carbohydrate intake. Now this is not effected through increased hepatic storage of glycogen, for exercise reduces the glycogenic load (§ 68). The disappearance of the glycosuria can occur, therefore, only through increased combustion.

PHYSIOLOGICAL DISTENSION OF THE LIVER BY GLYCOGEN

§ 65. The liver cell which is rich in glycogen is large compared with the cell which, through previous starvation, contains no glycogen: this has been demonstrated histologically, and the whole organ in these circumstances is 'very¹ large, and as it were swollen' (Foster). Now the capillaries of distribution of the portal vein ramify between the cells of the hepatic lobules, and it seems impossible that such an increase in volume of the hepatic cells can occur without some pressure being exerted upon these lobular capillaries: indeed, Foster² points out that some authorities have described the hepatic cells, swollen by glycogen, as compressing the lobular capillaries. And we are encouraged to agree with this on remembering that the blood pressure in these capillaries must be extremely low, seeing that they are formed by the subdivision of a vein which is itself formed by the confluence of other capillaries.

Now George Dancer Thane³ says:—'There are no valves

¹ *Text-book of Physiology*, Foster, 1895, p. 755.

Ib.

³ Quain's *Anatomy*, 1899, vol. ii. Part II. p. 543.

in the portal vein or in its larger tributaries, although such are known to exist in some animals. Valves are however present in the child in the veins of the stomach and of the wall of the intestine; but according to Hochstetter and Bryant they early become insufficient, and in the adult to a great extent disappear.' It follows, therefore, that any obstruction in the capillaries of distribution will tell back upon the capillaries of origin in the alimentary mucosae more truly and more directly than if the valvular apparatus in the portal venous system were fully competent; for the varying, but constantly recurring, pressure from adjoining viscera will be impotent to drive the blood onwards in the portal veins, as would not be the case were these veins provided with competent valves. It is easily conceivable then that, when the liver becomes distended by glycogen, there will arise a degree of mechanical congestion or tendency to stasis in the digestive mucosae. Such a vascular condition would be opposed to what obtains when food is introduced into the stomach of the hungry animal. Then, not only do the arteries of the organ dilate and largely increase the supply of blood, but, the passage through the liver being unobstructed, the circulation is rapid, so rapid that the blood in the gastric veins continues to preserve its arterial hue (Foster).¹ Manifestly, for active digestion, a free escape for the blood is as essential as an increased advent; wherefore it is probable that, as the liver becomes packed with glycogen, the activity of the digestive process and the rate of absorption lessen.

§ 66. The sense of hunger and of its satisfaction are doubtless complex in their mechanism, which probably includes the condition of the stomach as regards the absence or presence of material in contact with the mucous membrane, and also the condition of the blood as regards its carbon contents. But it seems to me that a scantiness and plenitude of hepatic glycogen, through their opposite effects upon the circulation in the alimentary mucosae, must be important items in the two groups of factors responsible respectively for the opposing sensations under consideration. And this on the following grounds:—1. Many conditions, which, we shall presently see, largely diminish the amount of glycogen in the liver, such as starvation, physical exercise, and cold weather, are admitted to be effectual in

¹ *Text-book of Physiology*, 1895, p. 426.

promoting a vigorous appetite; and the extreme difficulty experienced in suppressing for more than short periods the sensation of hunger by a purely proteid diet is probably, in part at least, attributable to the scanty accumulation of glycogen which follows a meal of this kind. 2. Pavy regards deficient hepatic glycogenesis (that is to say, deficient power on the part of the hepatic cells to dehydrate sugar into glycogen) as an essential factor in most cases of diabetes: the investigations pursued in this work generally confirm this view; and a ravenous appetite is certainly one of the most conspicuous clinical features of diabetes. 3. Although it has been demonstrated that distension of the stomach by innutritious foreign substances alleviates the sense of hunger, yet such alleviation is incomplete and short-lived. 4. There can be hardly any question that the absorption which follows digestion is of more physiological importance in abolishing hunger than the mere presence of food in the stomach. It is possible, nay easy, for anyone to leave the dinner table with a very distinct appetite, and yet to observe the total disappearance of appetite within a very short time. Medical men in general practice are frequently called upon in the middle of a meal to attend to some urgent case in the consulting-room; and several busy practitioners have informed me that, after remaining absent from the table, say, for fifteen or twenty minutes, they rarely if ever have any inclination to finish their interrupted meal. Such disappearance of appetite is not due to removal from suggestive sights, for the same may be observed by one who remains at the table. 5. Those physicians who, like George Keith, believe that a large number of morbid affections depend upon excess of food, and who consequently have raised the practice of dietetic restriction to the position of a dominant therapeutic procedure, lay great stress upon the importance of eating slowly, not in order to insure perfect digestion, but to alleviate hunger by means of less food. By eating slowly, absorption and, *inter alia*, the deposition of hepatic glycogen may be regarded as keeping pace more nicely with intake; and appetite, if, as I am arguing, it depends in great part upon paucity of glycogen in the liver, will succumb to a smaller intake than under rapid eating. Did the satisfaction of hunger depend in the main upon distension of the stomach by food, 'bolting' would be

preferable from the standpoint of the physicians referred to, inasmuch as by this means the maximum gastric distension would be attained.

§ 67. Thus it is open for us to ascribe to the glycogenic function of the liver two distinct, though correlated, uses :— (1) detention and temporary storage of sugar in the form of glycogen against hyperglycaemia and glycosuria ; and (2) regulation of digestion and absorption, perhaps also of the intake, of food generally. Hence we may regard the glycogenic function, not as a regulator merely of the sugar contents of the blood, but of the carbon or fuel contents generally—of pyraemia in short. In virtue of the glycogenic function, the liver may be said to act as a complex physiological valve, which regulates automatically and more or less accurately the supply of nutriment to the distributing circulation. At a later stage, it will be argued that the amount of stored hepatic glycogen—the degree of glycogenic distension—is in general an index of the degree of pyraemia.

§ 68. Physiologists are agreed that glycogen is derived chiefly from the carbohydrates, but to a less extent from proteids and gelatin ; and that fat in no degree contributes to the supply. And it has been demonstrated experimentally that glycogenic distension of the mammalian liver is favoured by *external heat*¹ (Külz) and *physical inactivity*¹ (Külz) : that, on the other hand, *starvation*² (Foster), a *purely proteid diet*³ (Saundby), external cold, *physical exercise*⁴ (Manché) and *pyrexia*⁵ (Bernard, Noël Paton), diminish the distension.

External heat and physical inactivity reduce respectively the demand for heat and force production, and both, therefore, are associated with diminished combustion : starvation and the enforcement of a proteid diet abolish and reduce respectively the supply of material out of which glycogen is formed, and the latter in addition increases combustion : external cold and physical exercise increase respectively the demand for heat and force production, and both, therefore, are associated with increased combustion ; while pyrexia, we shall see later, is

¹ Külz, quoted by Schäfer, *Text-book of Physiology*, 1898, vol. i. p. 918.

² *Text-book of Physiology*, Foster, 1895, p. 755.

³ *Renal and Urinary Diseases*, Saundby, 1896, p. 222.

⁴ Manché, quoted by Schäfer, *Text-book of Physiology*, 1898, vol. i. p. 918.

⁵ Bernard and Noël Paton, quoted by Saundby, *Renal and Urinary Diseases*, 1896, p. 299.

commonly associated, not only with a diminished intake of glycogen-forming material and an impairment of digestion and absorption, but also with an increase in the rate of combustion (§ 273).

§ 69. So far then we may conclude that glycogenic distension of the liver depends (1) directly (*a*) upon the supply of glycogen-forming material, and (*b*) upon the efficiency of digestion and absorption; and (2) inversely upon the expenditure of carbohydrate material by the tissues.

It follows from this, that glycogenic distension of the liver may be reduced by two seemingly opposed methods of dietetic management. 1. The abolition, or reduction to a minimum, of the proteid constituents of a mixed diet. In this case, the income will be restricted through a partial—probably a progressively increasing—abrogation of *function*, the functions of digestion and absorption; while expenditure, which is continuous, will gradually reduce the amount of glycogen already stored. 2. The abolition or reduction of carbohydrate food-stuffs, with or without an increase of proteid. Here distension will be reduced through a reduction of the *supply* of raw material out of which glycogen is mainly formed; and, if the supply of proteid is increased, as for example in the Salisbury diet, then increased expenditure by the tissues will still further reduce the hepatic distension.

It is certain that glycogenic distension may vary widely within physiological limits; and it is easy to conceive that, in certain circumstances, these limits may be exceeded. Glycogenic distension might then attain to pathological dimensions.

PATHOLOGICAL DISTENSION OF THE LIVER BY GLYCOGEN

§ 70. A pathological degree of distension of the liver by glycogen will, I submit, fully explain the phenomena of bilious attacks and biliousness of many clinical varieties. The evidence in support of this view may be thus generalised:—Conditions which favour glycogenic distension favour the occurrence of bilious attacks or biliousness: conditions which disperse glycogenic distension tend to prevent bilious attacks and to disperse biliousness.

We have seen that glycogenic distension is favoured by rich carbohydrate food, external heat and physical inactivity; and Harley¹ includes amongst the main proximate causes of bilious attacks and biliousness, errors in diet (especially excess in sugars, starches and fats), hot weather and deficient muscular exercise.

Again, we have seen that glycogenic distension is dispersed by starvation, external cold, exercise, pyrexia and a proteid diet; and the salutary influence of most of these upon bilious attacks and biliousness is widely recognized.

Harley² says that he has frequently cured his 'bilious patients with a day or two's starvation diet'; and I have known many persons who have learned through personal experience that a day's starvation is an effectual remedy for biliousness. The salutary influence of external cold is usually conspicuous in the bilious tropical resident who goes for a change to cooler regions; and exercise is proverbially hostile to biliousness. Pyrexia, though usually accompanied by dyspeptic conditions of its own, never fails in my experience to interrupt the recurrence of periodic bilious attacks, or to disperse (though this is, of course, much less conspicuous) the symptoms of biliousness. Though I cannot find this stated in medical works, I have no doubt, from frequent observation, of its truth. Finally, an exclusively proteid diet, or even a diet which is approximately so, has rarely, in my hands, failed to disperse both the allied conditions we are considering.

§ 71. The clinical fact that bilious attacks and biliousness are often treated successfully by an almost exclusively carbohydrate dietary may seem at first sight contradictory of the view that these affections depend upon glycogenic distension of the liver. From the success of a carbohydrate diet, it has been argued that the hepatic disturbance, responsible for bilious attacks and biliousness, concerns the proteid-modifying function of the liver, and that abstention from meat operates beneficially by relieving the strain upon this function. Now, without denying that cases exist in which nitrogenous excess leads to liver disorder, it will be clear to those who lay sufficient stress upon the influence of proteid supply on digestion and absorption, that the success of an exclusively

¹ *Diseases of the Liver*, 1883, pp. 245, 274.

² *Ib.* p. 245.

carbohydrate diet does not disprove the responsibility of glycogenic distension for bilious attacks: rather the contrary indeed. For, as already stated, it has been demonstrated experimentally that¹ 'the greatest accumulation of glycogen is effected, not by a pure carbohydrate diet, but by a mixed diet rich in carbohydrate' (Foster). The enforcement of a purely carbohydrate diet reduces glycogenic distension of the liver through a partial abrogation of the functions of digestion and absorption.

Harley² divides biliousness into three degrees, acute, sub-acute and chronic. Conformably, we may speak of acute, subacute (or recurrent) and chronic, pathological distension of the liver by glycogen.

§ 72. ACUTE DISTENSION.—Harley³ says, acute biliousness is due as a rule to some distinct error of diet, such as a surfeit of plum pudding or cheese cake. Both these articles of diet consist almost solely of purely carbonaceous, especially carbohydrate food-stuffs; and, as already stated, Foster insists that the addition of proteid is necessary to cause the greatest possible accumulation of glycogen in the liver. It is clear, however, that a surfeit of either of the articles of diet referred to by Harley would, in all probability, succeed a certain amount of meat.

Attacks so induced are sudden in their onset and subsidence and of short duration; and they are explicable by a large sudden irruption of glycogen-forming material into the portal venous system, with consequent acute glycogenic distension of the liver.

§ 73. The *mechanism* of such a bilious attack appears to be simple. Distension of the liver by glycogen will cause pressure on the intralobular capillaries of the portal vein. As a result, there will be mechanical congestion, perhaps stasis, in the capillaries of the gastric and intestinal mucosae. The congestion of the mucosae will be associated with some swelling. Such swelling, affecting the duodenal mucosa, will probably be sufficient to cause blocking of the orifice of the common bile-duct; for, as Lauder Brunton⁴ points out, 'the pressure under which bile is secreted is very low, so that a very slight obstruction

¹ *Text-book of Physiology*, Foster, 1895, p. 751.

² *Diseases of the Liver*, 1883, p. 274 *et seq.*

³ *Ib.* p. 280.

⁴ *Pharmacology, Therapeutics and Materia Medica*, 1885, p. 355.

to its flow through the common duct is sufficient to cause its accumulation in the gall-bladder and gall-ducts.' Blocking of the common bile-duct will necessarily involve blocking of the pancreatic duct, which opens by a common orifice with the common bile-duct. Thus there will be absence from the alimentary canal of bile and pancreatic juice; and it is probable that the gastric and other digestive juices will likewise be in abeyance. As a result, there will be total cessation of the processes of digestion and absorption, those processes which are responsible for the glycogenic distension of the liver. The clinical indications of the condition will be complete anorexia, nausea and later vomiting; while, in some few cases, the portal or retro-hepatic congestion will relieve itself by diarrhoea, and this will usually be bilious in character, at any rate inoffensive.

Usually, the vomiting occupies the apex of the attack: thereafter convalescence sets in. The vomiting will cause compression of the liver and distended gall-bladder between the abdominal wall and the diaphragm: thus the retained bile will be ejected into the duodenum and will usually find its way into the stomach, whence it may be vomited. In any case, fresh income of glycogen-forming material, and therefore fresh deposition of hepatic glycogen, will be precluded through the condition of the digestive organs; and the ever-present combustion in the tissues (temporarily exaggerated by the muscular exertion of vomiting) will gradually reduce the hepatic glycogen already deposited. So the glycogenic distension of the liver will be relieved, the mechanical stases dispersed, and convalescence established. The whole paroxysm appeals to me as a well-organized and most salutary strike, on the part of the organism in general and the digestive organs in particular, against the absorption of combustible material in excess.

§ 74. Harley¹ says that such acute bilious attacks, unlike the subacute or recurrent attacks to be next considered, are not accompanied by clay-coloured stools, nor by the signs of biliary colouring matter in the blood. Obviously, this is explained by the suddenness and evanescence of the attack: the retention of bile and its absence from the intestinal canal would be of too short duration to cause any of the phenomena of jaundice. On the same grounds, we may explain the absence of putrefac-

¹ *Diseases of the Liver*, 1883, p. 280.

tive decomposition of the intestinal contents and the observation that, if there is concurrent diarrhoea, this is simply bilious and inoffensive.

Such attacks have always been ascribed by the majority of the profession and by the general public to over-indulgence in rich and sweet foods; and this, in spite of the persistent endeavours of a minority to fasten the guilt upon meat and nitrogenous food-stuffs. The attacks often follow, especially in children, an isolated debauch on confectionery; and it is needless to assert that sweets, cakes, pastry and similar delicacies are peculiarly fitted to cause glycogenic distension.

§ 75. SUBACUTE OR RECURRENT DISTENSION.—Harley says that subacute biliousness is not due to isolated indiscretions in diet, but 'to ¹ a continued habitual indulgence in richly oleaginous ² and saccharine foods.' Such attacks are recurrent, frequently regularly recurrent or periodic; and we may suppose that the glycogen-forming material absorbed from the alimentary canal is in excess of the daily requirements, so that a gradually increasing accumulation takes place, leading eventually to pathological distension.

Except as regards the rate of the preceding accumulations these attacks seem identical in causation and mechanism with the more acute attacks just considered. But, being due to a slow and not to a rapid accumulation, they are of gradual onset and of longer duration. Hence retention of bile and its absence from the intestinal canal will probably be, in some cases, of sufficiently long duration to cause light-coloured stools ³ and perhaps even a slight degree of jaundice, as observed by Harley.⁴ Further, the more prolonged absence of deodorizing bile from the intestine, and the more prolonged inhibition of the normal chemical changes therein, will in all probability lead to putrefactive decomposition of the bowel contents and to the consequent passage of the foetid dejecta, so often observed after recurrent bilious attacks. Later, we shall see that all these phenomena may occur during or following typical migraine and many other affections associated with glycogenic distension of the liver.

§ 76. Recurrent bilious attacks have been variously described

¹ *Diseases of the Liver*, 1883, p. 283.

² The influence of fats is probably indirect: it will be considered later (§ 94).

³ *Diseases of the Liver*, 1883, p. 274 *et seq.*

⁴ *Ib.* p. 285.

by different authors. Eustace Smith¹ refers to them as Recurrent Gastric Catarrh, which, he states, may be febrile or more frequently non-febrile. Such are commonly attributed to cold, to indigestible food, etc.; but it is improbable that a child should catch cold periodically from purely extrinsic causes, and extremely unlikely that articles of food, which are ordinarily followed by no dyspeptic symptom, should become indigestible at regularly recurring intervals, except for some intrinsic reason. On the other hand, the hypothesis under which the catarrhal symptoms depend upon a mechanical congestion due to a regularly recurring glycogenic distension of the liver seems to cover the whole ground. And it is interesting and highly significant to note that the author quoted has arrived empirically at the self-same dietetic treatment that is deducible from the view just advanced: he advises an emetic, followed by a dietary which excludes all *sweets and rich carbohydrate foods*; and he goes so far in this direction as even to discourage the use of syrup as a medium for drugs.

§ 77. It has been argued that physiological distension of the liver by glycogen graduates imperceptibly into pathological distension. The clinical parallel to this seems to me complete and easy of observation by those who, like myself, are imbued with the principle of the gradations between health and disease. All shades of gradation between the strictly physiological sense of satisfied hunger and the grossly pathological bilious attack may be observed daily in general practice. There is a *recurrent*, sometimes an almost periodic, *anorexia*, which is a well-marked clinical condition and which can hardly have any pathological basis other than a recurrent glycogenic distension of the liver. In such cases, there may be no symptom except an absence of appetite, and the condition is of course self-curative if left alone; but attempts at forced eating show, by the dyspeptic symptoms set up, that physiological gastric digestion is in abeyance.

§ 78. Cases of dyspepsia have long been recognized in which the liver is supposed to play a dominant part: these have been termed hepatic or bilious dyspepsias. But I do not think that any definite tenable theory as to the mechanism of such cases has hitherto been framed. They have been ascribed somewhat vaguely to 'torpidity' of the liver, to deficient

¹ *Lancet*, 1880, vol. ii. pp. 805, 847.

secretion of bile or to an exaggeration of the physiological congestion which follows meals. But it is clear that an exceedingly large number of *intermittent*, *remittent* and *continued* dyspepsias are simply explicable on the view that they are *secondary* dyspepsias and depend upon undue distension of the liver by glycogen. In support of this view, clinical evidence, which to me seems irrefutable, is to be obtained from a consideration of the influence of the *quantity of food*, of *physical exercise* and of the *onset of diabetes*, upon dyspeptic states.

§ 79. Other things being equal, glycogenic distension of the liver, in persons living on an ordinary mixed diet, will vary directly with the amount of food; and Harry Campbell says:¹—‘Dyspepsia, being frequently the result of over-eating, may often be cured simply by cutting down the diet.’ I can fully confirm this, and I am convinced from my own experience that much of the difficulty met with in treating dyspepsia results from a tendency to under-estimate the importance of the quantitative factor.

§ 80. Other things being equal, glycogenic distension will vary inversely with the amount of physical exercise; and Fagge, speaking of the manifestations of ‘bilious dyspepsia’ in middle-aged persons, who take little exercise, says: ‘They²—are often at once removed by a few days’ shooting or hunting, or by any other active exercise which is sufficiently attractive to induce men to give up sedentary habits.’ Many persons have discovered for themselves that an attack of dyspepsia may be dispersed completely by a sharp walk. A medical friend of mine in North Queensland, long a sufferer from dyspepsia, finds that he remains completely eupeptic so long as he keeps up systematic exercise, and this in spite of a generous mixed diet. On the other hand, neglect of exercise for a few days is in his case inevitably followed by a return of the dyspepsia, even in spite of some care in diet.

Such cases are sometimes sought to be explained by supposing that exercise, through accelerating the circulation generally, accelerates the circulation through the digestive organs, thus raising their tone, whatever the exact significance pertaining to that expression. It is clear, as already argued,

¹ ‘Observations on Diet,’ *Lancet*, 1902, June 14, p. 1713.

² *Text-book of Medicine*, 1891, vol. ii. p. 332.

that the portal circulation will, through the removal of the glycogenic block, be accelerated, and secondarily the circulation through the digestive mucosae. But, apart from this, there is no reason to suppose that exercise increases the supply of blood to the digestive organs; nor is there any reason to think that anything, other than disease, can cause dilation of the arteries supplying the gastric mucosa, except the psychic stimulus of appetite¹ and the chemical stimulus of food² (Pawlow). Further, there is no reason to suppose that an increase of the blood-supply would be beneficial; and it is probable that exercise, by removing the mechanical obstruction to the efflux of blood from the stomach, conduces, in the absence of food, to a salutary anaemia of the organ.

§ 81. Other things being equal, hepatic distension by glycogen will vary directly with the capacity of the liver to dehydrate sugar and store it in the colloid form within the hepatic cells. In diabetes, Pavy assumes this capacity to be absent or, at least, inadequate; and we are accepting this view. Hence we shall expect in some cases an increase in digestive power and a subsidence of dyspeptic symptoms at the onset of diabetes. Now Fagge says:³—‘One of Dr. Pavy’s patients, who had before been a martyr to dyspepsia, said that his digestive troubles ended as soon as diabetes appeared.’ Williamson says:⁴—‘The digestive power of diabetic patients is generally very good, and persons whose digestion has previously been feeble often improve markedly in this respect after diabetes develops. Dyspeptic individuals, who have previously found it necessary to be very cautious in the choice of their diet, often lose all their digestive troubles after the onset of diabetes, and can take large quantities of food with impunity.’ And later I shall bring evidence to show that most recurrent affections, such as bilious attacks and migraine, which depend in part upon glycogenic distension of the liver, tend to cease abruptly on the supervention of diabetes or glycosuria. In fact diabetes implies loss of the capacity for glycogenic distension of the liver and for all the more or less conservative affections which depend upon this capacity.

¹ *Work of the Digestive Glands*, Pawlow and Thompson, 1902, p. 73.

² *Ib.* p. 93 *et seq.*

³ *Text-book of Medicine*, vol. ii. p. 572.

⁴ *Diabetes Mellitus*, 1898, pp. 203, 204.

§ 82. CHRONIC DISTENSION.—This corresponds to the chronic biliousness of Harley. Chronic biliousness, Harley says,¹ 'is in general only met with in adults, more especially those who have been for some years in hot climates . . ., is chiefly characterized by sallowness of the complexion and the "good-for-nothingness" of the patient's feelings,' and may extend in duration to months. The condition doubtless includes many of the milder cases known as 'tropical liver,' which Manson² ascribes to 'over-full and over-rich feeding, to over-stimulation by alcohol and deficiency of muscular exercise.' The pathological condition is usually considered to be in the first place one of physiological hyperaemia (active congestion), passing thereafter into pathological congestion with blood-stasis and diminished functional activity (Manson). Conformably, Professor J. Bauer says:³—'Since digestion always involves an increased flow of blood to the liver, it is conceivable that an excessive supply of food may induce an habitual hyperaemia of that organ, especially if there be superadded the consequences of a sedentary and inactive life.' But these views seem to explain little: certainly they do not explain why active physiological congestion should graduate into passive pathological congestion with blood-stasis.

§ 83. But the view about to be suggested will explain some such graduation. The digestion of a meal will necessarily cause an increased afflux of blood through the portal veins to the liver, such venous blood being highly charged with the products of digestion in the alimentary canal. Amongst such products will be a considerable quantity of sugar and perhaps other glycogen-forming material. There will thus be in the first place an active portal congestion of the liver. Now some, though as we shall see presently (§ 92) not all, of this glycogen-forming material is dehydrated by the liver cells and deposited therein as glycogen. As glycogen continues to accumulate, there will be a gradually increasing pressure upon the interlobular capillaries, which pressure will squeeze the blood back into the retro-hepatic portal venous system. Thus there will be, at this stage, a mechanical portal congestion behind the liver, but within the liver a tendency to anaemia, in so far, that is, as concerns the portal circulation.

¹ *Diseases of the Liver*, 1883, p. 277.

² *Tropical Diseases*, p. 338.

³ *Ziemssen's Handbook of General Therapeutics*, vol. i. p. 259.

But we have to consider also the hepatic circulation. It has already been argued that glycogen-formation is a function of the hepatic cells (§ 62); and later it will be argued that the exercise of this function involves a free supply of oxygenated blood through the hepatic artery (§ 442). There will thus be a vaso-dilation of this vessel and an active hepatic hyperaemia of the liver succeeding digestion; and if, as has been conjectured, the liver cells exert a continuous inhibitory influence in order to prevent the too rapid reconversion of glycogen into sugar (§ 62), then the active hepatic hyperaemia will be prolonged under conditions which demand a prolongation of the retention of glycogen in the liver. Nor will such active hyperaemia suffer much interference from the distension of the liver cells by glycogen; for the hepatic blood, unlike the portal blood, is supplied under the ordinary arterial blood-pressure.

Now conditions demanding a prolongation of glycogen in the liver undoubtedly obtain in the tropics. External heat will reduce the demand for heat-production by the tissues, physical inactivity will reduce the demand for force-production, and both, therefore, will tend to reduce the expenditure of fuel—one form of which is sugar—by the tissues; and if to these conditions be added over-rich and over-full feeding and over-stimulation by alcohol, it is clear that the deficiency of expenditure by the tissues will be increased, and by so much the necessity for retention of glycogen in the liver. Hence the anatomical condition in tropical liver will probably be a more or less chronic glycogenic distension accompanied by a more or less chronic arterial or active hyperaemia. There will also be a chronic mechanical portal congestion, but this will not affect the liver but the portal venous system behind the liver. Under this view, chronic biliousness or tropical liver is not a condition of 'torpidity' or functional inactivity of the organ. It is, on the contrary, a condition of strained physiological function, brought about by a relatively excessive fuel supply and by the consequent unphysiological demand for hepatic storage; and the congestion of the organ, which is so prominent a clinical feature of the condition, is probably the instrument whereby the strained physiological action is maintained.

The above would be true at any rate of the primary hepatic condition. But it would be of course impossible to deny the

probability of many further morbid changes occurring as results of the prolongation of this strained physiological condition: hepatitis of some kind is what we should naturally expect.

§ 84. The success of the treatment commonly prescribed for chronic biliousness or tropical liver is consistent with the view we have adopted. The treatment includes physical exercise, a change to a cool climate, purgatives and the avoidance of animal food. Exercise and cool weather diminish, as already stated, glycogenic distension of the liver by increasing combustion in the tissues. The omission of animal food (the chief ordinary source of proteid) from a mixed diet would, according to Foster, be succeeded by a diminution of the deposit of fresh glycogen probably through a reduction in the digestion and absorption of glycogen-forming material. And purgatives will have a doubly beneficial influence: (1) they will directly reduce the retro-hepatic portal congestion and thus relieve many symptoms dependent thereon; and (2) they will tend, as will be argued later (§ 245), to diminish fresh absorption, through hastening the onward progress of the contents of the alimentary canal.

§ 85. But the dietetic method most efficient for dispersing the common liver troubles of the tropics (as indeed of temperate climates) consists in the enjoinder for a time of a mainly proteid diet. Professor J. Bauer, speaking of cases in which there is a tendency to habitual hyperaemia of the liver,¹ lays stress upon 'a diet as simple as possible, which shall contain exactly the necessary amount of nutriment, especially in the form of lean meat, green vegetables, and not too large a quantity of white bread.' Those who have visited Carlsbad, the spa most famous for liver disorders, will recognize that the routine treatment there prescribed is peculiarly well adapted to reduce glycogenic distension. Regular exercise is insisted on: the food as a whole is considerably reduced; and carbohydrates, the chief source of glycogen, are reduced in far greater degree than any other class of food-stuff. The rationale of this therapeutic system seems clear. The *functions* of digestion and absorption are left unimpaired, if, indeed, as seems highly probable, they are not considerably improved in power. This, which from the standpoint of glycogenic distension would be

¹ Ziemssen's *Handbook of Therapeutics*, 1885, vol. i. pp. 259, 260.

disadvantageous, is unimportant here, since the *supply* of glycogen-forming material is rigorously retrenched. Moreover, expenditure of carbonaceous material by the tissues is increased by the exercise, and possibly also in some cases by a slight increase in the proteid, above the amount previously ingested. Such increased expenditure will hasten the delivery of sugar by the liver, and so relieve the glycogenic load.

§ 86. Comparing the two dietetic systems adopted in cases of glycogenic distension of the liver, namely, the system of reducing proteid and the system of reducing carbohydrates, we can hardly avoid being impressed by the theoretical superiority of the latter. In it, *function* of all kinds is, if anything, improved, and *supply* is regulated in accordance with the necessities of the case. In the former, reliance has to be placed on an impairment of one set of functions, the functions of digestion and absorption; and we have no guarantee that other sets of functions, for example those which are concerned with expenditure by the tissues, and function generally, will not be impaired concurrently: indeed, much evidence might be adduced to show that such occurs not infrequently. While it may be that there are cases which respond more happily to the former, yet I cannot doubt that those who have tried both systems will admit that the latter is practically, as well as theoretically, superior in the greater number: herein, theory and practice are at one.

§ 87. At this point, it became evident, if glycogenic distension is an underlying factor in many of the chronic forms of tropical liver disturbance, that attacks of intercurrent pyrexia should exercise a salutary influence in such cases; and, on ransacking my memory, it seemed that I could remember several instances of such salutary intercurrent pyrexia: in particular, I could recall one case, in which long-continued bilious symptoms had apparently been terminated by a compound fracture into the left elbow-joint, complicated by considerable septic pyrexia. But such evidence was vague and not very satisfactory, being manifestly open to the charge of personal bias. Accordingly I wrote to Major D. J. Buchanan, I.M.S., Editor of the 'Indian Medical Gazette,' Calcutta, requesting him to give me his experience on the point. In his reply, he said:—'My attention has not been called to the point you mention about the improvement following intercurrent

feverish attacks in liver cases, though when you mention it, I have seen such improvement, though I did not note the connection at the time. . . I have not seen the point raised before, though I went through all the literature of the subject before writing the article on "Hepatitis" in the new edition of Quain's Dictionary.'

The view of chronic biliousness and tropical liver, here adopted, implies the existence in high degree of the glycogen-forming capacity on the part of the liver: glycosuria (some forms at least), on the other hand, implies the absence or inadequacy of this capacity. Hence intercurrent glycosuria should disperse the manifestations of chronic biliousness and tropical liver, just as it does the manifestations of secondary dyspepsia, recurrent bilious attacks, and other affections depending on glycogenic distension of the liver.

§ 88. It may here be advisable to say that nothing which has been said as to the influence of carbohydrate food and glycogenic distension of the liver in promoting biliousness and bilious attacks need be regarded as excluding the possibility of an excessive ingestion of proteid leading in some cases to hepatic disorder. The liver is supposed to have a proteid elaborating function;¹ and it is easy to conceive that an excessive supply of proteid might interfere with the physiological performance of this function and so lead to pathological phenomena. There can be no question, too, that bile formation depends largely on the supply of proteid, and that a heavy proteid diet may lead to excessive secretion. This is seen with the Salisbury diet, which consists of lean beef (sometimes given in large quantities) and hot water. Under such a diet, however, there can hardly occur glycogenic distension and consequent bilious retention. The excess of bile appears in the motions and may manifest itself as bilious diarrhoea.

EFFECTS ON THE PORTAL CIRCULATION

§ 89. DIARRHOEA.—The tendency to stasis in the alimentary mucosa may be relieved in several ways: the vomiting

¹ Doubt has recently been thrown upon this. Schäfer (*Text-book of Physiology*, 1898, vol. i. pp. 902, 903) says:—'It may . . . be taken for granted that the great part of the proteid which is absorbed from the intestine passes on through the hepatic veins into the general circulation, without being stored or at once modified in the liver.' He places the site of temporary storage of proteid in the muscles.

accompanying the ordinary bilious attack is a means of relief : so is the diarrhoea which, in some cases, habitually replaces vomiting and terminates a period of biliousness. There is a special form of diarrhoea, which seems to me especially common in the tropics, and of which I have seen many examples. This consists of intermittent attacks of diarrhoea, occurring at irregular, but in some cases at fairly regular, intervals, independently of any marked exciting cause, dietetic or other. One of my patients was affected in this way for eleven years : the attacks were never separated by intervals longer than a month, and they were apt to occur more frequently : they lasted for a week and went off with slight dysenteric symptoms. A modified degree of abstention from carbohydrates completely removed the recurring tendency, but he can infallibly reinduce his attacks by returning to his former food habits : indeed, he has done so on many occasions (*vide* Case XXVIII). And I know of several similar cases in which recurrent diarrhoea, of many years' duration, coming on for the most part in the night, has been permanently removed by similar dietetic measures. In few of these, it is interesting to note, was there the slightest tendency to haemorrhoids.

Such cases of diarrhoea are commonly regarded as catarrhal and due to irritation of the alimentary mucous surface by improper food. Consequently, it is usual to prescribe a change from the ordinary mixed diet to one comprising only some form of fluid, or semifluid, carbohydrate food-stuff. This is regarded as bland and unirritating, and its prescription seems to be fairly successful. But it is open for us to regard these cases as catarrhal without abandoning glycogenic distension as a factor therein. For it may well be that various excitants, such as irritation by indigestible food, microbic infection, and even chills to the surface, find in the vascular stasis of the mucosae, induced by glycogenic distension, a favourable soil for their operation. Such, at least, appears to have been Murchison's view. Speaking of the effects of functional liver derangement (in all probability glycogenic distension), he says :¹—' In most of these cases there is evidence of more or less congestion of the liver : the circulation through the liver is impeded and there is a general stagnation of blood in the coats of the stomach and bowels. *This mechanical stagnation*

¹ *Functional Derangements of the Liver*, 1874, p. 92 *et seq.*

is very likely to be converted into an active congestion or a catarrhal inflammation, under the stimulus of irritating ingesta, so that even a small quantity of such a stimulus as alcohol may excite diarrhoea and vomiting.' (Italics mine.)

The commonly prescribed carbohydrate dietary may, in these cases, act beneficially in two ways, both consistent with the hypothesis of glycogenic distension of the liver: (1) being bland, it may be to some extent protective to the irritated mucosae; and (2) less absorption will follow than from a mixed diet, and, consequently, glycogenic distension will gradually subside. But a carbohydrate diet is not, in my experience, the shortest route to relief: temporary abstention from food is preferable, both from a theoretical and a practical standpoint; and next to this perhaps some aliment containing a minimum of glycogen-forming material, such as solution of egg-albumen, as recommended by George Keith¹ and others, on different grounds.

Before Murchison's time and even at a later date, the diarrhoea in such cases was often ascribed to excessive bile formation, which may of course be present. But a temporary retention of bile, brought about, as in the ordinary bilious attack, through congestive obstruction of the orifice of the common bile-duct, alternating with a more or less sudden evacuation when the bile tension in the ducts attains its maximum, will sufficiently explain the clinical phenomena; and, in these cases, the passage of loose motions, which are alternately light and dark in colour, is by no means infrequent.

Later, reasons will be given for believing that with women a tendency to hepatic distension by glycogen recurs at each menstrual epoch, and that this condition is prone to be more severe at about the menopause. Also it will be shown that some women are peculiarly liable to diarrhoea at both of these periods (Chapter VI).

If recurrent attacks of diarrhoea depend, in some cases, upon recurrent glycogenic distension of the liver, it is probable that the onset of diabetes would terminate them. I am unable to quote any case in which this happened; but constipation is the rule in diabetes, a fact which perhaps has some significance. Diarrhoea, dependent on glycogenic distension, will probably do more than merely relieve the

¹ *Fads of an Old Physician*, 1897, p. 151.

secondary retro-hepatic portal congestion: it will tend, as we shall see, through the acceleration of the intestinal contents, to restrict absorption of glycogen-forming material and so to lead to a reduction of the glycogenic distension upon which it depends (§ 268).

§ 90. HAEMORRHOIDS.—There can, I think, be little doubt that continued, or frequently recurring, glycogenic distension of the liver is one of the most important factors in the etiology of haemorrhoids. The mucous membrane of the rectum, down to its junction with the skin at the margin of the anus, is supplied with veins, which become tributary to the inferior haemorrhoidal veins, and thus empty into the portal system (Ball).¹ Any obstruction, therefore, in the circulation through the liver will bear heavily upon the haemorrhoidal area. This has long been recognized, but mainly in connection with cirrhosis.

The clinical evidence, connecting haemorrhoids with glycogenic distension of the liver, may be arranged as follows:—

1. Haemorrhoids commonly commence at that period of life when physical exercise is beginning to be abandoned: a sedentary mode of life has always been regarded as an important factor, though its influence has been otherwise explained.

2. Hirsch says:²—‘Justified as we are in designating haemorrhoids as an ubiquitous malady, we must at the same time admit that it is especially common in many regions within lower latitudes, particularly in the tropics.’

3. A combination of deficient exercise with a plentiful mixed diet and a hot climate is especially powerful to originate haemorrhoids.

4. Murchison regarded haemorrhoids as frequent attendants on functional derangements of the liver, and especially on the loaded state so common in ‘lithaemia’:³ Trousseau regarded them as one expression of the gouty diathesis. Later it will be argued that these constitutional states are identical (§ 858) and have for a common factor hyperpyraemia, a condition associated quite frequently, if not usually, with glycogenic distension of the liver (§ 95).

¹ *Rectum and Anus*, Ball, p. 230.

² *Geographical and Historical Pathology*, New Syd. Soc., vol. iii. p. 453.

³ *Functional Derangements of the Liver*, 1874, p. 95.

5. An almost exclusively proteid diet rarely fails to reduce the distension and size of haemorrhoids, and rarely to cause cessation of the bleeding: I have had several patients who were much annoyed by haemorrhage under an ordinary diet, but who quite ceased to be so on a modified plan of abstention from carbohydrates. Some of these can reinduce the bleeding by returning to their previous foods: one can do so with almost mathematical certainty. Some of these patients had determined on operation, but changed their minds on account of the relief they experienced from regulated diet.

6. On the view of the glycogenic function of the liver which is here adopted, glycosuria implies a relative incapacity on the part of the organ for glycogenic distension. Hence the onset of glycosuria (including some cases of diabetes) should afford some relief from haemorrhoids, as well as from the gastric manifestations (secondary dyspepsia, etc.) of glycogenic distension of the liver. Dr. W. J. Fearnley, resident medical officer of the Brisbane General Hospital, has supplied me with notes of a case which bears upon this point:—

A man of forty-four had suffered for ten years or more from dyspepsia, as evidenced by pain and flatulence after food, from constipation, and from *haemorrhoids* which occasionally bled. Four years ago he became diabetic. Since then he has been quite free from all the above-mentioned troubles.

I have yet to meet with a case in which the onset of glycosuria has failed to relieve considerably the pain, distension, or bleeding of pre-existing haemorrhoids. This fact has apparently escaped observation.

Nothing that has been said as to the influence of glycogenic distension of the liver in causing haemorrhoids is inconsistent with a due appreciation of other commonly recognized factors in this affection. The erect human posture is possibly a contributory factor in all cases: pregnancy and large abdominal tumours are doubtless the main factors in some; but the curative influence of diabetes (an affection commonly associated with torpid bowels) is against the view that habitual constipation alone is a factor of much importance.

§ 91. INTER-RELATIONS OF DIARRHOEA AND HAEMORRHOIDS.—There can be little doubt that both haemorrhage from piles and recurrent and other forms of diarrhoea are often

conservative and adapted to the relief of portal congestion, depending on glycogenic distension of the liver. The effect of a smart attack of diarrhoea in clearing up the symptoms of portal congestion has long been recognized; and all sufferers from piles consider haemorrhage, when not excessive, to be salutary. I know of many cases who have refused operation, because long experience had plainly demonstrated that the stoppage of the habitual loss coincided with a period of indifferent health and that a return of the bleeding brought with it relief. Since, then, both diarrhoea and haemorrhage may depend upon the same cause and are adapted to the same end, these affections are in a sense mutually antagonistic—they tend to be alternative, that is to say, rather than concurrent, and are not, as a rule, habitual in the same patient. I have already remarked on what seems to me the rather marked absence of haemorrhoids in those who are apt to suffer from frequent diarrhoea; and I am convinced that those who are affected with bleeding piles are free as a rule from recurring attacks of diarrhoea, even if they do not suffer habitually from constipation. The following case came under my observation:—

A gentleman suffered for ten years from haemorrhoids and recurring attacks of diarrhoea. At the end of that time, the haemorrhoids commenced to bleed and, for the following five years, he suffered frequently from haemorrhage, but from no diarrhoea. His piles were then ligatured and removed. A few months later, he recommenced to suffer from recurring diarrhoea. This was completely relieved by regulating the intake of carbonaceous material.¹

Haemorrhage from piles will have an influence beyond the mere relief of portal congestion: it will act, as we shall see later (§§ 154 and 267), as a means of decarbonizing the blood. Hence it will have important inverse relations with many affections ascribed in this work to hyperpyraemia. And the same will be true, perhaps to a less extent, of diarrhoea (§ 268).

¹ The dependence of haemorrhoids upon portal congestion, due to hepatic obstruction, is seen very plainly in the following case:—A woman of forty-five suffered from atrophic cirrhosis of the liver (alcoholic), and was much annoyed by haemorrhage from piles. Subsequently she suffered from ascites, for which she was tapped periodically for some years. From the commencement of the peritoneal effusion, the anal haemorrhage ceased, and the haemorrhoids became flaccid and ceased to protrude, even when the distension of the abdominal cavity was extreme. Clearly the peritoneal effusion acted as a newly acquired means of relief from the portal congestion.

RELATION OF GLYCOGENIC DISTENSION OF THE LIVER TO THE CARBON CONTENTS OF THE BLOOD

§ 92. We have seen that the amount of liver glycogen—the degree of glycogenic distension—tends to vary inversely with the rate of combustion in the tissues (§ 68). Now Bernard's theory assumes that the sugar which enters the general blood stream through the hepatic veins is utilized by the tissues as fuel. If this is true, it follows that the amount of sugar in the blood will tend to vary inversely with the rate of combustion. Consequently, it is not unnatural to infer that the rate of combustion in the tissues regulates the glycogenic distension of the liver indirectly through the medium of variations of the sugar contents of the blood,—in other words, that the liver pours sugar into the blood in response, and in proportion, to the withdrawal of sugar by the tissues for combustion. Thus the sugar contents of the blood would tend to uniformity. This view receives support from the demonstrated fact that not all the carbohydrate of a meal is detained in the liver as glycogen: some passes through the liver into the general blood stream (Schäfer).¹ And it may be that, with low sugar contents of the blood, less is detained as glycogen; and conversely.

But, if the rate of combustion determines the withdrawal of sugar from the liver, not directly, but by introducing variations in the sugar contents of the blood, then it follows that processes, other than combustion, which for any purpose withdraw sugar from the blood, will exert a like indirect influence upon the glycogenic distension of the liver. For example, if, as is generally believed, sugar is capable of being converted into fat, then the rate of fat-formation—a process which, we shall see later (§ 125), depends upon a vital capacity of the tissues—will have an important bearing upon glycogenic distension. In this connection, we may recall the fact that persons formerly included under the term 'bilious temperament' were usually spare of frame, that is, presumably, deficient in the fat-forming capacity. But what holds of fat-formation will hold of other processes, such as utero-gestation and secretion formation, which utilize sugar; and of

¹ *Text-book of Physiology*, Schäfer, 1898, vol. i. p. 917.

haemorrhage, which involves a direct loss of sugar from the blood amongst other effects.

But the carbon contents of the blood are not limited to sugar: the blood contains fat, carbonaceous material derived from the carbonaceous moiety of the proteid molecule whatever form that may take, and probably other carbonaceous compounds. Now fat, at least, is certainly capable of undergoing combustion or of being converted into tissue fat; and the probabilities are in favour of similar destinations for the other carbonaceous compounds. Thus carbonaceous material, other than sugar, is capable of replacing sugar to some extent—of acting as substitutive fuel, whether for combustion or storage. And we may hold such a view without denying that sugar and each individual carbonaceous material have special uses peculiar to themselves. But, if this is true, then glycogenic distension of the liver will be determined, not alone by the condition of the blood as regards its sugar contents, but by the condition of the blood as regards its carbon contents generally: glycogenic distension of the liver will tend to vary directly with the carbon or fuel contents of the blood—with the degree of pyraemia.

§ 93. This conclusion receives important direct support from a consideration of the clinical phenomena associated with menstruation. In Chapter VI, it will be argued that menstruation depends upon a carbonaceous accumulation in the blood, progressively increasing during the inter-menstrual period and attaining its maximum just anterior to the commencement of the flow. Further, it will be pointed out (1) that many women at this time suffer from symptoms, such as biliousness, dyspepsia, diarrhoea and haemorrhoids, which are clearly explicable only on the assumption of a degree of glycogenic distension of the liver which approaches the pathological; and (2) that all such symptoms tend to abate or disappear rapidly, when the menstrual haemorrhage has succeeded in dispersing the carbonaceous accumulation in the blood.

§ 94. The view that it is the total carbon, or fuel, contents of the blood which determines the degree of glycogenic distension of the liver, enables us to understand the influence of fats upon this organ. Fat is proverbially bilious. Harley¹

¹ *Diseases of the Liver*, 1883, p. 245.

says:—‘The two species of food which are in general found to be the most detrimental in the vast majority of hepatic cases, are the saccharine-forming and the fatty’; and I am convinced that in some cases an habitual slight excess of fats, as well as of carbohydrates, is capable of determining recurrent bilious attacks and other recurrent affections, dependent on a pathological degree of glycogenic distension of the liver (Case XI).

Now fats are taken up by the lacteals and enter the general blood stream without first passing through the liver; and it seems to have been thoroughly demonstrated that fats are not converted into glycogen. Nevertheless, it may be that fats exert an important influence upon the glycogenic distension of the liver.

The experiments which have shown that fats are not converted into hepatic glycogen were necessarily performed upon starving animals with fats alone: fat so given is followed by no deposition of glycogen in the liver. But fat, given as part of a mixed diet, or to a well-fed animal whose liver contains glycogen, might, by supplying the blood with an alternative fuel, retard the delivery of sugar by the liver and so indirectly prolong, and even permit of an increase in, glycogenic distension. On the other hand, the exclusion of fat from a mixed diet might, other things remaining equal, tend to increase the combustion of sugar; and such would be succeeded by increased delivery of sugar by the liver and by commensurate diminution of glycogenic distension. Hence a diet, such as the Salisbury, which practically excludes both carbohydrates and fats and consists of an excess of proteid, would be peculiarly fitted to reduce glycogenic distension of the liver. In it the supply of glycogen-forming material is largely retrenched: so is the supply of alternative fuel; while the expenditure of carbonaceous material of all kinds by the tissues is greatly increased (§§ 16, 243).

§ 95. The view, that in physiology glycogenic distension of the liver is an index of the degree of pyraemia, may be extended to pathology: pathological distension of the liver by glycogen may be regarded as an index of hyperpyraemia, which, I shall argue later, is probably in many cases merely a pathological degree of physiological high carbon contents of the blood or high pyraemia. Hence recurrent processes, such as

bilious attacks, instead of being due, as may seem to have been assumed, primarily to glycogenic distension of the liver, would be due primarily to hyperpyraemia and only proximately to glycogenic distension. The dispersion of hyperpyraemia would constitute the cardinal meaning of these processes: the glycogenic distension would be an essential instrument; and the dispersion of the glycogenic distension, a subordinate result. Later, bilious attacks, secondary anorexia and dyspepsia, etc., will be classed as pathological 'acarbonizing' processes, depending on hyperpyraemia; and chronic biliousness and similar chronic conditions, depending on chronic glycogenic distension of the liver, as hepatic manifestations of unrelieved hyperpyraemia.

There can be little doubt that it was the very common association of hepatic symptoms with the morbid affections which we are ascribing in this work to hyperpyraemia, that led Murchison to attribute practically the whole series of these morbid affections to functional derangement of the liver.

Later, it will be argued that the instrument, whereby the degree of pyraemia regulates the glycogenic function of the liver, consists of the vaso-motor mechanism (§§ 442 to 453).

POSSIBLE LATE RESULTS OF GLYCOGENIC DISTENSION OF THE LIVER

§ 96. As with the stomach, so with the liver, strained physiological action, though immediately conservative in nature, may eventuate in local disorganization, and so initiate a series of pathological conditions, more or less remote. Glycogenic distension, as already argued, is the primary hepatic condition in some of the chronic hepatic disorders of the tropics; and there is post-mortem evidence to show that, in the later stages, such cases may be complicated by true hepatitis. Many patients so affected present jaundice in various degrees of severity; and chronic jaundice is associated with its own train of phenomena and sequelae. Further, it is worth while considering whether the development of some of the more serious hepatic conditions, such as abscess, which are relatively common within the tropics, is not favoured by a state of more or less habitual glycogenic distension (compare § 175).

It seems certain that gall-stones are frequently associated

with the manifestations of hyperpyraemia and glycogenic distension of the liver. The statistics of Bouchard show this unmistakably. In the following table, taken from his work, nearly all the associated affections mentioned are affections which I am ascribing, in some cases, to the causes of hyperpyraemia, to hyperpyraemia or to its subordinate hepatic condition.

TABLE II.

*Personal Antecedents and Morbid Coincidences in 100 Cases of Biliary Lithiasis.*¹

Obesity	in 72 cases (§ 145)
Eczema	„ 41 „ (Chap. XXII)
Muscular rheumatism (lumbago)	„ 38 „
Migraine	„ 38 „ (Chap. IX)
Gravel	„ 34 „ (§ 636 <i>et seq.</i>)
Acute rheumatism	„ 28 „ (§ 664)
Chronic articular rheumatism	„ 28 „ (§ 857)
Haemorrhoids	„ 28 „ (§ 90)
Diabetes	„ 21 „ (§ 683)
Neuralgias	„ 17 „ (§ 473)
Asthma	„ 7 „ (Chap. IX)

The frequent association of gall-stones with gravel and urinary calculi has been noticed by a series of eminent physicians, amongst whom were Morgagni, Prout, Budd, Trousseau and Murchison. The association points, as we shall see later, somewhat strongly to hyperpyraemia as a common factor (§ 646).

But quite likely the connexion is less direct: it is at least equally explicable on the assumption that gall-stones do not depend upon hyperpyraemia and glycogenic distension, but own dietetic factors in common with these conditions. Both Murchison and Harley ascribe gall-stones to an excessive ingestion of starchy and saccharine food; and recent chemical researches bear this out in great part. These researches seem to show, however, that, while gall-stones are peculiarly liable to occur in those who indulge in starchy and saccharine excess, the most important factor is the deficiency of proteid which such food habits often imply. Mayo Robson says:²—‘It seems probable that free cholesterin in the bile-passages is due in some cases to a deficiency of its solvents in the bile, these solvents being the glycocholate and taurocholate of soda which

¹ *Les Maladies par Ralentissement de la Nutrition*, par Ch. Bouchard, 1890, pp. 88, 89.

² *Diseases of the Gall-bladder and Bile-ducts*, Mayo Robson, pp. 156, 157.

arise from the metabolism of nitrogenous foods. If the supply of nitrogen in the food be limited, the bile-salts are likely to be diminished, and cholesterin may be precipitated. This may serve to explain the presence of gall-stones in gouty persons, who, on account of their uric acid diathesis, limit their intake of nitrogen. The larger consumption of farinaceous food in Germany may serve to explain the greater prevalence of gall-stones there, than in England, where meat enters more extensively into the dietary'; and the sexual differences in food habits would explain also the marked preponderance of gall-stones in women¹ (autopsy percentages 20 against 4.4, Schroeder; 7.9 against 2.9, Brockbank).

THE MISSING GLYCOGENIC FACTOR IN MEDICINE

§ 97. If the views expressed in this chapter as to the importance of glycogenic distension of the liver in both physiology and pathology are accepted even in part, it will be matter for surprise that this hepatic factor has failed hitherto to enter into medical thought. The glycogenic function of the liver occupies considerable space in all works on physiology: in medicine it is seemingly ignored except in the case of the one affection, diabetes, in which the function is presumably lost. This disproportion is at first sight difficult to understand; but it becomes explicable when we bear in mind the preponderating influence, which the exclusively inductive method of investigation has exercised in modern medical science. The elucidation of the operation of glycogenic distension hardly lends itself to purely inductive methods. Probably in the great majority of cases, the distension disappears before death; and if, in some few, such as the case of sudden death from accident in a well-fed person, distension is present at the time, the occurrence of the fatal event determines, as we have seen, the rapid reconversion of all the liver glycogen into sugar. Hence glycogenic distension leaves no traces after death, and morbid anatomy and morbid histology fail us. We can only, it seems to me, arrive at this pathological factor through a process of deduction from physiology; but this is a method of investigation which is regarded as dangerous, and which, in consequence, is very generally discouraged.

¹ *Diseases of the Gall-bladder and Bile-ducts*, Mayo Robson, pp. 156, 157.

SUMMARY

§ 98. In this chapter, I have attempted to show that in health the carbon or fuel contents of the blood dominates the glycogenic function of the liver : that the glycogenic function of the liver subserves at least two physiological purposes, namely (1) detention and storage of sugar as glycogen against hyperglycaemia and glycosuria and against hypoglycaemia in the intervals between meals, and (2) the regulation of the general nutritious income from the alimentary canal through physiological distension of the organ by glycogen : that, in certain circumstances, glycogenic distension of the liver attains pathological dimensions, and that such pathological distension, which is always conservative and often, if not usually, salutary, may be acute, recurrent, or chronic, the clinical equivalents being the various forms of biliousness : that pathological distension, though conservative, represents the straining of a physiological function, and is, therefore, prone to be associated with, or succeeded by, secondary pathological conditions : that many of these secondary pathological consequences, for example haemorrhoids and diarrhoea, are again conservative, being adapted to relieve the portal back pressure upon which they proximately depend ; and that some of them, for example haemorrhage from piles and diarrhoea, are further adapted to reduce the carbon contents of the blood, and thus to disperse hyperpyraemia or a tendency thereto, the primary factor of the whole pathological sequence.

Thus the liver, by virtue of its glycogenic function, may be regarded as a complex automatic physiological valve, whereby the inflow of fuel to the general blood stream is regulated, more or less accurately, in accordance with the requirements of the tissues and in accordance with their capacities for physiological disposal. In those who are quite healthily constituted, the regulation is effected in a physiological manner ; and the clinical manifestations are those of comfort and satisfaction. In others, the regulation is pathological in nature ; and the clinical manifestations are distressing, if not extremely painful. But, between the most physiological regulation on the one hand, and the most pathological regulation on the other, all intermediate gradations are to be observed. Finally, it is clear that inadequacy of physiological regulation may be an important factor in pathological regulation.

CHAPTER IV

§§ 99–118

Carbon expenditure, or decarbonization of the blood: katabolism—Combustion a vital capacity of the nitrogenous tissues and a process of decarbonization—Variations in the rate of combustion: inherent individual variations: nutritional variations: variations depending on the supply of oxygen: variations in accordance with the demand for force and heat production: variations in accordance with the necessity for decarbonization or variations determined by the supply of fuel—Rhythmical fluctuations in combustion: daily fluctuations: fluctuations associated with menstruation and utero-gestation: seasonal fluctuations—Clinical evidence that the temperature of the body may be regulated by decrease of heat-production—Secondary results of strained combustion—Combustion inadequate for decarbonization—Summary.

§ 99. We have seen that the organism, confronted with an excess of carbonaceous material, is endowed within certain limits with the means of regulating the income to the general circulation. We have now to consider the means whereby the blood is normally cleared of carbonaceous material, which has passed the barriers of the digestive organs—expenditure of carbon or ‘decarbonization.’ Such expenditure may be by katabolism, by anabolism, and by direct loss or haemorrhage.

COMBUSTION A VITAL CAPACITY OF THE NITROGENOUS TISSUES AND A PROCESS OF DECARBONIZATION

§ 100. Heat production results from the katabolic changes occurring in the body. The majority of these, though they are much less simple than the term would imply, are spoken of generally as oxidative. Oxidative changes or combustion are continuous throughout the organism, but they are not uniform for the different tissues and organs. Foster says: ¹—‘The blood itself cannot be regarded as a source of any considerable amount of heat, since . . . the oxidations or other metabolic changes taking place in it are comparatively

¹ *Text-book of Physiology*, 1895, pp. 846, 847.

slight. The heat, evolved by the indifferent tissues, such as bone, cartilage and connective tissue, may be passed over as insignificant; and we cannot even regard the adipose tissue as a seat of the production of heat, since the fat of the fat-cells is in all probability not oxidised *in situ*, but simply carried away from its place of storage to the tissue which stands in need of it, and it is in the tissue that it undergoes the metabolism by which its latent energy is set free.'

Thus combustion is no mere result of the intake of combustible material, but is effected by means of the nitrogenous tissues—it is not a passive, but an *active or vital capacity of the nitrogenous tissues*. And, while it is probable that all nitrogenous tissues are endowed with this capacity in some degree, yet it is certain through experimental demonstration that the muscular and glandular tissues are so endowed in the highest degree. Even while at rest, combustion is continuous in the muscles, and during contraction combustion is greatly accelerated. During the accelerated combustion of muscular contraction, as we have seen (§ 6), there is no increase in the nitrogenous output, but the output of carbonic acid is largely increased. Hence it is inferred that the combustion bears solely upon the carbonaceous material which is perhaps stored temporarily somewhere within the muscular tissue¹ (Foster); and what is true of the accelerated combustion of muscular action, is probably true of the more 'subdued' combustion which is continuous. But such stored carbonaceous material must have been originally drawn from the blood stream, and it would have to be replenished thereafter from the same source. Hence it is open for us to regard combustion, whether in the resting or working muscles, or in the glandular and other tissues of the body, as a physiological process of blood decarbonization; and we may speak of it as 'katabolic physiological decarbonization.'

VARIATIONS IN THE RATE OF COMBUSTION

§ 101. It can be shown that the rate of combustion varies widely under a variety of conditions: some of these conditions are inherent, others nutritional and acquired: some concern the environment, others are purely or mainly personal.

¹ *Text-book of Physiology*, Foster, 1895, p. 164.

§ 102. INHERENT INDIVIDUAL VARIATIONS.—Combustion implies heat production, and Foster says:¹—‘Probably every species has what may be called its specific coefficient of heat production, the coefficient being the expression of the inborn qualities proper to the living substance of the species and of the individual.’ We may believe then that the rate of combustion is in some degree regulated by the capacity of the tissues inherent in the individual; and this, as we shall see, receives support from clinical observation.

Recent observations seem to render it probable that some of the individual variations in the rate of combustion depend on an internal secretion of the thyroid gland. Harry Campbell says:²—‘Thyroid secretion . . . plays the part of a bellows, causing the vital fire to burn more fiercely and increasing the output of urea, carbonic acid, etc. One can scarcely doubt, in short, that the differences of katabolic activity among normal individuals depend to a large extent upon the activity of the thyroid gland; and we may be sure that there are many kindred influences affecting the rate of katabolism of which we are as yet ignorant.’

§ 103. NUTRITIONAL VARIATIONS.—But individual differences in combustion capacity are not limited to those which are inherent or congenital. Combustion, being a vital capacity or function of the nitrogenous tissues, depends in great part upon tissue nutrition; and the due nutrition of all nitrogenous tissues implies a due supply of proteid food. Hence, as we have already seen (§ 16), an increase in the proteid supply is followed by a marked increase in the rate of combustion: on the other hand, a reduction in the supply will be succeeded by a fall in the rate of combustion.

§ 104. But conditions other than a deficiency of the proteid intake may lead to malnutrition of the nitrogenous tissues. ‘Liebermeister³ and other observers have . . . shown that the amount of urea excreted in the urine during fever surpasses by at least 70 per cent. that which is voided by a healthy person living on the same diet. Careful observations by Ringer in a case of ague established the fact of the same excess of excretion of urea for intermittent pyrexia’ (Fagge). Hence

¹ *Text-book of Physiology*, Foster, 1895, p. 850.

² ‘Observations on Diet,’ *Lancet*, May 24, 1902, p. 1487.

³ *Text-book of Medicine*, Fagge, vol. i. p. 38.

the fixed nitrogenous tissues must be largely disintegrated during pyrexia and be left in a state of more or less malnutrition. This anticipation is confirmed by the results of microscopic examination of these tissues in cases of scarlatina, typhoid fever, variola, erysipelas, diphtheria, septicaemia and other infectious diseases. The cells in such cases present the condition known as cloudy swelling, or parenchymatous or granular degeneration. Ziegler says:¹—‘This change is to be regarded as a *disorganization of the cell-protoplasm* following the absorption of liquid into its substance and leading to a partial separation of its solid and liquid constituents. *The nucleus not infrequently participates in these changes, undergoing a similar disorganization.* Recovery from a moderate degree of this degeneration is quite possible, in which case the cell is restored to its normal condition; but often there is a complete destruction of the cell, which then ultimately breaks up into finely granular fragments. Fatty degeneration is frequently associated with the degeneration under discussion.’

Conformably with the existence of such degenerative changes in the fixed nitrogenous tissues, it will be argued that during convalescence from fevers combustion is peculiarly apt to be retarded, and that hyperpyraemia sometimes results from the retardation (§ 230).

§ 105. VARIATIONS DEPENDING ON THE SUPPLY OF OXYGEN.

—High combustion capacity on the part of the katabolic nitrogenous tissues will be inoperative in the absence of a due supply of oxygen. The supply available may be reduced in various ways. Oxygen may be deficient in the surrounding atmosphere; or accident or disease affecting the air passages, such as laryngeal and tracheal obstruction, or lungs, such as pneumothorax and oedema, may limit the oxygen intake. So may arise acute asphyxia, a condition in which combustion, at first exaggerated in accordance with the exaggerated muscular effort of dyspnoea, rapidly fails as the available supply of oxygen becomes exhausted. Similarly, chronic asphyxial conditions may arise in various ways. Chronic bronchitis, emphysema, etc., may limit the oxygen intake: cardiac affections, through retardation of the circulation, may delay the delivery of oxygen to the tissues; and anaemia, implying as it does

¹ *General Pathology*, Dr. Ernst Ziegler, 1899. William Wood and Company, New York.

deficiency of haemoglobin, the oxygen-carrying constituent of the blood, will have a similar influence. As regards anaemia, it is probable that some cases arise through deficiency of proteid in the food (§ 204); and if so, then proteid deficiency will lead indirectly through anaemia, as well as directly through malnutrition of the nitrogenous tissues, to retarded combustion.

On the other hand, it is probable that an excess of oxygen or of ozone in the inspired air will lead, other things equal, to some increase in the normal rate of combustion.

§ 106. VARIATIONS IN ACCORDANCE WITH THE DEMAND FOR FORCE AND HEAT PRODUCTION.—Combustion, as we have seen, is greatly increased by bodily labour (§ 14): it is increased also in accordance with the demand for heat production (Foster).¹ Exposure of the surface of the body to cold is followed by a complex series of phenomena, adapted to maintain the body temperature uniform. Vaso-constriction of the cutaneous area occurs: the skin becomes anaemic. Along with this, there is internal vaso-dilation: this is sometimes placed in the splanchnic area, but it seems probable that the *muscular layer* is largely affected² (Winternitz). One tendency of these vascular changes is to secure a retention of heat. Concurrently, there is an increase in combustion and heat-production, as has been demonstrated calorimetrically. 'The muscles are placed in a condition of heightened tonus by cold and sometimes driven into spasm.'³ If the cold is intense the muscular spasm 'may increase to a general spasmodic quivering—the rigor':⁴ this still further increases combustion and heat-production, and so must be regarded as strictly conservative.

On the other hand, exposure of the body to external heat is followed by the reverse series of phenomena; but, in ordinary circumstances, these are less marked and indeed are not all invariably present. This seeming inconsistency will be considered more conveniently and more appropriately in the succeeding paragraph (§ 107).

§ 107. VARIATIONS IN ACCORDANCE WITH THE NECESSITY FOR DECARBONIZATION, OR VARIATIONS DETERMINED BY THE

¹ *Text-book of Physiology*, Foster, 1895, p. 849.

² Winternitz in Von Ziemssen's *Handbook, Therapeutics, Hydrotherapeutics*, p. 429.

³ *Ib.*

⁴ *Ib.*

SUPPLY OF FUEL.—Stewart says:¹—‘It might be supposed—and indeed has often been assumed, that heat would lessen metabolism as cold increases it; and there are indications that in the smaller animals this is the case, although the influence of heat seems to be much smaller than the influence of cold. But neither experimental results nor general reasoning have as yet shown that in man, either in the tropics (Eykman) or in the north temperate zone (Loewy), the chemical tone is diminished by a rise of the external temperature, much above the mean of an ordinary English summer, apart from the effects of muscular relaxation which heat induces. In a man indeed at rest in a hot atmosphere, the production of CO₂ and consumption of O are, if anything, greater than at the ordinary temperature. The regulation of temperature in an environment warmer than the normal seems in fact to be brought about more by increase in the loss than by a decrease in the production.’

There seems, however, to be a material difference of opinion as to the influence of hot climates upon the rate of combustion. Surgeon Lieutenant-Colonel Crombie² states that the amount of carbonic acid given off by the lungs is reduced in the tropics by about 20 per cent., but that with very high temperatures—95° F. and over—the respiratory exchange is on the other hand increased.

Nevertheless, even if it be true that as a general rule the output of carbonic acid remains undiminished in the tropics, the theory of hyperpyraemia constrains us to seek interpretation from a different view-point. It may be argued that insufficient allowance has been made for the food factor. A person, who is digesting and absorbing a constant amount, must eliminate *from his blood* a constant amount, of carbonaceous material—in short, expenditure must be commensurate with income: otherwise hyperpyraemia will result. Here it will no doubt be objected that combustion is not the only means of expenditure, and that carbonaceous material which is not burnt off and eliminated as carbonic acid is conveniently stored extra-vascularly as fat. But, in the succeeding chapter, it will be urged that fat-formation is no mere result of a

¹ *Manual of Physiology*, 1899, p. 499.

² ‘The Measure of Physical Fitness for Life in the Tropics,’ *Lancet*, December 14, 1901, p. 1671.

superfluity of fuel, but depends, in great part at least, upon an active or vital capacity of the nitrogenous tissues—a capacity with which the tissues of different organisms are endowed in widely different degrees: this, indeed, is a conspicuous clinical fact. It may be, then, that a person at rest in a hot atmosphere is but poorly armed with the capacity for rapid fat-formation, and if so, he will be dependent in a correspondingly higher degree upon combustion for adequate expenditure or decarbonization.

It is then, I submit, open for us to regard the continuance of the undiminished output of carbonic acid and the regulation of the body temperature by an increase in the heat loss, under the conditions specified by Stewart, as a conservative 'policy' adapted to avert hyperpyraemia. We need not infer, as seems to be generally inferred, that the organism 'prefers' (if the term be permitted) to regulate its temperature by increasing its heat loss, rather than by decreasing its heat production: we may infer instead that, under a constant supply of fuel, it may be driven to do so in self-defence: in other words, that combustion may be in part regulated by the necessity for decarbonization, or—which comes to the same thing—by the absorption of carbonaceous material, that is, by *the supply of fuel to the blood*. Strongly confirmatory of this view are the observations of Magnus Levy, Jacquet and Svenson (quoted by Herter and again referred to in § 143), to the effect that in corpulent persons, that is, in persons conspicuously well endowed with the fat-forming capacity, the post-prandial increase of combustion, as shown by the increase of oxygen consumption and of carbonic acid excretion, is much less than in more ordinary individuals.

The heat given off as a result of such combustion as is a response to the necessity for decarbonization must be regarded, as Maclagan would say, as an 'excretory product' in the strict sense of this term. If this argument is well founded, we must cease to wonder at Nature for adopting what appears at first sight a somewhat clumsy and expensive method of heat regulation: we must admire her for yet another example of her power of self-adjustment to varying and more or less deleterious conditions.

§ 108. The increased combustion called forth by the necessity for decarbonization enables us to understand the

increase in combustion which follows food. This increase may be inferred from our own sensations, but it has also been demonstrated by deliberate experimentation. That it is largely due to the presence of nutritive material in the blood in amount exceeding the average, and not solely, or even chiefly, to the mechanical and chemical work of digestion, seems to me assured by the following observations: 1. 'In¹ the dog it has been found that the rate of production' (of heat) 'increases after a meal, reaching its maximum from the sixth to the ninth hour, and then declining to the level which may be regarded as that secured by the general metabolism of the body' (Foster). Were the digestive work the chief source of the increase, it is clear the maximum would occur much earlier. 2. 'If² sugar be added to the meal, the rise becomes more marked at an earlier period' (Foster). It cannot be maintained that sugar requires for digestion more expenditure of energy than carbonaceous materials, such as the starches and fats: indeed, it is evident that it requires less. But it is clear, on this account, that sugar will gain more rapid entry into the circulation; and sugar is known to be one of the few nutritive substances which undergo absorption in the stomach³ (Schäfer). 3. 'Injections of sugar and peptone directly into the blood have been observed to occasion a considerable increase in the consumption of oxygen and in the production of carbonic dioxide'⁴ (Schäfer). The last observation seems conclusive.

It may be admitted, then, that, under ordinary human conditions, the body temperature in hot weather is regulated more by an increase of heat loss than by a decrease of heat production. But this is not an admission that high external temperature is incapable of bringing about a decrease of combustion. In order to substantiate such a contention, it would be necessary in the first place to eliminate variations of combustion dependent on variations of the carbon contents of the blood. This might be achieved by keeping the subject of experiment without food of any sort for such time as experience has shown to be necessary to render empty the alimentary canal of all nutritive material. Under these conditions, I would venture to predict, with all due deference to the

¹ *Text-book of Physiology*, Foster, 1895, p. 851.

² *Ib.*

³ *Text-book of Physiology*, Schäfer, 1898, vol. i. p. 432.

⁴ *Lectures on Chemical Pathology*, Herter, 1902, p. 446.

Baconian teaching, that variations of combustion would respond inversely with some delicacy to variations of external temperature.

§ 109. The failure to recognize the possibility of hyperpyraemia, and the consequent failure to realize that combustion is regulated in part by the demand for decarbonization, have led to some curious inferences. It has just been admitted that, under ordinary conditions, the temperature of the body is maintained constant in hot weather more by increased loss, than by diminished production, of heat. From this one physiologist is inclined to infer, that in warm climates not less, but if anything rather more, food than in temperate climates is necessary in order to supply the perspiration needed for the greater evaporation and discharge of heat by the skin. Now it is not easy to see what advantage could accrue from obtaining water, to be used in heat dissipation, by the combustion of food (carbohydrate) which is in itself a source of heat-production; nor why the additional water demanded should not be supplied by an increase in the fluid intake, especially in view of the thirst which is so commonly urgent in the tropics.

RHYTHMICAL FLUCTUATIONS IN COMBUSTION

There can hardly be a doubt that the various rhythmical fluctuations in combustion and temperature, which affect the organism, depend for the most part fundamentally upon the same factors as the less regular variations already considered. Still they are so important from the standpoint of clinical medicine, as to merit separate consideration here.

§ 110. DAILY FLUCTUATIONS.—It can be shown that combustion fluctuates rhythmically throughout the diurnal cycle. In the subjoined chart are recorded the variations in the temperature of the body, according to the observations of Liebermeister and Jürgensen, extending over a period of thirty hours. (Fig. 1.)

We see that from midnight to about 6 A.M. the temperature is low: that about 6 A.M. a rise begins, which continues throughout the forenoon: that during the afternoon and up to about 7 P.M. the temperature is fairly steady; and that thereafter there is a progressive fall.

§ 111. It is practically certain that these variations in

temperature are due in the main to variations in the production, and not to variations in the loss, of heat. Lockhart Gillespie says: ¹—‘If the day be divided into three periods of eight hours, one for work, one for rest, and one for sleep, we find that during the working hours, as many as 216,960 calories of heat may be produced in each, 140,000 during each of the resting hours, and only 40,000 during each hour of sleep.’ So far, then, from the reduction of temperature during the night being due to an increased heat loss, it is highly probable, bearing in mind the heavy fall in the heat production and also the conditions which usually surround the body during sleep, the warmth of bed, etc., that it occurs in spite of a diminished heat loss; and that the variations in combustion throughout

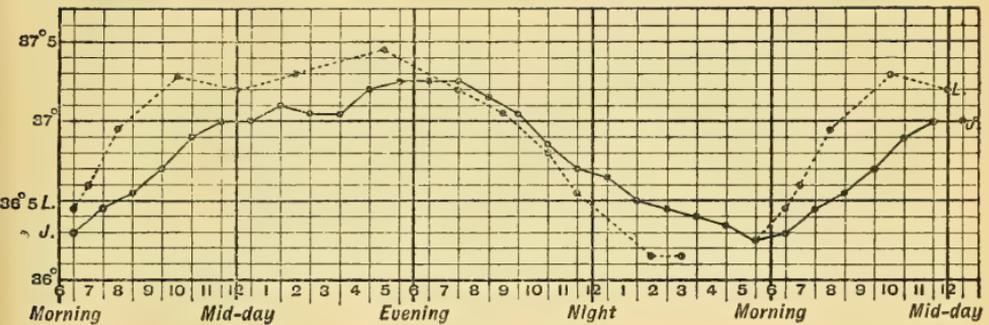


Fig. 1.

Daily variations in temperature observed by Jürgensen and Liebermeister. The observations extend over thirty hours. From Schäfer's 'Text-book of Physiology,' vol. i. p. 800.

the twenty-four hours are actually greater than thermometric observations might lead us to suppose.

As regards the causes of the fluctuations of combustion,² 'muscular activity and food appear to be the most important exciting factors' (Schäfer). Combustion rises and falls in accordance with the increased or diminished demand for force production and for decarbonization; and we must not omit to notice the varying demands for heat-production. In ordinary life, man is most active and takes food during the day: perhaps, too, at this time he is most exposed to cold. He is least active, takes no food, and is perhaps less exposed to cold, during the night. The daily fluctuations in combustion are rhythmical, because, in ordinary circumstances, the daily variations in

¹ *Nat. Hist. of Digestion*, A. Lockhart Gillespie, 1898, p. 336.

² *Text-book of Physiology*, Schäfer, 1898, vol. i. p. 801.

activity and exposure to cold and the daily supplies of food are rhythmical, being governed primarily by the rhythmical alternations of day and night. This is proved by the fact that continuous work, or even watching without much work through the night, inverts the fluctuations, or nearly so.

§ 112. But the waking and sleeping states, apart from muscular activity, food, etc., appear to exert an important influence. Sleep during the day causes a sharp fall, getting up in the evening causes a sharp rise, in the rate of combustion: this is clearly shown in the appended chart. (Fig. 2.)

Hence probably the extreme danger, long recognized by Arctic travellers, of sleep during exposure to very low temperatures. During the waking state the rate of combustion may

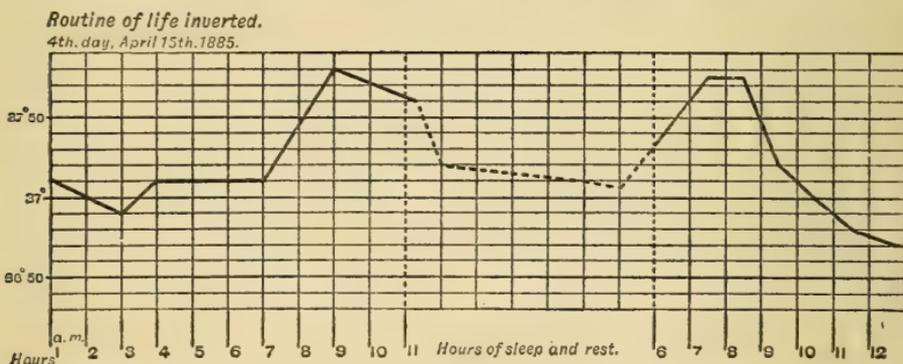


Fig. 2.

Variations in temperature due to sleep in the day-time, observed by U. Mosso.
From Schäfer's 'Text-book of Physiology, 1898, vol. i. p. 802.

be no more than sufficient to maintain the body temperature: at the onset of sleep the rate suddenly falls and thus becomes inadequate.

The fact that, in ordinary circumstances, combustion falls to its lowest point in the small hours of the morning, probably accounts for the number of instances in which death terminates exhausting diseases at about this time.

§ 113. FLUCTUATIONS ASSOCIATED WITH MENSTRUATION AND UTERO-GESTATION.—There is evidence showing that the menstrual rhythm is associated with a fluctuation in the rate of combustion. Rabuteau,¹ from experiments in metabolism, finds that during the whole of menstruation there is a diminution in the output of carbon. Later, it will be argued that this

¹ *Digest of Metabolic Experiments*, Atwater and Langworthy, 1898, p. 174.

retarded combustion is compensatory of the haemorrhagic decarbonization of menstruation (§ 156), and that it is preceded by a period of accelerated combustion, which may be regarded as a response to a gradually increasing demand for decarbonization.

The menstrual fluctuations in combustion are interrupted by pregnancy, but it seems undecided whether, during the latter physiological state, combustion is increased or diminished. In a case of pregnancy, observed by Scharling,¹ the exhalation of carbonic acid was increased to 885 cub. ins. per hour, the average hourly excretion being at other times 714 cub. ins. 'Oddi² and Vicaredi have published the results of experiments with rats, in which the influence of gestation on the respiratory quotient was studied. The conclusion was reached that gestation is characterized by increased combustion of carbohydrates in the body, while the nitrogenous material is used for the nutrition and development of the foetus.'

On the other hand, Reprev³ of St. Petersburg, from experiments on rabbits and dogs, concludes that 'during pregnancy less oxygen is exhaled' (? absorbed) 'and less carbon dioxide excreted than under normal conditions; that is, the oxidation processes are weakened.' It is impossible to decide between these conflicting statements; but it may be said that the last is more conformable with *à priori* anticipation. During pregnancy there must be an increased withdrawal of carbonaceous (as well as nitrogenous) material for anabolism, and consequently we should perhaps expect to find the necessity for katabolic decarbonization reduced. Fortunately a decision of this question is not necessary for the purposes of this argument.

§ 114. SEASONAL FLUCTUATIONS.—It seems probable that, in addition to the daily and monthly fluctuations in combustion, there are seasonal fluctuations also; but these are less well defined and have hardly been investigated. If such could be established, we might have an explanation of the occurrence of some of the diseases, ascribed in this work to hyperpyraemia, at special periods, such as gout in the late winter, etc. A special proclivity to disease at the spring and fall has long been

¹ *Human Physiology*, Austin Flint, pp. 147, 148.

² Quoted by Atwater and Langworthy, *Digest of Metabolism Experiments*, 1898 p. 172.

³ *Ib.* p. 344.

recognized in a vague kind of way. 'Folks who keep well in Spring and Fall will have their health throughout it all.' It has been my fortune to come across more than one out-of-the-way district in New South Wales, where the children, at both these periods, are still placed upon a course of brimstone and treacle, extending over nine consecutive mornings.

CLINICAL EVIDENCE THAT THE TEMPERATURE OF THE BODY MAY BE REGULATED BY DIMINISHED HEAT PRODUCTION

§ 115. Rapid heat production may often be inferred with probable correctness from the clinical evidences of rapid heat loss. These are matters of daily observation in hot weather and in the tropics: they consist, as might be anticipated, of intense subjective sensation of heat, flushing, profuse perspiration, etc., especially marked after meals and physical exercise. Now it has been inferred that the high combustion rate, which necessitates this rapid heat loss, depends in part upon the necessity for decarbonizing the blood; and, if this inference is correct, it will follow that these distressing phenomena may be in part averted by reducing the carbonaceous ingesta. The evidence which I possess upon this point is, from its amount in the aggregate, conclusive to my mind; yet, since it is purely clinical and therefore necessarily indirect, it is likely it will not favourably impress the reader.

Many of my patients, treated for various disorders, by regulation of the carbonaceous intake, bear witness to the relief they have experienced from the subjective sensation of heat, post-prandial flushes, profuse perspirations, and other manifestations of strained heat loss. One tells me, for example, that, whereas she was the one of a large household who chiefly suffered from hot weather, she now experiences much less discomfort on this account than any of the rest. Another has gone through a whole summer taking much bicycle exercise and wearing a starched shirt and high collar without inconvenience for the first time for many years; and so on. So uniform is the collected testimony of patients on this point, that it seems practically certain that, in their case, the regulation of the body temperature is carried out largely by diminished heat production and not solely, even if mainly, by increased heat loss.

SECONDARY RESULTS OF STRAINED COMBUSTION

§ 116. It may, I think, be reasonably urged that combustion, called forth by excessive carbonaceous intake and absorption (over-carbonization) and carried to the extent that the phenomena of heat dissipation become inconvenient and even burdensome, is the straining of a physiological capacity; and it can hardly be disputed that strained physiological action passes by insensible gradations into action, which is overtly pathological. Hence it will not be surprising to find a series of disorders commencing at this point. The morbid evolution may proceed in several directions. The discomfort attending the strained heat loss may lead to an endeavour to diminish heat production: this, if successful, may involve inadequate decarbonization and lead to hyperpyraemia, with any of its immediate or remote results. Or it may be that the dissipation of heat fails to be increased commensurately with the increased production of heat: in this case various pyrexial affections might arise; and it is believed by some that some of the ardent or thermic fevers of India, hyperpyrexial sunstroke¹ or heat apoplexy and other less clearly defined febrile states, arise essentially in this way: certainly the effect of direct heat abstraction by the cold bath in some of these affections seems to amount to a demonstration of the truth of such views. Finally, the phenomena of excessive heat dissipation may in themselves lead to disorders: 'prickly heat'² is almost certainly a proximate result of excessive perspiration: it is always regarded by the public as salutary, and probably with some reason, since it is at least an indication of an energetic attempt at compensation for rapid heat production. And it has often seemed to me that excessive perspiration is the most important factor in many cases of eczematous disease prevalent within the tropics.

¹ H. C. Wood in Parkes' *Hygiene*, 8th ed., p. 401.

² 'In prickly heat the vesicles formed are really retention cysts, caused by the scarf skin becoming sodden by the perspiration. The cells of the scarf skin become swollen by the imbibition of water, and thereby block the orifices of the ducts of the sweat glands. The sweat ducts themselves become distended and give rise to the minute discrete vesicles. By wearing underclothing of wool the perspiration, as fast as it is secreted, is carried away, so that the epidermis never becomes sodden, and the mouths of the sweat ducts remain patulous.'—Dr. George Gray (*Med. Annual*, 1901, p. 453), St. Lucia, West Indies.

COMBUSTION INADEQUATE FOR DECARBONIZATION

§ 117. The addition of fuel to an ordinary fire is succeeded by an increase in combustion, but this is true only within certain limits. If the fuel is added suddenly and in excess, a decrease, rather than an increase, in combustion ensues; and engineers inform me that accurately graduated stoking is a most important factor in maintaining the maximum rate of heat production. So it would appear to be with the organism: an increase in the carbon contents of the blood is followed by a corresponding increase in combustion by the tissues, but if the increased supply exceed the combustion capacity of the tissues, a retardation may ensue.

The vegetarian has been compared to 'an¹ over-heated steam engine' (Hueppe). The analogy is true only so long as combustion keeps pace with supply. Beyond this point, the vegetarian may be compared more aptly to an engine in which the fires have been slaked down by an excess of fuel, and in which, consequently, there is demanded either some further aid to combustion, such as extra draught of air, or a partial removal of the load.

A disproportion between carbonization of the blood and combustion is, as we shall see, a fundamental factor in hyperpyraemia.

SUMMARY

§ 118. In this chapter, I have attempted to show that combustion or oxidation is a vital capacity or function of the nitrogenous tissues: that, like all functions, it varies in power with the individual and with the supply of proteid in the food: that, from the standpoint of the theory of hyperpyraemia, it may be regarded as a process of katabolic physiological decarbonization: that, though continuous during life, it presents irregular and rhythmical variations: that some of these depend upon the supply of oxygen, others upon the demand for force and heat production, and others again upon the demand for decarbonization of the blood: that strained combustion, like all strained physiological functions, is prone to be associated with, or

¹ *British Med. Journal*, March 2 1901, Professor F. Hueppe.

followed by, secondary pathological conditions ; and that combustion may be strained to its limits and yet prove inadequate for decarbonization.

The regulation of combustion by the demand for decarbonization involves the principle, extremely important from the standpoint of the theory of hyperpyraemia, that the organism possesses the power, though only within certain limits, to increase the rate of combustion in response to an increase in the carbon contents of the blood : such increase may be direct, or indirect through physical exercise and consequent increase in the demand for force production.

CHAPTER V

§§ 119–153

Carbon expenditure or decarbonization of the blood (*cont.*): anabolism—Uterogestation and lactation—Secretion formation—Formation and deposition of muscle glycogen.—Fat-formation: the functional factor, an active or vital capacity of the nitrogenous tissues: the supply factor, a due amount of carbonaceous material in the general blood-stream available for fat-formation: a process of decarbonization: carbon equilibrium at various levels: limitations to the decarbonizing influence of fat-formation—Combustion and fat-formation correlated—Obesity—Leanness—Summary.

§ 119. We have considered the withdrawal from the blood of carbonaceous material, which is followed by its destruction in the tissues, and by its elimination as carbonic acid, with the production of heat or its equivalent in muscular work—*katabolic physiological decarbonization*. But carbonaceous material is withdrawn from the blood in various physiological processes for constructive purposes also. These processes we may classify under the head of *anabolic physiological decarbonization*. It is not, of course, customary to speak of anabolism as a source of expenditure; nor could we do so from the standpoint of the whole organism. But we may do so from the standpoint of the blood; for the blood is a current account, and material, transferred therefrom to a fixed deposit in the tissues, must be credited to the blood.

The anabolic decarbonizing processes include fat-formation, utero-gestation, and the formation of various secretions, such as milk, bile and sebum; and the fact that in many of these there is a withdrawal and anabolism of nitrogenous, as well as of carbonaceous, material, in no way negatives their decarbonizing influence.

All these anabolic processes depend fundamentally upon two factors: (1) a due supply of raw material, which for the present purpose may be regarded as carbonaceous; and (2) a vital or active constructive capacity on the part of the nitro-

genous tissues or bioplasm, especially concerned : in general terms, anabolism depends upon *supply and function*.

UTERO-GESTATION AND LACTATION

§ 120. It will be admitted that both these anabolic processes depend upon supply and upon function ; and that both are, *inter alia*, processes of decarbonization. During the whole of pregnancy and lactation, both nitrogenous and carbonaceous material continue to be withdrawn from the maternal blood for anabolism in amounts exceeding that which is withdrawn at other times. This amount probably increases progressively from conception to the termination of utero-gestation. Then there is an interval of a day or two between the end of labour and the establishment of lactation ; but the exaggerated expenditure is continued by the lochia, and it must be remembered that the great muscular labour involved in childbirth implies a heavy katabolic decarbonization. Obviously, from conception to the end of lactation, physiological decarbonization proceeds at a rate which is above the average at other times : it is, moreover, wholly continuous in place of being in part intermittent, as during the recurrence of menstruation. Hence we shall find that some physiological decarbonizing processes are partly inhibited and that many pathological conditions, depending on hyperpyraemia, remain in abeyance throughout the whole course of utero-gestation and lactation.

SECRETION FORMATION

§ 121. It will be admitted that all secretion formation depends fundamentally upon the two factors, supply and function. And it is clear that the formation of bile, sebum, and of all even partly carbonaceous secretions, may be regarded as anabolic decarbonizing processes, since the carbonaceous material, which enters into their composition, is drawn more or less directly from the general blood-stream. It is true that the influence of many such processes upon the composition of the blood can be but infinitesimal. Nevertheless, as we shall see later, they have important inverse relations with other processes, physiological and pathological, which operate to reduce the carbon contents of the blood.

FORMATION AND DEPOSITION OF MUSCLE GLYCOGEN

§ 122. Schäfer says: ¹—‘The muscles may contain as much as 1 per cent. of glycogen. Although this is not by any means as large as may be contained in the liver itself, the muscles may collectively hold as much as is present in the liver.’ This muscle glycogen varies in quantity, and its variations seem determined by conditions similar to those which determine the variations of liver glycogen. Thus Halliburton says: ²—‘The muscle glycogen disappears during starvation, but much more slowly than the hepatic glycogen’; and again:—‘During work the glycogen disappears, being perhaps transformed into sugar and the products of its combustion.’ The disappearance of glycogen during muscular activity ‘is held to be an argument in favour of this work being done at the expense of this carbohydrate’ (Schäfer).³ This is probably true, but it must be admitted that muscles are capable of utilizing other material as fuel. For, as Foster⁴ points out, ‘many muscles wholly free from glycogen are perfectly well able to carry on long-continued contractions.’

Since there are only traces of glycogen in the blood plasma (Schäfer)⁵ and since sugar is a constant constituent, it seems probable that the muscles obtain their store of glycogen from the latter and that, like the liver, they possess the power of dehydration. Conformably, Halliburton says⁶ that ‘some observers consider that the muscles have a glycogenic function apart from that of the liver.’ This view is supported by the fact, pointed out by Foster,⁷ that muscle glycogen is not quite identical with hepatic glycogen. We have seen that some of the carbohydrate of a meal, in the form of soluble sugar, passes through the liver into the general circulation (§ 92); and probably some of this is dehydrated and deposited in the muscles. It may be, also, that some of the sugar, resulting from the hydration of liver glycogen, becomes re-dehydrated by the muscles and deposited therein. In both cases, the act

¹ *Text-book of Physiology*, E. A. Schäfer, 1898, vol. i. p. 917.

² *Ib.* pp. 104, 105.

³ *Ib.* p. 915.

⁴ *Text-book of Physiology*, M. Foster, 1895, p. 764.

⁵ *Text-book of Physiology*, E. A. Schäfer, 1898, vol. i. p. 158.

⁶ *Ib.* p. 105.

⁷ *Text-book of Physiology*, M. Foster, 1895, p. 765.

of dehydration would be a means of removing superfluous sugar from the blood and thus of achieving decarbonization. But since the storage capacity of the muscles for glycogen is doubtless limited, the continued decarbonization of the blood by this means would be dependent on the continued combustion by muscle of the glycogen already deposited.

§ 123. What is the chief physiological advantage of the capacity possessed by the muscles for dehydrating and storing glycogen, the glycogenic function of the muscles? The intra-muscular deposition of glycogen occurs during the intervals of muscular activity: this is shown by the accumulation of glycogen which occurs in a muscle the motor nerve of which has been cut (Halliburton).¹ And it has been argued that such deposition is a storage provision to insure an adequate fuel supply against future contractions. This, however, can hardly be its sole essential object, since the blood always contains a certain percentage of sugar, even during starvation (Schäfer),² and a muscle in work can utilize as fuel sugar fresh from the circulating blood: this was shown by Morat and Dufour, who supplied a muscle with artificial blood and observed a much greater subtraction of sugar therefrom during contraction than during rest (quoted by Sajous).³ Considering everything, then, it seems to me that the glycogenic function of the muscles must be regarded, at any rate in part, as a subsidiary means of decarbonizing the blood, adapted to act in the intervals of the far more rapid katabolic decarbonization which occurs during muscular activity. On this view, the glycogenic function of the muscles would have two uses in common with the glycogenic function of the liver. Both functions would provide a store of fuel against future necessities, but both would be in addition charged with the duty of preventing undue accumulation of carbonaceous material in the blood. The muscular function, however, would operate in the latter respect merely upon the sugar contents of the blood, not, like the liver, upon the general carbonaceous contents. Further, the muscular function would operate by rendering expenditure more or less continuous, the liver function by regulating income.

It is, I suppose, technically incorrect to include under the

¹ *Text-book of Physiology*, E. A. Schäfer, 1898, vol. i. p. 105.

² *Ib.* p. 158.

³ *The Internal Secretions and the Progress of Medicine*, Chas. E. de M. Sajous, 1903, p. 352.

head of anabolism a process of simple dehydration such as the supposed glycogenic function of the muscles. Still the present is the only convenient connexion; and the process has much in common with the anabolic decarbonizing processes. By it, carbonaceous material in a fluid state is withdrawn from the circulation and transformed into a solid, at any rate a non-diffusible, state, capable of extra-vascular storage; and this, in all probability, is effected through a capacity of the nitrogenous tissues, whether directly or, as more recently surmised, indirectly through the action of an enzyme. Thus the formation and deposition of muscle glycogen depends, like all the anabolic decarbonizing processes, upon the two fundamental factors, function and supply.

FAT-FORMATION

§ 124. In fat-formation, as in all anabolism, two fundamental factors are essential, namely, *function* and *supply*. The functional factor, we shall see, consists of an active or vital constructive or anabolic capacity on the part of the nitrogenous tissues: the supply factor, of a due amount of carbonaceous material in the general blood-stream available for fat-formation.

§ 125. THE FUNCTIONAL FACTOR, AN ACTIVE OR VITAL ANABOLIC CAPACITY OF THE NITROGENOUS TISSUES.—Our knowledge of the deposition of fat in the cells of the connective tissue is far from complete. As to its essential nature two views are expressed: (1) 'that¹ the fat is brought to the fat-cell as fat and in some way taken up by the cell and deposited in the cell-substance with little or no change' (Foster); and (2) 'that² the fat is manufactured' by the cell-substance of the fat-cell 'in some such way as mucin or pepsine is manufactured by a mucous or a gastric cell' (Foster). The balance of experimental evidence is conclusive that fat may be manufactured as held under the second view; for it has been shown 'that³ only a small fraction of the fat stored up in the body can possibly come direct from the fat of the food' (Foster); and that, of the remainder, some at least, if not most, is derived from the carbohydrates. Clearly the fat, which is

¹ *Text-book of Physiology*, M. Foster, 1895, p. 808.

² *Ib.*

³ *Ib.* p. 809.

derived from the carbohydrates, is the result of a process of construction.

§ 126. Is this true also of the body-fat which is derived from the fat of the food? Not apparently without reserve. Schäfer says:¹—‘Dogs which have been starved for a considerable time, so that practically the whole of the body-fat has become removed, will, if fed upon an excess of mutton-fat and sufficient proteid, lay down a body-fat of a melting-point and composition very similar to mutton-fat. This shows that at least a portion of the fat introduced with the food has been, for a time at any rate, laid down directly as body-fat.’ But this seems more the exception than the rule. ‘A man² living upon mutton will have his body-fat, not of the consistency of mutton suet, but of the ordinary consistency of the fat of the human body, having a melting-point far lower and containing a much larger amount of olein in its composition’ (Schäfer).

It is probable therefore that most of the body-fat, even that which is derived from the fat contained in the food, is the result of a process of construction. If this is true, we must ascribe to the nitrogenous cells of the connective tissue (whether to these cells generally or to a special set thereof, is, for our present purpose, immaterial) this power of constructive metabolism or anabolism. In other words, fat-formation, as already stated, depends, in the main at least, upon a vital or active capacity of the nitrogenous tissues, which tissues cannot be regarded as mere passive receptacles for superfluous carbon.

The constituent factors of the anabolic fat-formation capacity of the tissues remain in great part obscure. It is undoubted that the capacity varies greatly with the individual. Foster says³ that ‘the power to store fat in adipose tissue is much more dependent on certain inborn qualities of the organism which we cannot at present define than on the kind of food: of two bodies living on the same diet and under the same circumstances, one will become fat while the other will remain lean.’ Some of these variations are almost certainly inherent or congenital; and it is clear that herein is ample

¹ *Text-book of Physiology*, 1898, vol. i. p. 931.

² *Ib.* p. 930.

³ *Text-book of Physiology*, M. Foster, 1895, p. 884.

room for the play of hereditary influences. At any rate, it is notorious that obesity and leanness tend to run in families.

§ 127. But the nutrition of the anabolic tissues must be an important factor. Hence for due fat-formation capacity, as for all functions, a due supply of proteid in the food is necessary. Conformably, it may be observed that the almost purely carbohydrate eater tends to be lean, even emaciated; and that, in many such cases, a marked increase in the deposition of fat may be achieved by adding to the proteid of the diet. Such cases occur with great frequency amongst women of European birth residing in the tropics. It must not be inferred that the leanness of the almost purely carbohydrate eater depends solely upon deficient anabolic capacity from deficient nutrition of the anabolic tissues. As will be argued presently, it depends largely upon deficient carbonization by the organs of digestion.

Many conditions seem to exert a definite influence upon the fat-formation capacity. Climate is one. Some persons are quite unable to accumulate fat in the heat of the tropics, but quickly succeed in doing so on a change to a cool climate. I do not think that the change operates solely through increasing appetite and intake: there seems also a direct stimulus to nutrition in external cold. The same is true to a less extent of physical exercise. Some persons increase in weight under an increase of exercise: most of the increase is doubtless due to increased appetite and intake, but not all, I am inclined to think.

§ 128. THE SUPPLY FACTOR, A DUE AMOUNT OF CARBONACEOUS MATERIAL IN THE GENERAL BLOOD-STREAM AVAILABLE FOR FAT-FORMATION.—The amount of carbonaceous material in the general blood-stream available for fat-formation will depend upon many complex factors. It will depend (1) directly upon the amount of carbonaceous material which enters the general blood-stream; and (2) inversely upon the amount of carbonaceous material which leaves the general blood-stream for purposes other than fat-formation.

1. The amount of carbonaceous material which enters the general blood-stream will depend directly (*a*) upon the intake of carbonaceous material with the food: (*b*) upon the activity of digestion and absorption; and inversely (*c*) upon the glyco-genic function of the liver.

2. The amount of carbonaceous material which leaves the

general blood-stream for purposes other than fat-formation will depend upon (a) the rate of combustion : (b) the amount of the menstrual flow ; and (c) the presence or the activity of anabolic processes, other than fat-formation, such as utero-gestation, lactation, and the formation of secretions other than milk.

§ 129. 1a. The dependence of fat-formation upon the intake of carbonaceous material is seen in the general rule that those who eat largely of starches, sugars, and fats tend to be plump, if not corpulent, while those who live mainly upon proteid tend to be lean. Though there are numerous exceptions, many lean persons may be fattened by simply increasing the intake of the purely carbonaceous food-stuffs ; and the great majority of the corpulent may be readily reduced in weight by cutting down the supply of these articles of diet and throwing the onus of nutrition in the main upon proteids.

§ 130. 1b. It has been already argued that the carbonization of the blood depends, *inter alia*, upon the efficiency of digestion and absorption ; and that both these functions depend, *inter alia*, upon the supply of proteid in the food (§§ 55 to 60). Hence, as a general rule, those whose digestive powers are strong tend to accumulate fat, while dyspeptics of all kinds tend to be lean. Deficiency of digestion and absorption is a second reason why the almost purely carbohydrate eater tends to be lean : he suffers from a deficiency of supply due to a deficiency of function.

§ 131. 1c. It has been argued that digestion and absorption depend inversely upon distension of the liver by glycogen, and this directly upon the capacity of the liver to dehydrate and store sugar as glycogen within the hepatic cells—upon the glycogenic function in short. Now Pavy, as we have seen (§ 63), has shown that this function may exist in all grades of efficiency ; and we have already noted the improvement in digestive capacity which so commonly follows the breakdown of the function on the supervention of diabetes (§ 81). Hence persons who are affected with a high grade of this capacity tend to be lean : they suffer from a deficiency of supply due to an exaggeration of a physiological function (a good example of a patient so constituted is detailed in full in §§ 554 to 566). On the other hand, it is highly probable, as will be argued presently (§§ 145, 146), that a dominant factor in some cases of obesity is a deficiency of the glycogenic function of the liver : persons so affected would suffer from an excess of supply due

to a deficiency of a physiological function. In both cases, the function at fault would be the function which normally regulates the carbonization of the blood (§ 67).

§ 132. The constituent factors of the glycogenic function of the liver are doubtless numerous and complex, and they remain for the most part obscure. But later (§§ 442 to 453) I shall argue that the function is to a large extent governed by variations in the supply of arterial blood through the hepatic artery. Such variations of blood supply occur, of course, through the influence of the vaso-motor system. And I shall argue further that the vaso-motor influence is determined by pyraemic conditions: that the responsiveness of the vaso-motor system to pyraemic conditions varies widely with the individual: that 'irritable' vaso-motor systems respond to low grades of pyraemia: that 'inirritable' vaso-motor systems respond only to high grades of pyraemia; and finally that, in many cases, such irritability and inirritability depend respectively upon the existence or absence of certain sources of reflex irritation of widely differing nature and location (§§ 510 to 568). It will follow that the existence of such sources of reflex irritation (such as eyestrain from ametropia, to take one widely prevalent example) not infrequently determine glycogenic distension of the liver, diminution of the inflow of carbonaceous material to the general blood-stream, and consequent deficient fat-formation through deficiency of supply. That this is the true pathological sequence is, I think, shown by the great increase of weight which in very numerous cases rapidly succeeds the removal of the source of reflex irritation.

At the present stage of this work, the above anticipation will, I do not doubt, appear in the light of a wild excursion into the regions of the unknown, if not into those which are, in the present state of knowledge, unknowable. But I would ask the reader to withhold any pre-judgment—to leave the question open until he has become acquainted with some of the numerous accredited facts of medicine which this series of hypotheses is capable of explaining.

§ 133. 2a. The margin of carbonaceous material in the general blood-stream available for fat-formation will obviously depend inversely upon the amount which is being withdrawn therefrom for energy production—upon the rate of combustion, that is to say. The rate of combustion, as already argued

(§§ 101 to 114), varies widely with a variety of conditions. Probably some individuals are endowed with an inherently high combustion rate; and such, other things being equal, would account for some cases of habitual leanness. Others lead physically active lives and these rarely become obese. In many cases, we may check increasing weight simply by enforcing physical exercise. And there are some in which a change to a colder climate has a similar influence. In all these cases, fat-formation is inhibited through restriction of supply; and the restriction of supply is achieved through exaggerated combustion. In more general terms, anabolism suffers through exaggerated katabolism.

§ 134. *2b.* In the succeeding chapter, it will be argued that the menstrual flow involves, *inter alia*, a loss of carbonaceous material. Such periodic loss will tend to reduce the margin of carbonaceous material available for fat-formation; and we shall see that there is a rather well-marked inverse relation between the amount of stored fat and the amount of the menstrual loss. Thus menorrhagia tends to inhibit fat-formation through restriction of supply; and the restriction of supply is achieved by an exaggeration of the direct loss of carbonaceous material involved in an exaggeration of the menstrual flow.

On the other hand, it will be pointed out that many obese women menstruate but slightly; and that a sudden increase of weight often concurs with a stoppage, or marked diminution, of the menstrual loss (§ 183).

§ 135. *2c.* The inverse relation between fat-formation and other anabolic processes is often very conspicuous in pregnancy, especially advanced pregnancy. Many pregnant women tend to become thin, and the unusual sharpness of their features has often been observed. The same inverse relation is often to be seen during lactation. Many women, though retaining their general health, become markedly thin when nursing and recover weight rapidly after the child has been weaned. In both pregnancy and lactation, any diminution of fat-formation which may occur is of course due to restriction of supply; and the restriction of supply is due to the intercurrent super-added anabolic functions.

In the domain of pathology, the same inverse relations may be observed between fat-formation and the malignant

anabolism of cancer and sarcoma; and the same explanation will be sufficient in many other cases.

§ 136. A PROCESS OF DECARBONIZATION.—Since the raw carbonaceous material (so to speak) for anabolism has to be withdrawn by the manufacturing tissues from the blood, fat-formation must be a decarbonizing process: we may regard it as the chief member of the class of anabolic physiological decarbonization. And the adoption of this view does not in the least degree prejudice the many well-recognized uses of fat when stored within the tissues of the organism.

Generally speaking, the clinical evidence of the decarbonizing influence of fat-formation is to be found in the inverse relationships which are to be observed between fat-formation and other processes tending to decarbonize the blood. Many of these are physiological and have been, to some extent, already considered. But many are pathological, depend upon hyperpyraemia and are adapted to disperse this condition: these will be considered later (Chapters IX, XIV, XVI and XVII).

Meanwhile, it may be pointed out that fat persons, *especially those who are adding to their weight*, are proverbially well, physically and mentally: as a class, they are hearty, good-tempered and optimistic; and this is naturally, and no doubt correctly, ascribed to the physiological excellence of their blood. Weir Mitchell says:¹—‘The gain of fat up to a certain point seems to go hand in hand with a rise in all essentials in health, and notably with an improvement in the colour and amount of the red corpuscles.’

The corroborative evidence as to the salutary influence of rapid fat-formation, which is to be found in medical literature, is extensive. But, in order to appreciate this evidence, it is often necessary to invert the commonly accepted order of cause and effect. For, usually, when the disappearance of an accustomed disorder coincides roughly with an increase in the deposition of fat, we are apt to assume that the former event antecedes, and indeed permits of, the change in the nutritional state. This is doubtless true in many cases—the familiar expression ‘laugh and grow fat’ will not always call for inversion; but, in others, it is reasonable to think that the increased fat-formation decarbonizes the blood and thus dis-

¹ *Fat and Blood*, 1900, pp. 16, 17.

perses disorders depending on hyperpyraemia; and herein, it seems to me, consists a most important, though certainly not the only, bond between a high state of nutrition and good health.

§ 137. CARBON EQUILIBRIUM AT VARIOUS LEVELS.—It is obvious that, in ordinary circumstances, fat-accumulation has a strong tendency towards self-limitation. Assuming a constant food supply, sufficient under constant conditions to cause a gradual increase in weight, sooner or later a time arrives when further augmentation ceases. Clearly, other things being equal, weighty persons require for carbon equilibrium a larger supply of carbonaceous food than those who are light. The operation of this law is conspicuous in an obese person who is undergoing weight reduction by means of a mainly proteid diet. The food supply and other things remaining constant, the loss of weight is at its maximum during the first week: it has amounted in very corpulent persons to a stone (Case LVIII). Thereafter, the weekly reductions progressively decrease, and finally cease. Obviously, the loss of weight in any given week is a measure of the carbonaceous deficiency in the diet during that week; and the deficiency is directly as the weight.

§ 138. This may be explained, in part at least, on the following grounds:—1. Fat, being a living tissue, is subject, in common with all living tissues, to ordinary 'wear and tear,' and this has to be made good by supply. Other things being equal, the amount so lost will be proportionate to the amount existing in the body, but it will be in any case comparatively insignificant: 2. The call for heat-production, and therefore for fuel, is proportionate to bulk. This does not conflict with the known fact that, in bulky persons, the heat loss is relatively less.¹ Reubner has shown that 'the ¹ smaller produce relatively more heat in proportion to their weight than the larger animals, and that the heat-production is proportional to the surface of the body.' Consequently, it still remains true that the total heat-production, and therefore the total demand for fuel, increases with increasing weight; though such increase is proportionate to the increase in surface which necessarily accompanies the increase in weight, and not to the increase in weight itself: 3. Weighty persons, in order to attain the same dynamic result, must utilize more energy, and therefore more

¹ *Text-book of Physiology*, Schäfer, 1898, vol. i. p. 853.

carbonaceous matter, than those who are light: it is self-evident that a man of twenty stone expends twice the energy expended by a man of ten stone, in walking the same distance. Manifestly, a person who has increased in weight will be, other conditions remaining constant, in a position to eliminate physiologically by combustion more carbonaceous material than before.

To this it may reasonably be objected, that increasing obesity leads to a diminution in the amount of physical exercise; and there can be no question that this is true of some. But I do not believe that it is true of the majority. With most persons, exercise in middle life is governed by business necessities, rather than by considerations of hygienic expediency; and practically, the average individual takes the same amount of exercise every week. His habits tend to become fixed: he walks the same distance to the station in the morning and in the evening: spends the same time in his office; and passes his evenings and holidays according to the same routine.

§ 139. The formation and deposition of fat within the tissues may, as already argued, be regarded as a conservative device, whereby the healthy organism is enabled to withdraw from the blood-stream and store conveniently a surplus of carbonaceous material, thus averting hyperpyraemia. But, under ordinary conditions of life, fat-formation is more than this. The increasing store raises *pari passu* the demand for fuel, so that the surplus becomes a diminishing quantity and eventually disappears: carbon equilibrium is then attained upon a higher level. In the absence of some such automatic regulation, persons digesting and assimilating even a slight excess of carbonaceous food would tend to increase in weight indefinitely; and those whose carbonaceous intake is slightly deficient for equilibrium would tend to waste indefinitely.

It follows, other things being equal, that those who are lean do not require, cannot easily dispose of, and therefore should avoid, much carbonaceous food, because their small bulk demands comparatively little energy whether as force or heat. If such persons eat largely of carbonaceous food-stuffs and succeed in digesting and absorbing them, hyperpyraemia is more probable than in those who are stout. But many persons, we shall see, are lean through deficiency of the anabolic fat-

formation capacity—through a deficiency of this function and not through any deficiency in the supply of carbonaceous material in the blood available for fat-formation. Such persons will have a double reason for avoiding any carbonaceous excess.

§ 140. These theoretical deductions seem fully confirmed on appeal to clinical observation. We are all familiar with the thin wiry individual, who is never happy unless he is taking exercise and who suffers in health from even a temporary sedentariness. Usually, in such cases, we ascribe the leanness to the activity, and the activity to an innate restlessness of disposition, as in the remark, credited to Liebig, that a restless pig will never fatten. This may be true of some; but it is open for us to invert the accepted order of cause and effect, and to regard the restless activity as a *subconscious but conservative habit*, compensatory of deficient fat-formation capacity and adapted to avert hyperpyraemia. Similarly, from the usual standpoint, the corpulent individual, who has discovered, quite unconsciously perhaps, that he retains his health and comfort without much exercise, is regarded as fat because he is physically lazy. Here again the prevalent view may be true of many, but it is open for us to consider the converse.

What is true of those who are naturally lean applies, but with diminished force, to those who have been reduced by diet to thin proportions. Such patients, though they retain the anabolic fat-forming capacity, have lost to some extent their capacity for combustion. On returning suddenly to their original allowance of carbonaceous food, they may reaccumulate fat with great rapidity, but this does not always occur. Sometimes they commence to suffer from headaches and from other affections, which, it will be argued, depend upon hyperpyraemia.

§ 141. LIMITATIONS TO THE DECARBONIZING INFLUENCE OF FAT-FORMATION.—As long as we continue to regard the existence in the blood of a margin of carbonaceous material available for fat-formation—the supply factor, that is to say—as the chief, if not the sole, factor essential to fat-formation, so long probably shall we remain blind to the possibility of fat-formation being inadequate to the demand for decarbonization. And it goes without saying that the invariable adequacy of fat-formation would entirely preclude the possibility of hyperpyraemia. But the view that fat-formation depends

upon function—upon the anabolic fat-forming capacity of the nitrogenous tissues—as well as upon supply, at once suggests the idea of a possible inadequacy. We realize that there is no reason for believing that the capacity to construct fat is unlimited, any more than is any other physiological capacity.

As just pointed out, however, fat-formation, by raising the demand for energy-production and so the rate of combustion, leads indirectly as well as directly to decarbonization. But the rise of combustion depends largely upon continuance of habits as regards physical exercise. And it happens not infrequently that increasing corpulence leads to diminished physical exercise. In this event, more and more strain will be thrown upon the anabolic fat-formation capacity, with the result that, ultimately, physiological decarbonization may become inadequate and hyperpyraemia arise. Hence, as we shall see, all the clinical manifestations of hyperpyraemia are prone to arise in the obese. But it is obvious that these must then be regarded as having arisen to a larger extent in spite, than in consequence, of the increased deposit of fat. And it is certain, as I shall have frequent occasion to point out, that all hyperpyraemic manifestations are far more easily controlled or dispersed in the fat, than in the lean. The mildness and comparative curability of glycosuria in the corpulent has long attracted attention; but ample evidence can be adduced to show that the same is true of the majority of hyperpyraemic affections. Many of my obese patients suffered from typical migraine, asthma, chronic bronchitis, etc.; and usually, the recurrent or chronic affection ceased very rapidly after the commencement of treatment, dietetic and hygienic, directed against the hyperpyraemia: in not a few, this result was attained before any great reduction of weight had been brought about. Thus *à priori* reasoning and experience are here in complete accord.

In addition to causing a diminution of much-needed physical exercise, excessive obesity may injuriously affect the organism in many ways both more directly and more complexly. The mere mechanical crowding of important organs—the heart and lungs especially—may seriously obstruct their work; and it may be, as has been held, that fatty degeneration, consecutive to fatty infiltration, plays a part in the general failure. Though, as already argued, it is one of Nature's most

physiological means of decarbonization, yet we must admit that fat-formation, if strained, may terminate, like all strained physiological functions, in action which is overtly pathological. Physiological fat-formation passes by imperceptible gradations into pathological obesity, and so may become the starting-point of a series of disorders and degenerative processes which need not here be specifically considered.

COMBUSTION AND FAT-FORMATION CORRELATED

§ 142. It is clear that both increased combustion and increased fat-formation may be a response to a surplus of carbonaceous material in the circulation: the organism utilizes both its katabolic and its anabolic capacities for decarbonization; and these, in a state of health, we may suppose bear a certain relation to each other and are together sufficient. But there is clinical and experimental evidence to show that individual organisms vary considerably in the use they make of these two capacities respectively.

Georges Hayem says: ¹—‘Certain individuals, generally those somewhat obese, have always a cool, even a cold, skin, while in lean persons the skin is usually warm.’ This observation is explicable only on the hypothesis that the obese depend for decarbonization more upon anabolism, the lean more upon katabolism or combustion, which implies a higher rate of heat dissipation. And it explains what was to me one of the great surprises of practice in the tropics, namely, that so many persons, with a distinct tendency to corpulence, continue to endure for long periods the intense heat with, as a rule, less discomfort and less deterioration of health than others who are lean. Such observations remain inexplicable, so long as we continue to believe that heat-formation is in general a constant quantity, and that the temperature of the body is regulated chiefly by variations in heat loss.

§ 143. Experimental evidence is strongly confirmatory of the adopted view. Herter ² quotes the experiments of Jacquet and Svenson, and points out that, ‘while the obese patient shows no diminution in the intensity of metabolic

¹ *Physical and Natural Therapeutics*, Hayem and Hare, 1895 p. 96.

² *Lectures on Chemical Pathology*, 1902, pp. 445, 446.

combustion in the fasting condition, he may react much less strongly to the influence of food than the ordinary individual. Thus Magnus Levy found an average augmentation of 27 per cent. in the O_2 consumption after breakfast, while Jacquet and Svenson found only an increase of 12 to 21 per cent. under similar conditions in one of their obese patients. Three hours after breakfast the increase in the consumption of O_2 still amounted to 16 per cent. in the normal subject, whereas in the corpulent person an increase was barely perceptible at this time. The influence of digestion exhibits itself normally in an increase of the CO_2 output, as well as in the greater consumption of O_2 . In an obese subject the CO_2 output, like the O_2 used, is much less augmented by a meal than is ordinarily the case. The observations on the respiratory exchange of gases thus indicate that the processes of combustion in the cells are much less actively stimulated by food in persons that are obese than in normal persons. The increased combustion that normally follows the absorption of food is also of shorter duration in the subject of obesity. In other words, the over-fat individual differs from the normal in that he saves considerable food material during the period of food absorption. It has been estimated that an obese person may save 11 grams of fat per day in consequence of this diminished oxidation; that is to say, 11 grams of fat which would have been burned by a normal person under similar dietetic conditions. Such a saving as this would account, at least in part, for the obesity of some persons.'

The theory of hyperpyraemia enables us to read this argument and to interpret the facts, upon which the argument is based, in the following way:—In the absence of food, combustion is regulated in the main by the necessity for force and heat-production. Hence there is no reason why the fat and the lean should differ materially from each other during fasting. After food, on the other hand, combustion will be regulated in part by the necessity for decarbonization. But obese persons, being highly endowed with the power of rapid fat-formation (anabolic decarbonization), will not find it necessary, in these circumstances, to increase combustion (katabolic decarbonization) to the same extent as lean persons, who are but poorly endowed with the power of fat-formation. In both cases, the maintenance of a certain pyraemic uniformity

will be the goal; and the organism will strive to attain this goal by means of its individual capacities.

§ 144. It has been argued that both combustion and fat-formation depend, *inter alia*, upon a due state of nutrition of the nitrogenous tissues; and that both functions may be increased in power in appropriate cases by an increase in the supply of proteid. Hence those who regard an increased deposit of fat as invariably due to retarded combustion would have to admit that an increase in the proteid supply is capable of both hastening and retarding combustion; which seems absurd. But there is no contradictoriness in the two results on the view herein set forth. The proteid increase would accelerate the combustion which had been retarded: it would raise also the anabolic capacity for fat-formation which had been in abeyance; and it would operate in both cases by increasing, through improved nutrition, a physiological capacity of the nitrogenous tissues.

Further, though I am incompetent to demonstrate it experimentally, I am convinced from clinical observation that both the anabolic and katabolic functions in question may be increased concurrently in the same individual. For example, many women, living on a mainly carbohydrate diet, not only become emaciated, but exhibit many of the phenomena of retarded combustion: their extremities are cold and pallid, and it is obvious that they dissipate but little heat. In such, the administration of a due supply of proteid is often rapidly succeeded, not only by a conspicuous increase in the deposit of fat, but by an almost equally conspicuous increase in the signs of combustion.

In many of these cases, the result is, of course, due simply to an increase in the digestion and absorption of food—in the carbonization of the blood, that is: such have been suffering merely from a modified degree of starvation. But, in others, there have long been present some of the manifestations of hyperpyraemia, such for example as recurrent sick-head-aches or the high tension pulse: in these, the carbonization of the blood has been excessive, at least relatively as regards decarbonization: consequently, the recovery of health and nutrition must be ascribed to increased katabolic and anabolic decarbonization (combustion and fat-formation).

OBESITY

§ 145. From a consideration of the physiological factors concerned in fat-formation, it is, of course, easy to deduce the numerous possible physiological factors concerned in obesity. The subjoined is a classified list :

- I. A well-developed anabolic fat-formation capacity (function).
 1. Inherent, congenital or hereditary.
 2. Acquired.

- II. An excessive margin of carbonaceous material in the general blood-stream (supply).
 1. Through excess of income, due to an excessive intake of carbonaceous food, combined with a powerful capacity for digestion and absorption and a low grade of the glycogenic function of the liver.
 2. Through deficient expenditure.
 - a. On combustion.
 - b. On direct loss, as in deficient menstruation.
 - c. On other forms of anabolism.

On the view of fat-formation here adopted, a well-developed, that is rapidly acting, anabolic fat-forming capacity (I.) is of course essential in all cases of obesity : its existence is demonstrated by the fact that in the obese the post-prandial increase of carbonic acid output is distinctly below the average ; and obesity consists largely in a preponderating tendency to decarbonize by anabolism. It is obviously impossible to determine to what extent this capacity is inherent, congenital or hereditary, or to what extent it may be acquired.

But the factor of supply (the existence of a margin of carbonaceous material in the general blood-stream) is doubtless in all cases equally essential. This margin may depend upon excess of income (II. 1). Though it is often stated that many fat persons have habitually small appetites, yet I am convinced from long observation that such is not the general rule. The majority have hearty appetites, especially for the more highly

carbonaceous food-stuffs, the sugars and starches; they are endowed, too, with conspicuously powerful digestions, and suffer little from any kind of discomfort after food. I have known huge mixed meals ingested in such cases without the slightest degree of sleepiness following. Now it is clear that all these special endowments could be explained by a low grade of the glycogenic function of the liver, resulting in deficient regulation of the nutritious income to the general blood-stream through glycogenic distension of the liver.

§ 146. Only on such a view can we explain the extremely frequent association between obesity and glycosuria—an association noticed for many years, but hitherto unexplained, so far as I know. In both these clinical conditions, there would be a low grade of the glycogenic function of the liver, and this would tend to increase the carbonaceous income to the general blood-stream. In obesity without glycosuria, the excess of carbonaceous income would be fully compensated by a high grade of the anabolic fat-forming capacity. In obesity with glycosuria, such compensation would be inadequate, at any rate as far as the sugar contents of the blood are concerned. While in glycosuria without obesity, such compensation would be almost wholly absent and by so much would the glycosuria be severe. These deductions are in full accord with clinical experience as to the relative severity of glycosuria in the fat and in the lean.

Usually, the association is that the obesity antecedes, perhaps by long periods, the onset of the glycosuria and tends to diminish thereafter: in such cases, probably, the deficiency in the glycogenic function is inherent or congenital; and we could account in this way for many cases of early obesity. But sometimes the obesity and the glycosuria commence simultaneously; and then there can be no question as to the dependence of both conditions upon deficient glycogenic function of the liver. In such cases, the functional incapacity is manifestly acquired; and it is highly probable that it may be acquired though many intercurrent factors. The following is a case which seems to illustrate fully this view:—

A gentleman, aged 36, well nourished, but by no means obese, had suffered throughout the greater part of his life from typical periodic migraine. He was known not to be glycosuric, since his proposal for life assurance for a considerable amount had recently been accepted

without loading. He contracted typhoid fever which turned out to be prolonged and somewhat severe. During the fever, his migraine attacks ceased—as they always do in these circumstances; nor did they recur during convalescence as they usually do. During early convalescence he rapidly put on weight, and very soon became obese. Concurrently, his urine was found to be loaded with sugar. Two years later, he remained both glycosuric and obese, but in apparently good general health. His migraine had not returned.

Migraine, I shall argue later, is a recurrent process adapted to disperse hyperpyraemia and operating through recurrent glycogenic distension of the liver. Clearly, on this view, the lost power of hepatic glycogenesis, due in all probability to some pyrexial tissue damage, was responsible alike for the cessation of the migraine, for the glycosuria, and, to a large extent at any rate, for the obesity.

I shall further argue that, in some cases, deficient hepatic glycogenesis may depend upon a certain loss of function of the vaso-motor system (§ 689).

§ 147. But the margin of carbonaceous material in the general blood-stream available for fat-formation may depend essentially upon deficient expenditure (II. 2.). Deficient expenditure may consist of a deficiency in some form of direct loss, such as amenorrhoea or the cessation of some pathological form of haemorrhage (for example, that which occurs from piles) to which the organism has become accustomed (II. 2. *b.*); and both these occurrences may, as we shall see later, be succeeded by obesity. Further, the deficiency of expenditure may consist perhaps in the absence of some special anabolic function. It might be argued, from a biological standpoint, that utero-gestation is a physiological function, normal to the reproductive period of life in women, and that celibacy is a result of civilization and therefore in a sense abnormal; and it has been remarked, I think with truth, that unmarried women tend earlier in life to obesity than women with families. Lactation would be another normal anabolic process; and women who do not nurse their children likewise run some added risk of becoming obese.

§ 148. But the most important form of expenditure, responsible in this connexion, is combustion (II. 2. *a.*). We often speak of obesity as resulting from retarded metabolism—katabolism would be a better word—meaning thereby that

carbonaceous material which, under quite normal conditions, would be burnt off and eliminated, is, through a relative failure of combustion, stored up in the tissues as fat. This view must be regarded as incomplete, though not of course erroneous. For it ignores the constructive capacity of the nitrogenous tissues, and seems to regard the whole process of fat-formation as a mere extra-vascular oozing of superfluous carbonaceous material into passive receptacles.

It may be admitted that, other things remaining constant, fat-formation will depend upon the width of the carbonaceous margin in the blood. An increase in the rate of combustion will decrease the carbonaceous margin and may render it a minus quantity. So will arise a decrease in the rate of fat-formation or even an absorption of fat already deposited. Such is the tendency of increased muscular exercise; and such undoubtedly is one of the actions of thyroid extract which forms so useful an addition to the dietetic treatment of obesity. On the other hand, any retardation in the rate of combustion, whether dependent on diminished physical exercise or other causes, will increase the width of the carbonaceous margin, and so may determine obesity. Hence obesity often follows reduced muscular activity and not infrequently arises post-pyrexially. But in all such cases, we must believe that previously the fat construction capacity of the tissues was not strained to its utmost limits and that sufficient reserve power remains for the additional work; for it is inconceivable that a mere failure of combustion could add to an active capacity of the tissues.

LEANNESS

§ 149. From a consideration of the physiological factors concerned in fat-formation, it is of course easy to deduce the numerous possible physiological factors concerned in the clinical condition of leanness. The subjoined is a classified list:—

- I. Deficiency of the anabolic fat-formation capacity (function).
 1. Inherent, congenital or hereditary.
 2. Acquired through malnutrition, as from deficient proteid.

II. Deficient margin of carbonaceous material in the general blood-stream (supply).

1. Through deficient income.
 - a. From deficient intake of carbonaceous food.
 - b. From deficient digestion and absorption.
 - c. From exaggerated hepatic glycogenesis.
2. Through excessive or additional expenditure.
 - a. On combustion or katabolism.
 - b. On direct loss, as in the haemorrhage of menstruation.
 - c. On other forms of anabolism.

The anabolic deficiency (I.) is well illustrated in those lean persons who habitually decarbonize to a more than average degree by combustion (as shown by marked post-prandial increase of carbonic acid output), whose heat-loss consequently is raised proportionately, and whose skin, as pointed out by Hayem, tends to be habitually warm.

II. 1. *a.* is illustrated in those human races who live mainly on flesh food, and in the carnivora: II. 1. *b.*, in many chronic dyspeptics; and II. 1. *c.* will be more fully dealt with in discussing pathological prepotency (Chapter XIII). Here it may be remarked that if, as already argued, the carbonaceous margin in the general blood-stream, which is responsible for some cases of obesity, depends essentially upon a low grade of the glyco-genic function of the liver, then it is reasonable to ascribe some cases of habitual leanness to a relatively high grade of the same function. And I shall argue later that, in some cases, exaggerated hepatic glycogenesis depends upon a certain 'irritability' of the vaso-motor system, which in turn may depend upon the existence of certain sources of peripheral irritation (§§ 512, 513).

II. 2. *a.* is illustrated in the leanness of the working man and of those who lead a life of strenuous physical exertion, also in pyrexia: II. 2. *b.* in some cases of menorrhagia and other less physiological forms of recurrent or chronic haemorrhage; while II. 2. *c.* may be seen in some cases of utero-gestation and prolonged lactation, and in practically all malignant, and some benign, tumours.

§ 150. But, in addition to the already mentioned factors which diminish or abolish the carbonaceous margin in the

general blood-stream and so inhibit fat-formation, there is a long series of pathological processes, such as some of the paroxysmal neuroses and allied vaso-motor affections, which have highly important relations with the physiological process of fat-formation. These pathological processes, I shall argue, depend upon hyperpyraemia and are adapted to disperse this humoral condition: they are to be regarded as ultra-physiological reinforcements of inadequate physiological action (§ 349). And since fat-formation is one of the most important physiological actions which remove carbonaceous material from the blood, it follows that deficiency of fat-formation is often an important cause of these processes. But it must be admitted that by no means infrequently this sequence of cause and effect is inverted: the pathological processes become important factors in deficient fat-formation. This happens whenever these pathological processes become 'prepotent' over the physiological processes which in health regulate the carbonaceous contents of the blood; and such 'pathological prepotency,' we shall see, may arise under a great variety of circumstances (§§ 514 to 568). It will be recognized, of course, that, while the deficiency of fat-formation which leads to the pathological processes depends on a deficiency of *anabolic function*, the deficiency of fat-formation which results from the pathological processes depends on a deficiency of *supply of material*.

§ 151. Practically, leanness depends doubtless in all cases upon some combination of the pathological factors enumerated. The leanness or tendency to emaciation, which affects women who live mainly on carbohydrates, especially those who reside in the tropics, has already been ascribed to deficient carbonization of the blood, to deficient anabolic decarbonization, or to both. In any of these cases it is due primarily to a deficiency of function dependent on malnutrition of the nitrogenous tissues; and in the majority of cases it may be removed and replaced by due fat-deposit, by simply insisting upon increased intake of meat or other digestible and assimilable proteid.

The leanness so often associated with hyperpyraemic affections may, as already argued, be due in great part to deficiency of supply—absence of the carbonaceous margin available for fat-formation—caused by the hyperpyraemic affections which have become prepotent over fat-formation. In this case, the

leanness will be most effectually treated by the cure of the hyperpyraemic affections; and this will resolve itself into the discovery and removal of the factors responsible for the pathological prepotency (§ 580).

But, in all cases, in view of the danger of hyperpyraemia, leanness should be treated by so arranging the diet that the carbonaceous income to the general blood-stream does not leave a carbonaceous margin therein which is beyond the anabolic fat-forming capacity of the tissues. At the same time, we may seek to raise this capacity in many cases by adding to the proteid intake. When these indications are fulfilled, we shall expect the storage of fat to augment gradually. As the weight of the body increases, so will increase the capacity for combustion, and by so much will diminish the danger of hyperpyraemia. This is not the customary mode of procedure. We commonly prescribe from the commencement a considerable excess of carbonaceous material, a practice which almost inevitably follows from the prevalent conviction that such food-stuffs, provided only that they undergo digestion and absorption, necessarily undergo rapid combustion or storage—from the view which tends to ignore the importance of the anabolic fat-forming capacity of the tissues.

§ 152. Harry Campbell has seen cases in which 'the weight is actually increased by cutting down a diet that has been excessive';¹ so also have I in some numbers. And though in many the result was attained through improved digestion and absorption, and consequent increased width of the carbonaceous margin in the blood, yet in others such explanation would not hold. Many of these latter had always possessed conspicuously strong digestive powers, and the improved nutrition can only have been due to improved anabolic function, consequent on appropriate graduation of the supply.

I had often feared to reduce the carbonaceous intake in the case of an emaciated patient who had been crammed with starches and sugars without benefit, arguing vaguely that one who remained so thin upon an excess of fat-forming food might fall dangerously away on a less amount. But in most cases the argument is fallacious and the fear groundless. An emaciated patient placed upon a mainly proteid diet, which necessarily implies a considerable reduction in the carbonaceous

¹ 'Observations on Diet,' H. Campbell, *Lancet*, May 24, 1902, p. 1487.

intake, does not necessarily lose weight: indeed, he not infrequently gains materially. Although the dietetic practice here suggested applies to many cases in which there is organic disease, I am not now referring to such as are other than functional.

SUMMARY

§ 153. In this chapter I have argued that all anabolism—including even the formation of muscle glycogen, which cannot in a strict technical sense be considered anabolic—may be regarded, *inter alia*, as a means or process of decarbonization: that all anabolism depends fundamentally upon two factors, function and supply: that in fat-formation, the most important member of the class, the functional factor, consists of an active or vital anabolic capacity of the nitrogenous tissues, which varies widely in power with the individual, but which depends, *inter alia*, as do all functions, upon the supply of proteid: that the supply factor consists of a margin of carbonaceous material in the general blood-stream available for fat-formation: that such carbonaceous margin depends upon the income of carbonaceous material to the general blood-stream and upon expenditure of carbonaceous material in other directions by the general blood-stream: that the income depends *directly*, not only upon the intake, but upon the complex function of carbonization and therefore upon the supply of proteid, and *inversely* upon the glycogenic function of the liver, which again depends upon many factors to be referred to in more detail hereafter: that the expenditure in other directions by the general blood-stream depends upon many conditions, such as the occurrence of conception, lactation, external temperature, physical exercise, and the intervention of disease: that the accumulation of fat tends to raise the expenditure of carbonaceous material, thus progressively narrowing the margin available for fat-formation and precluding further accumulation; and that, in some circumstances, fat-formation may prove inadequate to disperse the margin of carbonaceous material in the general blood-stream, left by other forms of expenditure, thus permitting hyperpyraemia to arise.

CHAPTER VI

§§ 154–185

Carbon expenditure or decarbonization of the blood (*cont.*): haemorrhage a means of decarbonization through direct loss—The meaning of menstruation: possible objection to the adopted theory—Symptoms of menstruation—Amenorrhoea: amenorrhoea due to absence of carbonaceous surplus (supply): amenorrhoea due to imperfect discharging capacity (function): amenorrhoea of anaemia—Puberty and climacteric—Katabolic, anabolic and haemorrhagic decarbonization correlated—Summary.

§ 154. Excluding accidents, haemorrhage may be physiological (menstruation), pathological (epistaxis, haemoptysis, haematemesi, haemorrhoidal, etc.), or employed therapeutically (venesection). Loss of blood, however induced, is succeeded by increased absorption of fluid from the tissues, indicated clinically by thirst and followed by fresh fluid intake. The effect upon the mass of blood remaining is therefore dilution: the percentage of total solids falls; and therein is involved a fall in the percentage of carbonaceous material. Hence haemorrhage is a means of decarbonization; and the carbonaceous material is removed from the blood directly, without, that is to say, undergoing katabolism or anabolism.

The clinical evidence of the decarbonizing influence of haemorrhage consists in the fact that many affections (such as migraine, asthma, some convulsions, together with morbid conditions, such as high pulse-tension), which we shall regard as common manifestations of hyperpyraemia, may be dispersed, temporarily or for longer or shorter periods, by loss of blood. In this connexion we may recall the once prevalent practice of venesection.

THE MEANING OF MENSTRUATION

§ 155. Excluding the lochial discharge, no form of haemorrhage other than menstruation can be considered physiological;

and even of menstruation it has been said:—‘There¹ is no physiological condition so nearly resembling disease, as that which produces every month in an adult woman a change so profound that it has been looked upon as the expression of a morbid condition.’

According to Stewart,² women lose throughout the reproductive period of life, in the intervals of utero-gestation and lactation, at each menstrual period, from 100 to 200 grams of blood—‘that is to say $\frac{1}{40}$ to $\frac{1}{20}$ of the whole of the blood in the body’; and since normally no failure of health ensues, it is certain that the loss is recuperated in some way. Now the periodic loss comprises both carbonaceous and nitrogenous material, and it is conceivable that the compensation for the loss consists of some economy in the other sources of expenditure of these materials.

§ 156. The economy in carbonaceous expenditure seems not to present much difficulty of discovery. It is known that in males the evolution of carbonic acid undergoes a progressive increase from the age of 8 to the middle period of life³ (Tilt). On the other hand, ‘the⁴ absolute increase in the evolution of CO₂ with age in the female is arrested at the time of puberty and remains stationary during the menstrual period, provided the menstrual flow occur with regularity. . . . After the cessation of the menses, the quantity gradually increases’ up to the age of 60 (Austin Flint). Not only is the progressive increase in the evolution of CO₂ inhibited during menstrual life, but Rabuteau⁵ has shown, by a series of observations, that each individual menstrual period is associated with a marked fall in the excretion of this gas. Conformably, ‘when⁶ the menses are suppressed there is an increase in the exhalation of CO₂, which continues until the flow becomes re-established’ (Austin Flint).

Thus it would appear that, with women during menstrual life, katabolic is replaced in part by haemorrhagic decarbonization. But, since menstruation is not continuous but regularly intermittent, it is probable that towards the end of the intermenstrual period, there is in the blood a tendency to

¹ Guerin, quoted by Dr. Helen McMurchy, *Lancet*, October 5, 1901.

² *Manual of Physiology*, 1899, p. 824. ³ *Change of Life*, Tilt, 1882, p. 56.

⁴ Austin Flint, *Human Physiology*, pp. 147, 148.

⁵ Dr. Helen McMurchy, *Lancet*, October 5, 1891.

⁶ Austin Flint, *Human Physiology*, p. 148.

the accumulation of carbonaceous material. The dispersion of this accumulation, I shall argue, constitutes the chief meaning of menstruation.

§ 157. The economy in nitrogenous expenditure seems also quite conspicuous. Experiments were made at the Charité Hospital, Berlin, by Schrader¹ on ten women to determine the excretion of nitrogen before, during, and following menstruation. The food was kept constant, and 'in every case except one the excretion of nitrogen in the urine and faeces was diminished during menstruation.' Rabuteau² also reports the results of a similar experiment which 'covered nineteen days, including three days before and eleven after the menstrual period.' The daily diet was uniform throughout. 'The³ average amount of nitrogen (calculated from the urea) excreted in the urine per day during the menstrual period was 7·8 grams: before and after this period, 9·2 and 8·5 grams respectively. In the author's opinion the excretion of urea is diminished during menstruation.' Dr. Helen McMurchy thus summarizes the fluctuations in nitrogenous excretion during menstrual life: 'Daily⁴ excretion of urea—maximum, just before menstruation—minimum, just after menstruation. Gradual increase from minimum to maximum.'

The diminution noted by Rabuteau in the daily output of nitrogen (amounting on the average to one gram) seems to correspond fairly well with the amount of proteid material lost daily in the menstrual haemorrhage—1 gram N = 2·14 grams urea = 6·42 grams proteid = about one ounce of blood, which is regarded as the average amount lost daily during menstruation. And it might perhaps be inferred that nitrogenous material, as well as carbonaceous material, tends to accumulate in the blood during the intervals of menstruation, and that both accumulations are discharged at each period. But we have argued *à priori* that there are objections to the idea that nitrogenous material tends to accumulate in the blood (§ 11), which objections do not apply to the idea of a carbonaceous accumulation. *And it is certain that the general phenomena of menstruation are explicable on the assumption of a purely carbonaceous accumulation.*

¹ *Digest of Metabolic Experiments*, Atwater and Langworthy, 1898, p. 174.

² *Ib.*

³ *Ib.*

⁴ 'Physiological Phenomena of Menstruation,' *Lancet*, October 5, 1901.

§ 158. It may be argued that the menstrual loss, which depends upon, and discharges, the carbonaceous accumulation, necessarily involves a loss of nitrogenous material; and that the nitrogenous loss, so occasioned, is compensated by an economy in the normal daily output of urea, both at the time during menstruation and to a less extent thereafter. On this view, there would be in the blood neither a pre-menstrua excess, nor, except perhaps to a very slight extent, a post-menstrual deficiency, of nitrogenous material. The nitrogenous constitution of the blood would remain uniform; but there would be an alternation in the modes of expenditure. This would accord with the principle formulated by Stewart (already quoted § 5), that the healthy body lives up to its income of nitrogen, lays by nothing for the future, but becomes suddenly economical in the pinch of necessity. And nitrogenous equilibrium would continue, without serious interruption, throughout the reproductive period of healthy adult non-pregnant women, as it does at other periods of her healthy adult life, and as it does in healthy adult males.

§ 159. I am assuming, then, that a surplus of carbonaceous matter in the blood, calling for periodic discharge, determines the menstrual flow; and it is admitted by all that the evolution of ovarian activity at puberty initiates menstruation, and that the ovaries continue to dominate this function until the menopause. Consequently, bearing in mind the inverse relations between the menstrual flow and the output of carbonic acid, it is reasonable to infer that the ovarian influence operates by determining, *inter alia*, the metabolic modifications, which entail a retardation of combustion and so lead to the carbonaceous surplus.

This carbonaceous surplus may be regarded as a preparation for increased anabolism—for the special anabolic effort of utero-gestation. It is admitted that, during every inter-menstrual period, important changes occur in the ovaries and uterus. The changes in the ovaries concern mainly the process of ovulation; they are periodic, but not regularly so. The changes in the uterus are, on the other hand, regularly periodic: hence they may, or may not, coincide with ovulation. The uterine changes comprise a growth of stroma and vessels during the pre-menstrual week, a breaking down of vessels during the menstrual week, followed by periods of recupera-

tion and rest (Heape).¹ The local anabolic changes are regarded by all physiologists as a preparation for the function of utero-gestation.

Now, if the mature female organism is accustomed to institute periodic preparations of *mechanism* for the super-added function of utero-gestation, is it not reasonable to suppose that it may institute also periodic preparations for the additional *supply* of material which will be demanded by the superadded function? To my mind, such a supposition presents no great difficulty. As regards the presumed absence of any nitrogenous intermenstrual accumulation, we may explain this on the grounds that such is unnecessary; for it has been argued that the accretion of nitrogenous material, unlike the accretion of carbonaceous material, is determined by increased function, and therefore *follows* the demand for increased material (§ 10).

In the absence of conception, the carbonaceous surplus would tend to accumulate and require, as already argued, periodic dispersion; and menstruation would constitute the means of such dispersion.

Except that they do not restrict the anabolic surplus to carbonaceous material and locate it in the blood, the above is the view formulated by Geddes and Thomson. These authors say: ²—‘If the female sex be indeed preponderatingly anabolic, we should expect this to show itself in distinctive functions. Menstruation is one of these, and is interpretable as a means of getting rid of the anabolic surplus, in absence of its consumption by the development of offspring,—just as it is intelligible that the process should stop after fertilization, when replaced by the demands of the practically parasitic foetus. In the same way the occurrence of lactation, after this internal parasitism has been terminated by birth, is seen to be reasonable. The young mammal is thus enabled to become what is practically a temporary ecto-parasite upon the unfailing maternal anabolic surplus; and, when lactation finally ceases, we have the return of menstruation from which the whole cycle may start anew. So in the widely different, yet deeply similar, world of flowers, the distinctly anabolic overflow of nectar ceases at fertilization, and the surplus of

¹ *Menstruation and its Disorders*, Giles, 1901, pp. 12, 13.

² *Evolution of Sex*, Geddes and Thomson, p. 245.

continual preponderant anabolism is drafted into the young seed or fruit.' The absence of the anabolic surplus from the blood during lactation would supply us with a reason why few women conceive until after weaning.

§ 160. The inability of the purely local view to explain fully the phenomena of menstruation is thus voiced by Macnaughton Jones: '—' We do not find any accurate explanation of many of the phenomena of menstrual life. There is a something in these not to be explained by any anatomical or physiological facts connected with ovulation. The effects of its mysterious influence on the entire being of the woman may not be measured by any descriptive language. The explanation is not in the swollen or sensitive ovary, nor in any changes that occur in the parenchyma, in the maturation and rupture of the Graafian follicle, in the accompanying congestion of the Fallopian tube, nor yet in the swelling, proliferation and disintegration of the epithelium of the uterine mucous membrane.'

Nevertheless, since throughout biology there are innumerable instances of double and multiple adaptations, the view here adopted does not contravene, but rather includes, the narrower view that the endometrial changes preceding menstruation are a preparation for the impregnated ovum. We may indeed reasonably regard these endometrial changes as the initial steps of that increased anabolic decarbonization which, we have seen, is substitutive of retarded katabolic decarbonization, and which attains its end in the reproduction of the species.

On no other theory can we explain the not very infrequent continuance of menstruation, in some cases for long periods, after the complete ablation of both ovaries. I am aware that some gynaecologists believe this phenomenon to be explicable in all cases by a small piece of ovarian tissue having been left behind, or by the existence of a third ovary which has been overlooked. But, if this were so, why should not such post-operative menstruation continue up to the natural menopause, instead of gradually ceasing in the course of a few months or years as it does in the majority? And how is it possible to overlook a third ovary or to leave behind ovarian tissue

¹ *Diseases of Women*, Macnaughton Jones, 1897, p. 145.

unintentionally, in cases (which must be fairly common) such as the following?—

The patient, a woman of 30, was in the Trendelenburg position : the cavity of the pelvis was empty of small intestine and well illuminated : there was a complete absence of adhesions : the broad ligaments were healthy and lent themselves to the formation of long and excellent pedicles. Both appendages were completely removed ; and yet the patient continued to menstruate regularly and rather profusely for eighteen months, after which cessation gradually supervened.

§ 161. On no other theory, than the one here adopted, can we explain the phenomena of vicarious menstruation, such as haematemesis, haemoptysis, epistaxis, haemorrhage from piles, ulcers, sinuses, etc., in none of which can there be any question of the disintegration of recently formed mucous membrane (§§ 669 to 671).

The conception that menstruation is a periodic decarbonizing process, depending upon an intermenstrual accumulation of carbonaceous material, is by no means new. West¹ writing in 1879 says :—‘ It is a law of the female economy that for some thirty years of life, unless interrupted by pregnancy or its results, a certain quantity of blood shall be periodically discharged from the system. This periodical discharge alone engaged the attention of observers in bygone times, and various hypotheses were framed, which, differing in other respects, yet agreed in this—that they all regarded the menstrual function as a great depurative agent, a means supplemental to the lungs themselves, *for eliminating superfluous carbon from the system.*’ (Italics mine.) This aspect of menstruation would seem to have sunk into the background during recent years.

§ 162. But, while we may believe that menstruation is a haemorrhagic decarbonizing process, we are not called upon to deny that the organism brings to bear upon the intermenstrual accumulation many of those means upon which it is accustomed to rely in amenstrual life in order to meet a tendency to hyperpyraemia. And many considerations go to show that, towards the end of the intermenstrual period, when presumably the carbonaceous accumulation is commencing to be burdensome, most of the physiological means, both those which re-

¹ *Diseases of Women*, West and Duncan, 1879, p. 40.

strict the income, and those which promote the expenditure, of carbonaceous material, are in exaggerated operation.

§ 163. Amongst the commonest preliminary symptoms of menstruation, is a certain degree of loss of appetite with or without dyspeptic manifestations. Such symptoms depend, in all probability, upon exaggerated hepatic glycogenesis and a consequent tendency to glycogenic distension of the liver. Not infrequently they overstep the physiological boundary line and expand into the manifestations of pathological distension of the liver by glycogen, such as distinct anorexia, nausea, vomiting and even diarrhoea. In any case, however, they will insure some restriction of the carbonaceous income.

§ 164. But there is also unmistakable evidence of exaggerated expenditure about this time. Giles¹ has shown 'in a composite chart of the temperature in relation to menstruation based on fifty observations,' that while during menstruation the morning, evening and mean temperatures are below the average, especially towards the end of the period, these temperatures are all above the average during the week which precedes menstruation. This premenstrual increase of temperature is ascribed by Giles² to a general increase of metabolism. In different words we may ascribe it to combustion, increased in accordance with the growing necessity for decarbonization. (Compare §§ 107 to 109.) Presently I shall argue that such increased combustion may, in some circumstances, attain to pathological dimensions (§ 179).

§ 165. But a close observation of the immediately premenstrual period seems to show that, at this time, there is often a subconscious impulse to increase physical exercise, and so to increase combustion by means of an increased necessity for force production (§ 106). Dr. Helen McMurchy³ finds that an increase of nervous energy, as exemplified by an anxiety to 'finish up things' or a 'feeling as if you couldn't do enough,' is present in 44 per cent. A physician informs me that his wife becomes markedly energetic on the day or two before menstruation: she frequently commences a general housecleaning, or she may make some trifling excuse to go for long bicycle rides. I knew a lady who had a curious fancy for

¹ Reproduced by Dr. Helen McMurchy, *Lancet*, October 5, 1901.

² *Menstruation and its Disorders*, 1901, p. 16

³ *Lancet*, October 5, 1901.

making frequent alterations in household arrangements: she would turn the drawing-room into the dining-room, or completely alter the disposition of the furniture in either, or, again, change her bedroom from one end of the house to the other; and recently, on making inquiry, I find that such domestic revolutions were undertaken almost invariably when menstruation was impending. Many cases are known to me of young women who habitually spend the entire day in domestic occupations, but who take long walks at the near approach of the menstrual period; and one of these, recognizing the regular increase of energy which in her case heralds the catamenial flow, deliberately postpones to that time any specially arduous piece of work.

The same subconscious impulse to increase combustion through physical exercise is present, as already pointed out (§ 140), more or less habitually in some healthy persons who are deficient in the fat-forming capacity; and the tendency to hyperpyraemia, which is the underlying factor in both instances, may lead, as we shall see later, in others less happily constituted, to various pathological forms of exercise. Such, we shall see, is the meaning of the premenstrual exacerbations of asthma, epilepsy, angina, mania, etc.

§ 166. Such considerations encourage us to speculate as to the 'evolutionary origin' of menstruation. The phenomena of rut in the lower animals are commonly regarded as largely analogous to the phenomena of menstruation. Rut, however, is not, except in a few cases, accompanied and relieved by haemorrhage. But Mr. Le Souef, superintendent of the Sydney Zoological Gardens, informs me that rut is, in the majority of female animals under his care, accompanied by almost complete indifference to food and by restlessness and consequent great increase of physical exercise. May not the decrease of carbonaceous income and the increase of katabolic carbonaceous expenditure, so attained, be correlative of the haemorrhagic carbonaceous expenditure of menstruation in the human female? And if so, could we not ascribe menstruation to the evolution of the sentiment of modesty—to the strictly human desire to conceal the condition of sexual unrest? It seems to me that this conception demands no special effort of imagination; for, as we shall see, menstruation, even in the present stage of evolution, depends to a great extent directly

upon food and inversely upon the amount of physical exercise. On this view, menstruation would be a comparatively recent evolutionary development: it would be a physiological capacity which has but recently in the evolution of mankind escaped from the pathological domain. (Compare § 923.) Hence possibly its still persisting semi-pathological characteristics.

§ 167. A POSSIBLE OBJECTION TO THE ADOPTED THEORY.—Out of the old plethora theory of menstruation arose ‘the¹ view first propounded by Stadlin, that menstruation consists in a casting off of unnecessary pabulum, which is retained if conception occurs for the nutrition of the foetus.’ The objection to this theory is thus stated by Giles:²—‘To make this theory fit in, it was assumed that sixteen or eighteen ounces of blood was lost at each menstruation’ (whereas it is now known that the amount lost is much less than this on the average), ‘and it was then pointed out that this amount multiplied by ten (the number of suppressed periods) corresponded with the weight of the child at birth.’

The theory of menstruation here adopted may be regarded as a specification of Stadlin’s theory; and possibly a similar objection may be preferred against it. But the restriction of the accumulated ‘pabulum’ to carbonaceous material defeats such possible objection; for, as already argued, the loss by the menstrual flow is probably only a portion of the total loss of carbonaceous material depending on prior accumulation; and it is highly probable, as we have seen, that the effect of such total extra loss upon the composition of the blood is supplemented by periodic restriction of income.

SYMPTOMS OF MENSTRUATION

§ 168. The view that menstruation depends upon a progressively increasing accumulation of carbonaceous matter in the blood and that it is a periodic decarbonizing process, adapted to prevent a condition of physiological high pyraemia from passing over into one of pathological hyperpyraemia, justifies us in placing the menstrual process upon the border line between physiology and pathology. Accordingly, we shall find that many of the phenomena usually regarded as

¹ *Menstruation and its Disorders*, 1901, Giles, p. 10.

² *Ib.*

the normal symptoms of menstruation (1) can be explained by the carbonaceous accumulation which presumably attains its climax on the first day of the flow, or by secondary conditions depending thereon; and (2) may be looked upon as minor grades of the more distinct pathological manifestations which, I shall argue later, depend upon hyperpyraemia.

The tendency to hyperpyraemia may explain, as has been already argued, the increase of temperature which occurs during the premenstrual week. It may explain also the general malaise, irritability, demented depression, weariness, lassitude and headache, so often experienced: the marked tendency to catarrh (compare § 651): the outbreak or exacerbation of acne, with marked increase of the greasiness of the hair (very common phenomena: compare § 823): eczema, pruritus, herpes, etc. (compare §§ 823, 824): dimness of sight (compare § 795); and many other symptoms. And it will fully explain, as we shall see later (§ 616), the menstrual fluctuations in the excretion of uric acid, demonstrated by Haig.

Elsewhere it has been assumed that glycogenic distension of the liver is some index of the carbon contents of the blood or pyraemia, and that it tends to vary directly accordingly (§ 92). Consequently, we shall expect to find that the onset of menstruation is associated in some cases with symptoms pointing to glycogenic distension of the liver. Nor are we disappointed. Some impairment of appetite is almost constantly present; and this may expand in some cases into distinct anorexia, nausea, and vomiting, such as occurs in an ordinary bilious attack. Dr. Helen McMurchy¹ refers to digestive disturbances, such as flatulence, occurring in 55 per cent.: constipation in 41 per cent.: diarrhoea in 45 per cent. And it may usually be observed that women affected with non-bleeding haemorrhoids suffer more severely from pain and distension when the menstrual flow is impending than at other times. All these affections, as already argued, may depend upon glycogenic distension of the liver (Chapter III).

§ 169. But, if menstruation is a decarbonizing process, we should expect all its symptoms—those which depend upon the carbonaceous accumulation in the blood and those which depend upon the subordinate glycogenic distension of the liver—to undergo marked accentuation under conditions which

¹ *Lancet*, October 5, 1901.

prevent or retard the escape of blood. That this happens, is one of the oldest of all clinical observations; and this fact is fully recognized, if indeed it is not over-estimated, by all women. Not only are the ordinary menstrual symptoms exaggerated, under these conditions, but more serious phenomena, presumably depending on a pathological degree of carbonaceous accumulation in the blood or hyperpyraemia, or on a pathological degree of glycogenic distension of the liver, are liable to make their appearance. Tilt says:¹—‘I have even seen jaundice occur in young women, from the sudden suppression of the menstrual flow, and have then noticed a persistent loss of appetite for months’; and, later in this work, we shall see that many of the typical expressions of hyperpyraemia, such for example as acute arthritic gout, have been observed to make their first appearance in these circumstances (§ 588).

Many of the phenomena of menstruation seem to depend directly upon the vaso-motor action, which, I shall argue, is one of the commonest results of carbonaceous accumulation in the blood, whether physiological or pathological in degree; but these will be considered more conveniently at a later stage of this work (§§ 458 to 460).

AMENORRHOEA

§ 170. On the theory here adopted, the functional activity of the ovary determines menstruation through a modification of metabolism, whereby continuous katabolic decarbonization is in part inhibited in favour of periodic haemorrhagic decarbonization. This conception will serve to explain many of the phenomena associated with amenorrhoea. Menstruation will depend primarily upon at least two conditions: (1) upon supply, namely, the existence of the carbonaceous surplus in the blood; and (2) upon function, namely, the due capacity on the part of the menstrual mechanism for the discharge of blood. In default of either, amenorrhoea will result; but the two varieties, so induced, will naturally have associated phenomena and results which diverge widely.

§ 171. AMENORRHOEA DUE TO ABSENCE OF THE CARBONACEOUS SURPLUS (SUPPLY).—This form of amenorrhoea must be

¹ *Change of Life*, 1882, p. 269.

regarded as strictly conservative: it may be physiological or pathological. It is exemplified in the amenorrhoea of pre-menstrual and post-menstrual life, of pregnancy and lactation, of starvation, of prolonged pyrexia, and probably of chronic exhausting diseases generally. In healthy females before puberty and after the menopause, decarbonization of the blood would, on this view, follow lines substantially identical with those of healthy males. Combustion and fat-formation, aided by other minor forms of anabolic decarbonization, would together serve to prevent any serious degree of carbonaceous accumulation. During the whole of pregnancy and lactation, from conception to the involution of the mammary gland after weaning of the child, carbonaceous material is being withdrawn from the maternal blood for anabolism in amounts above the average at other times. It is true, there is a narrow gap in the continuous anabolic decarbonization, lasting a few days from the end of the third stage of labour to the full establishment of the lacteal secretion; but it must not be forgotten that the muscular exertion of labour implies a heavy katabolic decarbonization, and that blood in some quantity may be lost towards the end of, and succeeding, labour. During starvation, carbonaceous income from the alimentary canal ceases and carbonaceous accumulation will be impossible. During pyrexia, as will be argued (§ 273 *et seq.*), both income is restricted and expenditure increased; and the same is true probably of many chronic exhausting diseases.

§ 172. AMENORRHOEA DUE TO IMPERFECT DISCHARGING-CAPACITY ON THE PART OF THE MENSTRUAL MECHANISM (FUNCTION).—Here the cessation of the flow cannot be regarded as conservative: we may perhaps regard it generally as an unfortunate accident. The conditions which prevent the escape of blood from the generative organs, except such as consist of gross lesions like atresia, do not seem to be well understood. This is because the mechanism of menstruation has not been fully worked out. Later, however, I shall argue that menstruation is essentially a vaso-motor process (§§ 454 to 465); and then it will be admitted that, amongst the factors responsible for imperfect discharging-capacity of the generative organs, must be included an inability on the part of the vaso-motor system to institute the vascular changes essential for menstruation.

In this form of amenorrhoea, the carbonaceous surplus in

the blood will tend to increase. The organism, deprived of its accustomed outlet for periodic haemorrhagic decarbonization, will be driven to make other arrangements. It may find another outlet for the discharge of blood, as in vicarious menstruation: failing this, it may, as we have seen (§§ 156, 165), increase combustion (katabolic decarbonization) directly or indirectly; and it is a matter of common observation that women, in these circumstances, are liable to increase rapidly in weight (anabolic decarbonization). These efforts at increased expenditure may be associated with increased efforts to restrict income, as shown by the frequent occurrence of symptoms, such as anorexia, dyspepsia, and biliousness. But probably all such alternative devices are at times inadequate; and then a condition of hyperpyraemia will ensue—a condition which may lead to many overtly pathological affections to be more fully considered hereafter.

§ 173. AMENORRHOEA OF ANAEMIA.—But it may be that amenorrhoea is conservative and yet does not depend upon the absence of the carbonaceous surplus. During chlorosis and anaemia of other kinds, menstruation is always reduced and may cease entirely; and such cessation is usually attributed to an endeavour on the part of the organism to conserve haemoglobin which is already deficient in the blood. This is reasonable, and, if true, it will cause no surprise that the carbonaceous accumulation tends to increase in these circumstances. It is certain at any rate that anaemic conditions are very liable to be complicated with dyspepsia, anorexia, sick headaches and with high pulse-tension, all of which conditions will be regarded as common manifestations of hyperpyraemia; and the ordinary plumpness of chlorosis may perhaps be looked on as due to a slight exaggeration of anabolic decarbonization, substitutive of the absent haemorrhagic decarbonization of menstruation and of the retarded katabolic decarbonization, occasioned by diminished haemoglobin and diminished oxygen carrying power of the blood.

PUBERTY AND CLIMACTERIC

§ 174. The foregoing considerations will assist us to explain many of the special phenomena observable at the two most critical epochs of woman's life, namely, puberty and the climacteric or menopause. If menstruation depends both upon the

carbonaceous surplus and upon a due discharging capacity on the part of the generative organs, it follows that, for the physiological performance of the menstrual function, an accurate relation between the two named conditions is essential; and it is easy to realize that at no period will the accuracy of this relation be more liable to disturbance, than at the commencement and at the termination of menstrual life. For example, at puberty the metabolic modifications introduced by the evolution of ovarian activity may give rise to the carbonaceous surplus in the blood before the evolution of the discharging mechanism is sufficiently advanced to assure adequate haemorrhagic decarbonization; and conversely, at the menopause involution may have reduced the discharging capacity of the menstrual mechanism, before the metabolic reversion to the ante-pubertal or male type has succeeded in promoting adequate substitutive physiological decarbonization, katabolic or anabolic.

Hence, at both these epochs there will be a special tendency for the premenstrual accumulation to become exaggerated, and so will arise some of the manifestations of hyperpyraemia. George J. Engelmann says: ¹—‘Colds, headaches, neuroses and slight disturbances of all kinds attain their greatest frequency in the year preceding puberty, as shown by the statistics of the schools of Sweden and Denmark.’ The special proclivity to manifold disorders and diseases at the menopause calls for no insistence.

The similarity of the affections occurring at puberty and the menopause is voiced in the following passage from West and Duncan’s work on Diseases of Women.² ‘The very accidents, to which there is a disposition when menstruation ceases, may also precede its occurrence. If menstruation is postponed beyond the ordinary period, the system suffers in the same way as it does at its cessation. The same double duty is thrown on the liver, the same disposition to its disorder exists, the same tendency to congestion of different viscera manifests itself, and frequently the same outbursts of haemorrhage give temporary relief to the congestion.’ And Tilt says: ³—‘Menstruation is likely to end as it begins, and storms at puberty foretell a

¹ ‘Age on First Menstruation on the North American Continent,’ *New York Med. Journal*, February 8, 1902, p. 221.

² *Diseases of Women*, 1879, p. 41.

³ *Change of Life*, 1882, p. 77.

stormy change of life. Diseases which precede first menstruation may be expected to precede its cessation.'

§ 175. But the affections which are prone to arise at puberty and the menopause are not special to these periods. They are the same as those which are prone to arise at any period of menstrual life, whenever the flow becomes checked or inadequate to the discharge of the carbonaceous surplus. They are, it is true, most common at puberty and the menopause, but only because it is at these two periods that the menstrual loss is peculiarly liable to be inadequate.

Like the affections which are liable to arise on the sudden checking of the flow during menstrual life, the affections of puberty and the climacteric may be regarded for the most part as exaggerations of the common premenstrual and menstrual symptoms. Most of these will be considered more conveniently later: the gastro-intestinal affections, depending, as they probably do, upon a pathological degree of glycogenic distension of the liver, may be referred to here.

Tilt gives a table which shows 'that¹ 354 kinds of gastro-intestinal suffering were noted at the change of life in 500 women, many of the 354 presenting several kinds of gastro-intestinal disturbance.' He adds:—'The practical bearing of the table is the great liability to *biliousness*, *dyspepsia*, *diarrhoea* and *piles*,' but 'it² gives no idea of the obstinacy of the biliary symptoms in many of these cases.' A study of the clinical histories of Tilt's cases shows that, in many, the affections enumerated recurred or became exaggerated with a monthly periodicity: from this, it may be inferred that they depended on a recurrent glycogenic distension of the liver, indicative of a recurrent tendency to hyperpyraemia which the generative organs had become, through involution, inadequate to relieve.

The climacteric affections referred to by Tilt include, in addition to a heterogeneous list of dyspeptic and bilious conditions, jaundice, vomiting, diarrhoea, any of which may be more or less periodic, constipation, haemorrhoids, and what must be regarded as vicarious menstrual losses, such as recurrent haemorrhage from piles, recurrent entorrhagia and haematemesis. He also mentions, on the authority of Sir H. Halford, a case of climacteric abscess of the liver. (Compare § 96.)

¹ *Change of Life*, 1882, p. 266.

² *Ib.* p. 267.

§ 176. That the disorders met with at the menopause depend in great part upon hyperpyraemia, is further rendered probable by Tilt's experience of the dietetic management most suitable at this period. This author says:¹—'Having shown that the debility often experienced at the change of life sometimes depends upon the frame being oppressed by an overplus of blood, for which there is no longer a monthly drain, it is rational that, on the very first appearance of the irregularities characteristic of this epoch, women should curtail, rather than augment, the amount of food and stimulants to which they have been accustomed. When in the family-way or nursing, or so long as the menstrual flow remains regular and abundant, many women can, without inconvenience, take meat three times a day, and beer and wine at both luncheon and dinner; but when the surplus blood produced by high feeding can neither be well employed nor regularly ejected, it increases all the sufferings of the change of life, and brings on obstinate biliousness and constipation.' He advises a breakfast of toast or bread and butter, with weak tea, etc.; and but one dinner a day. 'Dinner² should be a plain meal; fish and white meats, such as fowl or veal, in preference to beef or mutton; more of the crust than the crumb of bread, and jellies and ice in preference to puddings. If, on the contrary, all sorts of *farinaceous food, pastry and cakes* be indulged in, the natural consequence will be a desire to prolong sleep, a distaste for exercise, and a tendency to congestions, bleedings, inflammations and gout, or women may become distressingly stout.' (Italics mine.) My own experience is confirmatory. I have found that, in otherwise healthy women, climacteric disorders, so often the despair of the family physician, are as a rule readily amenable to dietetic and hygienic treatment adapted to reduce the carbon contents of the blood (Case LXXIII).

§ 177. Before leaving the subject of the menopause, it will be well to anticipate a very probable objection to the hyperpyraemic theory. On this theory, the pathological phenomena associated with the menopause depend upon, and imply, a diminution of the accustomed menstrual haemorrhage—an inadequacy of haemorrhagic decarbonization. But it is a prevalent conviction amongst the general public, and I think within the medical profession also, that at the menopause menstrual losses are apt

¹ *Change of Life*, 1882, p. 110.

² *Ib.*, p. 111.

to be excessive. This seemed a serious bar to the hyperpyraemic theory. Accordingly, for some years I kept a careful look-out for cases in which the menopause was associated with increased menstrual loss; and, as a result, I was forced to conclude that such cases are far less common than is generally thought, if indeed they are not quite exceptional.

This being so, it was gratifying to find this conclusion more than confirmed by Handfield Jones.¹ This observer 'critically analyzed, in his practice, all those cases where the patients had complained of excessive loss, attributed more or less confidently to a disturbance "natural" to the period of the climacteric. From these cases he isolated a group in which an obvious gross lesion, such as carcinoma of the cervix, a considerable fibroid, etc., was easily detected. There then remained a large number where the cause of the haemorrhage was not so readily explained. Here, if anywhere, ought to be found the material to justify the view that at the menopause frequent and excessive haemorrhage is to be expected in the natural order of things. Yet, on analysis, it was discovered that, with one or two doubtful exceptions, every one of the so-called functional haemorrhages could be referred to a definite, though perhaps relatively slight, structural cause, upon the removal of which the haemorrhage ceased.'

KATABOLIC, ANABOLIC AND HAEMORRHAGIC DECARBONIZATION CORRELATED

§ 178. It has been argued that combustion and fat-formation are both decarbonizing processes, and that they are to some extent mutually substitutive (§§ 142 to 144). In the present chapter, it has been argued that menstruation is a periodic decarbonizing process. Consequently, menstruation should have conspicuous relationships with both combustion and fat-formation; and these relationships should extend to all other forms of anabolic decarbonization. Further, such relationships should be those of alternation and should be most conspicuous at those epochs of life at which the metabolic balance is undergoing modification.

The alternation of menstruation with the anabolic processes of pregnancy and lactation has been referred to in other words.

¹ *Medical Annual*, 1903, p. 468.

So has the alternation with combustion. The relatively high and low temperatures of the pre-menstrual and menstrual weeks respectively are probably examples of this alternation ; and so almost certainly is the increased output of carbonic acid, which occurs whenever menstruation is suppressed from causes other than the absence of the carbonaceous surplus.

§ 179. It would seem that the presumed pre-menstrual increase of combustion may, in circumstances which interfere with the menstrual discharge, become exaggerated and attain to pathological proportions. Trousseau thus commences his ninety-second lecture : ¹—‘ Gentlemen :—An error of diagnosis, which you saw me commit the other day, affords me an opportunity of entering into some details regarding an affection to which I give the name menorrhagic fever. A young woman of 17, who had been ill for six days, was admitted as a patient to Saint Bernard’s ward. She was born in the country ; and had only resided four months in Paris. Like most new-comers she did not menstruate. From the commencement of her indisposition, she complained of headache, giddiness and insomnia. She had epistaxis, loss of appetite, foul tongue and diarrhoea. The pulse was febrile ; and there had been no cessation of fever. I concluded that the case was one of dothienteria. On the following day the catamenia appeared, and the fever abated. The menstruation was normal ; and two days after the appearance of the sanguineous discharge, health was completely re-established. Gentlemen, this is not the first case of the kind which has presented itself in our wards : not a year passes without my calling your attention to such cases, of which sometimes I am led to form an erroneous diagnosis.’

§ 180. At the climacteric, when menstruation ceases permanently, there is, as we have seen, a permanent increase in the output of carbonic acid. An increase in the output of carbonic acid implies an increase in combustion, and consequently in heat-production ; and an increase in heat-production, when not associated with an increase in the temperature of the body, is necessarily associated with an increase in the dissipation of heat from the body. Conformably, Harry Campbell says : ²—‘ Many women at the climacteric and for years afterwards, as late as the age of 70 or more, are, as is well known, very

¹ *Clinical Medicine*, New Syd. Soc., vol. v. p. 212.

² *Flushing and Morbid Blushing*, H. Campbell, 1890, p. 49.

susceptible to heat and insensitive to cold. They clothe themselves more lightly than ordinary individuals, and are seldom seen sitting near the fire. One infirm patient told me that even in the depth of winter she could not bear an extra blanket. Cold weather seems to suit such: during hot weather, on the other hand, they are apt to suffer great exhaustion and discomfort. This susceptibility to heat and insensitiveness to cold is attributed by Tilt to an excessive production of heat in the body.' There can, I think, be hardly a doubt that the opinion of Tilt is correct; and I am convinced, from my own observations, that the phenomena just described occur for the most part in women who do not become markedly corpulent at the menopause—in women, that is to say, in whom anabolic does not readily take the place of haemorrhagic decarbonization.

§ 181. Physical exercise and exposure to cold, as we have seen (§ 106), increase materially combustion and the excretion of carbonic acid: a poor diet tends to diminish the carbonaceous income to the blood; and all these conditions are observed to alternate, to some extent, with menstruation—to diminish, that is to say, the amount of the flow. On the other hand, the opposite conditions are known to add to its amount.

Playfair says: 'Rich diet, luxurious living . . . will have an injurious effect in increasing the flow, which is therefore less in hard-worked country-women, than in the better classes and residents in town. It is more abundant in warm climates, and our country-women in India habitually menstruate overprofusely, becoming less abundantly unwell when they return to England. The same observation has been made with regard to American women residing in the Gulf States, who improve materially by removing to the Lake States. Some women appear to menstruate more in summer than in winter. I am acquainted with a lady who spends the winter in St. Petersburg, where her periods last eight or ten days, and the summer in England, where they never exceed four or five. The difference is probably due to the effect of the over-heated rooms in which she lives in Russia.' Tilt² says that the influence of heat on menstruation is shown 'by menstruation usually making its first appearance in summer in the temperate

¹ *Midwifery*, 1898, vol. i. p. 75.

² Tilt on *Uterine Therapeutics*, 1878, p. 252.

regions of the globe; and by its premature or too frequent occurrence in young women exposed to the unusually intense heat of kitchens and washhouses.'

§ 182. The influence of temperature is shown by many other observations. 'Menstruation usually appears in France and Italy at 14 or 15, in Germany and Denmark at 16 or 17. In the United States and Canada, the average age is 14. Menstruation appears earlier in the south than the north' (G. J. Engelmann).¹ Among the Esquimaux women, 'Cook,'² the ethnologist of the Peary North Greenland expedition, found that menstruation only began after the age of 19, and that it was usually suppressed during the winter months, when there was no sun, only about one in ten women continuing to menstruate during this period. It was stated by Velpeau that Lapland and Greenland women usually menstruate every three months, or even only two or three times during the year. On the Faroe Islands, it is said menstruation is frequently absent. Among the Samoyeds, Mantegazza mentions that menstruation is so slight that some travellers have denied its existence. . . . Among the Indians in North America, again, menstruation appears to be scanty. Thus Holder, speaking of his experience with the Crow Indians of Montana, says:—"I am quite sure that full-blooded Indians in this latitude do not menstruate so freely as white women, not usually exceeding three days." Among the naked women of Tierra del Fuego, it is said that there is often no physical sign of the menses for six months at a time. These observations . . . indicate on the whole that primitiveness in race is a very powerless factor without a cold climate' (Havelock Ellis). But the climatic is probably only one factor of many, in the scanty menstruation of the races referred to. Primitive habits imply usually much physical exercise; and food is a most important factor. The Crow Indians, as already mentioned (§ 40), were almost purely meat eaters: the Fuegians live mainly on raw fish; and a proteid diet, such as these, implies a low carbonaceous intake and a high rate of combustion—a small income and a relatively large katabolic expenditure.

§ 183. The alternation of menstruation with fat-formation is hardly less conspicuous than that with combustion. It is,

¹ *Med. Rev.* June 1903, p. 23.

² *Studies in the Psychology of Sex*, Havelock Ellis, 1901, pp. 52, 53.

so far as I have been able to discover, the rule rather than the exception for women with a tendency to corpulence to menstruate less profusely than women of a lean habit. Checked menstruation is often followed by a rapid increase of weight. The following is a case typical of this common event :—

Miss D— : aged 30 : hospital nurse : left England in September for Queensland. At the beginning of the voyage, she weighed 10 st. 8 lbs. Menstruation ceased on board ship, as it so frequently does. In January of the following year, she weighed 12 st. 5 lbs., a gain of nearly two stones in less than four months.

Of course it is not intended to be inferred that the *whole* gain of weight resulted from the saving of a few menstrual losses.

Obesity is a frequent sequel of the menopause. Tilt says :¹— ‘Of 383 women in whom there had been no menstrual flow for five years, 121 had grown stouter than before. . . . Three out of 383 became suddenly fat at cessation.’ Many pastoralists have assured me that, as a general rule, kine which fatten readily are poor breeders ; and a similar observation has been made concerning the human female. May it not be that in such there is a deficiency of the anabolic surplus for reproduction? If so, the infecundity of the obese would be comparable with the infecundity of nursing women.

§ 184. But the alternations of menstruation with other decarbonizing processes are not limited to such as are physiological. Menstruation has conspicuous inverse relations with a multitude of pathological processes, all of which may be regarded as reducers, or as attempts at reduction, of the carbon contents of the blood : some of these tend to restrict the carbonaceous income, others to increase the carbonaceous expenditure, others again to act in both ways combined. Some of these have been already referred to : many others will be considered hereafter.

SUMMARY

§ 185. In this chapter, I have attempted to show that the evolution of ovarian activity at puberty determines a modification of metabolism, whereby combustion, or katabolic decarbonization, is retarded in anticipation of the increased anabolic

¹ *Change of Life*, 1882, pp. 66, 67.

demands of maternity: that, when conception occurs, the carbonaceous material, so saved from destruction, is devoted to the anabolism of the offspring while a parasite, to its nutrition through lactation when an ecto-parasite: that, in the absence of conception, the saved carbonaceous material tends to accumulate in the blood: that such accumulation is tolerated, without protest from the organism, for a time: that later, usually within three weeks, the accumulation tends to become burdensome: that then the organism institutes some of its accustomed measures to restrict further accumulation: that these consist of (1) an increase of expenditure, through a rise in the rate of combustion which occurs directly as a response to the accumulation, and sometimes indirectly also, through a subconscious impulse to increase physical exercise, and (2) a restriction of income, through glycogenic distension of the liver and its results: that the remainder of the accumulation is discharged with the menstrual flow; and that this series of events continues to recur, except when interrupted by pregnancy or other less physiological conditions, until the *involution* of ovarian activity at the climacteric determines reversion to the ante-pubertal or male type of metabolism.

CHAPTER VII

§§ 186-252

Hyperpyraemia—Physiological variations in the carbon or fuel contents of the blood: pyraemic variations—The blood in starvation—*A priori* probability of hyperpyraemia—The food factor in hyperpyraemia: deficient nitrogenous intake: excessive carbonaceous intake—Functional factors in hyperpyraemia: a powerful digestive and absorptive capacity: deficient hepatic regulation: deficient katabolic decarbonization or combustion: deficient anabolic decarbonization, especially fat-formation: deficient haemorrhagic decarbonization or menstruation: mental strain and psychical factors—The principles of treatment of hyperpyraemia: treatment of hyperpyraemia through increased expenditure: treatment of hyperpyraemia through restriction of income: the two dietetic methods, that by reduction of the proteid, and that by the reduction of the carbonaceous, intake, compared—Diatheses—Summary.

PHYSIOLOGICAL VARIATIONS IN THE CARBON OR
FUEL CONTENTS OF THE BLOOD: PYRAEMIC
VARIATIONS

§ 186. The carbon or fuel income to the blood will depend upon the intake, and upon the efficiency of digestion and absorption: the carbon or fuel expenditure will depend upon the carbon or fuel income (to some extent), and upon the efficiency of decarbonization, katabolic, anabolic and haemorrhagic. In health, there will be a general balance between income and expenditure, and this will tend to maintain a uniform mean level in the carbon or fuel contents of the blood—a uniform mean pyraemia. But, since some of the factors of the income (intake and digestion at least) are intermittent or remittent, and, since some of the factors of expenditure (katabolic and haemorrhagic decarbonization) are irregular or periodic, it is to be anticipated that the carbon or fuel contents of the blood will not be absolutely uniform, but will present certain variations. These variations, we may suppose, are, in the healthy state, restrained within physiological limits by a series of balancing agencies. The carbon or fuel contents of

the blood will be prevented from falling to a pathological level by hunger and fresh intake; and, in the absence of food, the stored carbonaceous material (glycogen, fat, etc.) will be drawn upon for the same purpose. Again, the carbon or fuel contents of the blood will be prevented from rising to pathological heights by another series of balancing agencies. Amongst these will be the diminution in the rate of digestion and absorption, and probably in intake from lessened appetite, through glycogenic distension of the liver: the power within certain limits possessed by the organism to increase combustion in response to the presence of extra carbonaceous material or fuel in the circulation: the unconscious or subconscious, but wholly beneficial, impulse to increase combustion by physical exercise in accordance with the necessity for decarbonization: the power to form fat and glycogen, utero-gestation and other anabolic capacities: the periodic haemorrhage of menstruation; and possibly other physiological functions, less well understood.

THE BLOOD IN STARVATION

§ 187. The physiological variations in the carbon contents of the blood, occurring in ordinary circumstances, are due, as we have seen, to the irregularities of the income and expenditure. The ordinary income in the absence of food necessarily ceases, and then the organism commences to draw carbonaceous material from the stores contained in its tissues. This is a state of things which, it is now admitted, may continue for some time without material harm. Under these conditions, the variations in the carbon contents of the blood, which depend primarily upon the irregularity of the food supply, will cease: so will fat formation; and so also will combustion, in so far as it is a response to the demand for decarbonization. But combustion, in so far as it is a response to the demand for such force and heat-production as remain essential to life, will continue.

Now it seems reasonable to suppose that the blood will withdraw from the extra-vascular stores of the tissues just so much carbonaceous material as, but no more than, it is expending to meet these vital necessities; and if so, the carbonization of the blood will cease to be regulated in part by *supply*,

as it is in ordinary circumstances—it will be regulated altogether by *demand*.

The carbon equilibrium of the blood, under these conditions, will be as true as is presumably the nitrogenous equilibrium of the blood under most physiological conditions. All variations in the carbon contents of the blood will tend to disappear and to be replaced by a certain uniform minimum level; for variations in the rate of combustion, irregular or rhythmical, will be without effect, since they will now determine the income to, as well as the expenditure by, the blood; and hyperpyraemia will of course be impossible.

§ 188. Conformably with this conception, Foster says:—‘In starvation, as in ordinary circumstances, the several tissues struggle to keep the blood in an average condition.’ But it is clear that the struggle during starvation is of a nature different from what occurs when ample food is being taken. In the latter case, the struggle is often to attain decarbonization: in the former, it must always be to attain carbonization.

§ 189. There can, I think, be little doubt, as Harry Campbell¹ points out, that, in ordinary circumstances, that is to say, under a sufficiency in the quantity and frequency of meals, ‘most of the energy expended by the organism is . . . derived from the food recently taken.’ The modern civilized organism has become unaccustomed to draw to any large extent upon its stored fuel. Hence the sudden withdrawal of food is apt to be followed by unpleasant sensations of debility. This may be but temporary, however. A personal friend of mine, an officer in the North Queensland native police, was employed in tracking an escaped prisoner in the Carpentaria district. Expecting to finish the expedition in two or three days, he furnished himself with rations for that time only. But the expedition lasted twelve days, and for the last nine he was totally without any kind of food except water, although he covered on an average ten miles a day on foot over rough country. He tells me that the first thirty-six hours of abstinence were by far the most distressing, and that thereafter he remained comparatively comfortable, and was by no means exhausted at the end. It is conceivable that the organism takes some little time before it is able to replenish its blood-

¹ ‘Observations on Diet,’ *Lancet*, May 24, 1902, p. 1488.

stream satisfactorily from the long-disused fuel supply stored in the tissues.

In accordance with the *à priori* impossibility of hyperpyraemia during starvation, we shall see later that most of the clinical manifestations of this blood-state may be dispersed wholly or in part, by abstention from food.

À PRIORI PROBABILITY OF HYPERPYRAEMIA

§ 190. Since, under the conditions of modern civilization, the intake of fuel, regulated as it is in great measure by taste rather than by appetite, is not of necessity accurately graduated to the demand for energy production: since the glycogenic function of the liver, which largely regulates the processes of digestion and absorption and therefore the carbonization of the blood, is liable to wide variations in capacity: since the rate of combustion varies with the individual, with the nutrition of the tissues, and with conditions—such as exposure to cold and physical exercise—which are either largely accidental or chiefly voluntary: since the power of fat-formation, the most important form of anabolic decarbonization, which in the ideal state might be supposed to supplement adequately decarbonization by combustion, is often manifestly deficient: since the capacity for the formation and deposition of muscle glycogen is probably limited: since menstruation, or physiological haemorrhagic decarbonization, depending as it does upon many conditions, local and general, as well as upon the existence of the carbonaceous surplus in the blood, is liable to be inadequate or deferred: since, in general terms, the removal of carbonaceous material from the blood, unlike the removal of nitrogenous material, depends only within narrow limits upon supply, and is not therefore accurately self-regulating:—it will not be surprising if at times the amount of carbonaceous material in the blood rises above the capacity of the organism for physiological disposal. This is not generally admitted. It is held, on the contrary, that carbonaceous material, which is not required at the time for fuel, is conveniently stored extra-vascularly in the form of fat, glycogen, etc.; and conversely, that carbonaceous material, not so stored, is rapidly oxidized by the tissues and eliminated in the form of carbonic acid, the heat produced being dissipated by a commensurate increase of heat loss. In short,

it is assumed by implication that the aggregated capacities of the organism for the physiological disposal of carbonaceous material are (except in the case of glycosuria) throughout life adequate on all occasions to the demand. Now this, it seems to me, is a larger assumption than any which is demanded by the theory of hyperpyraemia; for surely an occasional inadequacy is more probable than an invariable adequacy.

§ 191. We must of course freely admit that the aggregated capacities of the organism *are in the great majority of cases* fully adequate to the physiological disposal of carbonaceous material: indeed, it is an essential part of this argument that physiological health connotes a certain accuracy in the balance between the income to the blood and the expenditure by the blood of carbonaceous material. But the *à priori* argument adduced gives us the right to demand some proof of the assumed invariability of the relation: in the absence of such proof, to question the truth of the assumption: to assume in turn provisionally that, in certain circumstances, the balance may be imperfect; and that, as a result of an imperfection, whereby the income exceeds the expenditure, carbonaceous material may accumulate in the blood to an ultra-physiological or pathological degree. For the hypothetic humoral condition resulting from such an accumulation, I can find no better term than 'hyperpyraemia.'

§ 192. Since we have but an inadequate knowledge of the chemistry of the carbon compounds which normally constitute the fuel of the blood, of pyraemia, that is to say, it would be premature to attempt a chemical definition of the load which is responsible for hyperpyraemia. We must suppose that the sanguineous load is at any rate *primarily* carbonaceous, not nitrogenous: that it is something which is capable of being utilized as fuel by the katabolic tissues and of being built up into fat by the anabolic tissues: that it is dispersable by exaggerations of those physiological means which in health restrain the carbon contents of the blood from rising unduly; and that it is derived from the carbonaceous portion of the food supply.

§ 193. If we take as an average normal diet the mean of Moleschott's, Ranke's, Pettenkofer's and Voit's diets for a man in ordinary work, we obtain proteid 4·31 ounces, fats 3·53 ounces, and carbohydrates 11·71 ounces (B. Yeo).¹ One third

¹ *Food in Health and Disease*, B. Yeo, 1897, p. 193.

of the proteid (1.43 ounces), containing a little carbon and practically all the nitrogen, is rapidly discharged as urea (Foster).¹ The remaining two thirds of the proteid (2.88 ounces), together with all the fats and carbohydrates, contain carbon but no nitrogen; and it is from some or all of the members of this group, which constitutes 93 per cent. by weight of the total food supply, that the hyperpyraemic load must be derived.

§ 194. As the result of such an intake as the above, the blood is found to contain glucoses or monosaccharids, saccharoses or disaccharids, and probably amyloses or polysaccharids, such as glycogen, together with glyco-proteids and fats; and it is hardly probable that this list exhausts the carbonaceous compounds of the blood. As to the chemical constitution of the hyperpyraemic load the following possibilities suggest themselves:—1. It may consist of an increase of one or more of the carbonaceous compounds referred to. 2. It may consist of a proportionate increase of all. 3. It may have a varying chemical constitution, consisting now of an increase of one, now of several, anon of all. 4. It may consist in some cases, more especially in those in which the paroxysmal manifestation is preceded presumably by a more or less prolonged period of hyperpyraemia, of some carbonaceous compound, more stable in nature, that is, less rapidly dispersable than any which exist normally in the blood.

All these questions should be left absolutely open for the present. Nevertheless, the view that the chemical constitution of the hyperpyraemic load varies in different cases seems probable when we come to consider its numerous and complex modes of origin in different cases. But there is one consideration which makes it highly probable that hyperpyraemia, *in some cases*, is a mere quantitative exaggeration of pyraemia, whatever the chemical constitution of that physiological condition of the blood. The consideration referred to is the argument for 'pathological prepotency' of the paroxysmal neuroses and 'relative hyperpyraemia,' which is detailed in Chapter XIII. This argument is, I think, tenable only on the above view.

§ 195. Under this last view, hyperpyraemia is pathological in the sense that it is a condition, which the *unaided and*

¹ *Text-book of Physiology*, M. Foster, 1895, p. 810.

undirected physiological capacities are unable to deal with satisfactorily, and which, as we shall see, demands the intervention of extraordinary measures that we are accustomed to speak of as *pathological*. Otherwise, it is but an exaggeration of the high carbon contents of the blood which, I have argued, is normally recurrent; and the two pass by imperceptible gradations into each other. But, since the capacities for dealing with carbonaceous material in a physiological manner, vary within wide limits with the individual and with his environment, it follows that, in such cases, hyperpyraemia is a relative term and has no necessary connexion with an absolute excess of eating and drinking. In other words, what is physiological high carbon contents or high pyraemia for one individual may be pathological hyperpyraemia for another; and what is physiological high carbon contents or high pyraemia in one set of circumstances may be pathological hyperpyraemia in another.

§ 196. But in other cases—and this refers especially to cases in which there is presumably a prolonged antecedent hyperpyraemia, such as articular gout and many of the manifestations of unrelieved hyperpyraemia—it is probable that there becomes developed some more stable compound than any which are present normally in the blood: that this is carbonaceous in nature, or at least subject to the laws of carbonaceous metabolism; and that, on account of its stability, it demands a more than ordinarily intense or prolonged process of a carbonization, pyrexial or other, for its complete dispersion. (Compare Case LVIII, also § 955.)

In this connexion, it may be apposite to introduce the following statement by Professor J. Bauer: ¹—‘ In the opinion of several authorities, as F. W. Beneke, A. Cantani, etc., a diet, in excess of the individual requirements, gradually leads to imperfect elaboration of the nutriment taken, and “ to a retardation of metabolism.” The existence of these derangements of function, which are the commencement and causes, or the accompaniments, of many diseases, is due, according to Dr. Beneke, to the fact that a part of the food ingested is not reduced within a certain time to the ultimate products of normal assimilation, viz. urea, carbonic acid, and water, and the immediate consequences are that the products leave the

¹ Von Ziemssen's *Handbook of General Therapeutics*, 1885, vol. i. p. 157.

body, partly in earlier stages of splitting up than they would under normal conditions, and partly in the natural and ultimate forms, but in abnormally small amounts. Evidence of this incomplete metabolism is to be found in an abundance of oxalic acid in the urine.'

§ 197. The hyperpyraemic load has been referred to as primarily carbonaceous. The qualification is essential; for later, experimental and other data will be adduced in support of the view that at least one nitrogenous waste material, namely, uric acid, tends to accumulate in the blood concurrently with, *but as a result of*, the carbonaceous accumulation (§ 631); and it may be that other less well investigated waste products have a similar tendency.

§ 198. It may be advisable here to insist that the term hyperpyraemia does not imply a full description of the condition of the blood in any case: it has reference merely to one item therein, the proportion or nature of the carbonaceous accumulation. Consequently, hyperpyraemia may coexist with blood-states which differ from each other in many important respects: it may coexist, for example, in one case with anaemia, in another, with the opposite condition; and so on.

THE FOOD FACTOR IN HYPERPYRAEMIA

§ 199. On the definition of hyperpyraemia adopted, it is presumable that the imperfection of equilibrium, implied in that term, may concern either the carbonaceous income, or the carbonaceous expenditure, of the blood: the one may be relatively in excess, the other relatively deficient. But the carbonaceous income to the blood will depend upon the carbonaceous intake and upon the efficiency of digestion and absorption; and similarly, the carbonaceous expenditure by the blood will depend upon the carbonaceous income and upon the efficiency of katabolic, anabolic, and haemorrhagic decarbonization.

So far all seems simple; but the question becomes much complicated by the facts (1) that the efficiency of digestion and absorption is inversely correlated with the efficiency of the glycogenic function of the liver; and (2) that the efficiency of the carbonizing functions (digestion and absorption), of the

chief regulative function (hepatic glycogenesis), and of the decarbonizing functions (katabolic, anabolic, and haemorrhagic), probably all depend in some part upon the nitrogenous income derived from the proteid intake. Consequently, in considering the food factor in hyperpyraemia, we shall have to differentiate sharply the fuel or carbonaceous intake contained in the carbohydrates, fats, and proteids from the nitrogenous intake contained in the proteids alone.

§ 200. In the table on the following page, I have attempted to delineate the main steps by which fundamental errors of diet, depending in all probability primarily on advancing civilization, tend to the production of hyperpyraemia. The steps are of course largely provisional, pending much fuller knowledge in all branches of physiology, but it would not be fair to regard them as purely speculative, since most of them will be found to conform generally with clinical observation.

§ 201. The fundamental dietetic errors, as shown in the table, may be divided into two primary classes: (1) *errors immediately and adequately adjusted by the self-regulating power of the organism*; and (2) *errors not immediately and adequately adjusted*.

Errors which are immediately and adequately adjusted by the self-regulating powers of the organism cannot constitute primary factors of disease, although they may easily become important secondary factors, where pathological processes have already commenced. Of such a nature are a *deficient carbonaceous*, and an *excessive nitrogenous, intake*. In healthy organisms, the former will be associated simply with hunger which will lead to an increased intake: the latter, with commensurately increased nitrogenous excretion (§ 5).

Errors which are not immediately and adequately adjusted by the self-regulating powers of the organism may constitute primary factors of disease. Of such a nature are a *deficient nitrogenous*, and an *excessive carbonaceous, intake*.

§ 202. DEFICIENT NITROGENOUS INTAKE.—Whilst a large section of the medical profession has long concerned itself with inveighing against the vice of excessive meat eating, a smaller but increasing section has taken up an opposite position, and is commencing to prescribe an excess of proteid as a temporary therapeutic measure in many diverse pathological conditions.

TABLE III

Advancing civilization, involving the decay of instinct, imperfectly compensated by growth of reason and knowledge

Fundamental dietetic errors

Errors immediately and adequately adjusted by the self-regulating powers of the organism

Errors not immediately and adequately adjusted

Deficient carbonaceous intake, adjusted by hunger

Excessive nitrogenous intake, adjusted by commensurate nitrogenous excretion

Deficient nitrogenous intake

Excessive carbonaceous intake

Adjustment to the deficiency (?)

Adjustment inadequate

Malnutrition of the tissues of the digestive organs, leading to reduced absorption of carbonaceous material (carbonization) and reduced nitrogenous absorption

Malnutrition of the general nitrogenous tissues, leading to deficient physiological decarbonization

Hyperpyraemia

Evolutionary adjustment to the excess, probably by diminished absorption

Evolutionary adjustment inadequate

Adjustment by the individual organism

Adjustment by the individual organism inadequate

Hyperpyraemia

Incidental adjustment, e.g. pregnancy and various pathological processes

Adjustment attributable to the carbonaceous excess

Restriction of income

Increase of expenditure

Some functional and structural disorders of the alimentary canal, such as primary oral, gastric and intestinal, dyspepsia: protests against excessive supply and barriers against excessive intrusion (Chap. II).

Digestion and absorption restricted by physiological distension of the liver (Chap. III).

Increased katabolic decarbonization or combustion, either direct or through increased muscular exertion, in both cases compensated by increased heat-loss (Chap. IV).

Increased anabolic decarbonization, especially fat-formation (Chap. V).

Increased haemorrhagic decarbonization or menstruation (Chap. VI)

In an editorial entitled 'The¹ Food Factor in Education,' the 'British Medical Journal' voices a growing conviction that the train of symptoms, occurring in the young, which is commonly ascribed to 'overpressure' or overstrain of the mental faculties, and which is observable with increasing frequency of recent years, is, in reality, dependent upon insufficient nourishment. 'In these cases symptoms distinctly referable to the nervous system are those most frequently encountered, but muscular weakness, accompanied by more or less anaemia, is scarcely less common; while a disturbance of the digestive organs is often met with, which no care can prevent from constantly recurring, although it may be relieved at the moment by appropriate treatment.' The writer appends a series of tables of school dietaries. From a study of these, he draws the following, amongst other, conclusions:—that in English girls' boarding schools 'the quantity of meat supplied would seem to be far too little'; and that in 'most public schools the defects are similar . . . namely, a very insufficient quantity of meat and nitrogenous food.'

The causes which lead to a deficient nitrogenous intake are various. Those who are very poor find it difficult to obtain a sufficiency of meat or other animal food, the main sources of nitrogen: such are apt to live almost exclusively upon the cheaper carbohydrate food-stuffs, some of which, it may be mentioned, have, through modern methods of manufacture, become deprived of much of the nitrogenous material they naturally contain. But poverty is by no means the only cause of deficient nitrogenous intake: many persons at the present day, especially women, habitually eschew meat and animal food, whether they are influenced thereto by taste, by sentimental motives, or by pseudo-scientific theories: this, I am inclined to think, is especially true of the tropics and hot climates generally.

§ 203. The effects of a deficient nitrogenous intake will vary according to many circumstances. Individuals seem to differ widely as regards the amount of proteid essential for the maintenance of perfect health. We have seen that nitrogenous equilibrium is possible with the most different amounts of proteid in the food (§ 4); and it is not unreasonable to suppose that with some races, whose environment has for long periods

¹ *Brit. Med. Journal*, April 4, 1903, pp. 798, 799.

precluded an abundance of nitrogenous food, the organism has undergone, through natural selection, a process of gradual adjustment, more or less perfect, so that what would be in other races a deficiency is with them a sufficiency.

In the absence or inadequacy of such adjustment, a deficient nitrogenous intake will lead to malnutrition of the nitrogenous tissues, and this will involve impairment of function. But the effect upon the carbon contents of the blood will vary according as the functional impairment bears preponderatingly upon the carbonizing, or upon the decarbonizing, functions.

§ 204. Should the carbonizing functions be preponderatingly impaired, the carbon contents of the blood will tend to fall through restriction of income: should the decarbonizing functions be preponderatingly impaired, the carbon contents of the blood will tend to rise through restriction of expenditure. But such restriction of expenditure may not be due solely to the direct influence of impaired nutrition of the fixed nitrogenous tissues. 'It has¹ been proved that, with a diet composed of exclusively non-nitrogenous food, the percentage of haemoglobin in the blood undergoes a notable diminution' (B. Yeo); diminution of haemoglobin will involve impaired oxygen-carrying power on the part of the blood; and this will add to any already existing deficiency of combustion or katabolic decarbonization. The fact that deficiency of proteid intake tends to cause anaemia, as well as deficient fat-formation, whether through deficiency of supply or through deficiency of anabolic capacity, possibly explains an observation of Weir Mitchell,² that anaemic obesity is a rare condition. It must be admitted, however, that minor grades of *embonpoint* are common in anaemia, witness the plumpness of chlorotic girls.

Conformable with the deductions just made as to the varying influence of deficiency of proteid upon the carbon contents of the blood, are numerous clinical observations that the affections, which are regarded in this work as manifestations of hyperpyraemia, are in some cases averted or relieved, in others precipitated or accentuated, by a reduction of the proteid intake (§§ 342 to 345 inc.). Manifestly, in such cases, there must be other factors which determine the preponderating incidence of the malnutrition; but, as to the

¹ *Food in Health and Disease*, B. Yeo, 1897, p. 460.

² *Fat and Blood*, 1900, p. 24.

nature of such determining factors, I must freely admit I have no knowledge.

§ 205. A deficient nitrogenous intake, having for its preponderating effect deficient decarbonization by the tissues, seems to me one of the most important modes of origin of hyperpyraemia. Many women of the poorer classes, needlewomen and such like, who subsist for the most part upon bread-stuffs, tea, and sugar, suffer from recurrent bilious attacks, migraine, neuralgia, etc., affections which will be regarded in many cases as manifestations of hyperpyraemia; and the same is true, to some extent, of women of all classes, especially of those who live in warm countries. All such tend to be anaemic and thin; and they contribute largely to the roll of neurasthenics.

§ 206. EXCESSIVE CARBONACEOUS INTAKE.—It will not, I think, be difficult to show that advancing civilization tends generally towards an increased carbonaceous intake. Civilized communities draw the two most important classes of their food-stuffs, proteids and carbohydrates, in the main from the animal and vegetable kingdoms respectively. Increasing knowledge has modified both considerably. Scientific breeding has improved the quality of meat, and modern culinary art has rendered it much more palatable and, perhaps, more digestible. The carbohydrate food-stuffs have become, through modern methods of manufacture, more refined and less bulky, because more freed from indigestible material. Such changes, together with diminished cost, all tend to increased intake. The number, not less than the cheapness, of carbohydrates tends to increase. Sugar, as a common article of diet, is comparatively new, and there can be no doubt that its consumption is enormously increasing. The cheapness of sugar involves the cheapness of jam and of confectionery generally, the use of which articles of diet continually increases; and it may be remarked that excess in the soluble carbohydrates is especially likely to be associated with excess absorption, since such food-stuffs call for but little digestive preparation.

§ 207. We may conclude, therefore, that civilization, by adding to the pleasures of the table, has resulted in the regulation of the intake by *taste*, rather than by *hunger*, and so has destroyed the accuracy of the relation between supply and demand—in other words, that we have lost in great part

through civilization the conservative influence of a coarse and monotonous dietary. Russell H. Chittenden says: ¹—‘Sir William Roberts has well said that the palate is the dietetic conscience, but he adds that there are many misfit palates, and we may well query whether our dietetic consciences have not become generally perverted through a false mode of living. The well-nigh universal habit of catering to our appetite on all occasions, of bowing to the fancied dictates of our palates even to the extent of satiety, and without regard to the physiological needs of the body, may quite naturally have resulted in a false standard of living in which we have departed widely from the proper laws of nutrition.’

§ 208. It is not, I think, often possible to throw the blame for hyperpyraemia upon any one class of food-stuff. It seems improbable that fats are in general largely responsible, if only for the reason that they do not conduce to excess, at any rate, in temperate and tropical climates; and it may be that some fats are more readily assimilable by the tissues than other carbonaceous foods (compare § 126). It seems probable that carbohydrates are often largely responsible: at least, there can be little doubt that excess in carbohydrates is a common food fault, especially with women and children.

Two thirds of proteid are carbonaceous, and an excessive proteid intake may theoretically involve an excessive carbonaceous intake; yet, practically, bulk and monotony would preclude such excess. Were it probable, however, for an excessive carbonaceous intake to occur on a purely proteid diet, hyperpyraemia could hardly result, because of the largely increased katabolic decarbonization incited thereby (§ 16). Still, the amount of proteid in a mixed diet is, as we shall see, an important factor in conducing to hyperpyraemia, through its influence on the digestion and absorption of carbonaceous material.

§ 209. The nature of the articles of diet which contribute to the carbonaceous excess will have considerable influence. Sugar is, perhaps, the worst article of diet: it is very liable to be taken in excess: it needs little digestive preparation; and it is one of the few substances which undergo absorption from the stomach (Schäfer).² On the subject of ‘sugar-gluttony,’ Pro-

¹ ‘Physiological Economy in Nutrition,’ Russell H. Chittenden. *Popular Science Monthly*, June 1903, p. 124.

² *Text-book of Physiology*, Schäfer, 1898, vol. i. p. 432.

fessor Ogston expresses himself with no uncertain voice.¹ 'He had had many years of medical experience among children who, though not actually delicate, were not of the strongest constitution, and he was persuaded that to such children the present-day gluttony of sugar was a real and spreading evil. There were some children in whom the tendency to sugar-gluttony had become so strong that their infatuation for it resembled the craving of the drunkard for his dram. Such saccharo-maniacs showed early disappearance of the teeth from decay. Edentulous subjects were to be found in large numbers among adolescents, particularly in towns where, in contrast to what was the case a generation ago, there had sprung up a gigantic trade in all kinds of sweet-stuffs, so cheap as to be within the means of all, and of a nature to constitute a serious danger to the rising generation; and he would not be surprised if future observers were to place the evils of sugar-gluttony on a pedestal as conspicuous as the drink question in causing deterioration of individuals and races. It would be of no small benefit if measures could be devised to mitigate this danger to school children.'

Alcohol is not always regarded as a food, yet it contributes to the production of hyperpyraemia: it needs no digestive preparation; and 'it is said² to lessen the amount of carbon dioxide in the air of expiration' (Parkes) probably by retarding combustion. A combination of sugar and alcohol would seem to be peculiarly deleterious, both *à priori* and from observation. Alcohol³ has been shown to promote the absorption of sugar from the stomach (Schäfer), and port wine—containing as it does glucose, the form of sugar which needs the least digestive preparation for absorption—is notoriously the worst of all beverages in at least one affection due to hyperpyraemia, namely gout.

§ 210. The effects of an excessive carbonaceous intake will vary with many circumstances. Many Asiatic and other races consume carbohydrate material, much in excess of their demands for heat and force-production, and apparently in excess of their fat-forming capacity; and it is not unreasonable to suppose that, in such races, the organism has undergone, through

¹ *Brit. Med. Journal* February 6, 1904, p. 330.

² *Practical Hygiene*, Parkes, 1891, p. 336.

³ *Text-book of Physiology*, Schäfer, 1898, vol. i. p. 432.

natural selection, a process of gradual adjustment to the excess. Such adjustment would in all probability be by means of restricted absorption, so that much of the excess merely passes through the alimentary canal.

§ 211. In the absence or inadequacy of *evolutionary adjustment*, adjustment may occur by the individual organism. This may be *incidental*—it may depend, that is to say, upon causes other than the carbonaceous excess. An example is the physiological process of utero-gestation: many women enjoy perfect health only during pregnancy. Other examples are physiological conditions, such as hard physical exercise, exposure to cold, etc., and various pathological conditions, such as the specific fevers to be considered later.

§ 212. In the absence of incidental adjustment, adjustment may be secured by processes dependent upon the carbonaceous excess; and such processes may operate *through restricting the carbonaceous income to the blood*, or *through increasing the carbonaceous expenditure by the blood*.

§ 213. The carbonaceous income to the blood may be restricted through the nature of the diet. Upon a mainly flesh diet, the amount of faeces discharged is much less than upon a mainly vegetarian diet. This is fairly conspicuous in man, but more so in the lower animals: 'flesh eating' animals pass but one stool in several days, whilst those whose food is restricted to vegetables pass several stools in every twenty-four hours (Schmidt and Strasburger). Now it is admitted that a vegetable diet promotes, through its bulk, increased intestinal peristalsis: this we are accustomed to ascribe solely to the indigestible material contained in such a diet. But there are grades of digestibility in all food-stuffs; and it seems not unreasonable to suppose that a diet, even if consisting in the main of material which is capable of complete digestion and absorption when taken in moderate or small amounts, will, when taken in considerable bulk, so increase peristalsis as to restrict absorption decidedly. If so, this would constitute an item (not, perhaps, a very important one) in the regulation of the carbon contents of the blood; and habitual constipation, which, we shall find, frequently accompanies and intensifies the manifestations of hyperpyraemia, would be in such cases an index of unduly rapid

¹ Review on *The Faeces of Man in Normal and Pathological Conditions*, by Professor Schmidt and Dr. Strasburger, *Brit. Med. Journal*, Feb. 1, 1902, p. 276.

or complete absorption.¹ It is on such grounds that the salutary influence of purgation in many hyperpyraemic conditions will be explained.

§ 214. In Chapter II, I have argued that some functional disorders of the alimentary canal, such as primary oral, gastric and intestinal dyspepsia, and even some structural degenerations, such as dental caries, may in some cases depend upon an excessive carbonaceous intake, and may be interpreted as protests against such excess. Such, it was suggested, may act to some extent as barriers against the intrusion into the blood of excessive carbonaceous material. These dyspeptic and degenerative conditions must, of course, be regarded as pathological, but it is convenient to refer to them here.

§ 215. All such primary apeptic conditions may, however, be absent, or, if present, inadequate. Then the liver may act as a second line of defence, checking through the glycogenic distension, which itself depends upon absorption, the further digestion and absorption of carbonaceous material in the alimentary canal, and so restricting the carbonaceous income to the general circulation, as argued in Chapter III.

§ 216. Failing restriction of income, the organism will be driven to secure adjustment by increased expenditure. This it may achieve in several ways.

§ 217. As argued in Chapter IV, *katabolic decarbonization or combustion* may be increased either directly—combustion increased in accordance with the demand for decarbonization—or indirectly, through increased physical exercise—combustion increased in accordance with the demand for energy-production.

§ 218. ANABOLIC DECARBONIZATION may be increased commensurately, as argued in Chapter V. This applies mainly to *fat-formation*, the most important of the physiological anabolic decarbonizing processes; but the minor members of the same class, such, for example, as sebum-formation, may often be observed to share concurrently in the decarbonization (§§ 833, 834).

§ 219. Finally, a portion of the excess may be got rid of by an increase in the periodic process of *haemorrhagic decarbonization* or menstruation: we have seen in Chapter VI that menstruation tends to vary directly with the supply of food, and inversely with the rate of combustion and fat-formation.

¹ The excess absorption associated with habitual constipation has been demonstrated experimentally by Baron Oefele, *Brit. Med. Journal*, Jan. 7, 1905, p. 24.

§ 220. The increase of function, which is attributable to, and compensatory of, an excessive carbonaceous intake, will vary widely with the individual in accordance with his individual capacities and proclivities: compensation may be by restriction of income, by increase of expenditure, or by any combination thereof.

§ 221. Alternation in these various processes, whereby adjustment to the excess of carbonaceous material is secured, may often be observed in the individual at different periods of his lifetime; and such alternations are as true, and nearly as conspicuous, as the alternations of the similarly acting pathological processes to be considered hereafter (§ 341). As examples of the alternation of the above physiological processes may be mentioned the alternations between menstruation and pregnancy, between menstruation and combustion, between menstruation and fat-formation, between combustion and fat-formation, and between restriction of the carbonaceous income and any of the above. All these have been already referred to.

§ 222. Failing evolutionary adjustment and adjustment by the individual organism, whether incidental or attributable to the carbonaceous excess, an excessive carbonaceous intake will result in hyperpyraemia. Hence we return to the general statement that hyperpyraemia arises through an imperfection in the balance between the carbonaceous income and the carbonaceous expenditure of the blood, whereby the former exceeds the latter. But since, in addition to the supply of carbonaceous material, the income depends upon the carbonizing functions and the expenditure upon the decarbonizing functions, it may be said, in still more general terms, that hyperpyraemia arises through a faulty relation between supply and function; and that, in any individual case, the primary fault may concern the one or the other.

§ 223. In Table III, the influence of faulty supply has been set forth under the head of *excessive carbonaceous intake*: and so, under the head of *deficient nitrogenous intake*, has the influence of faulty function, in so far as this is due to this particular dietetic error. But faulty function depends upon many conditions other than dietetic errors; wherefore, it will be well to consider the functional factors of hyperpyraemia more fully.

FUNCTIONAL FACTORS IN HYPERPYRAEMIA

§ 224. Since hyperpyraemia depends upon an imperfection in the balance between the carbonaceous income and the carbonaceous expenditure of the blood, whereby the former exceeds the latter, it follows that the functional factors concerned may consist of a relative excess of the carbonizing functions or of a relative deficiency of the regulative and decarbonizing functions. The carbonizing functions are the functions of digestion and absorption in the alimentary canal: the regulative function, referred to here, is the glycogenic function of the liver; and the decarbonizing functions comprise combustion, fat-formation, etc., and menstruation (katabolic, anabolic, and haemorrhagic decarbonization). It seems probable that variations of capacity in any of these functions may be to some extent due to hereditary influences.

§ 225. A POWERFUL DIGESTIVE AND ABSORPTIVE CAPACITY.—If, as already argued, primary dyspepsias, oral, gastric, and intestinal, together with some degenerative conditions, such as dental caries, may be preventive of hyperpyraemia (§§ 41, 49 and 54), then the absence of such affections may conduce to hyperpyraemia. Now the absence of such affections is amongst the most powerful factors of strong digestive and absorptive capacities; and we shall find that, in many of the most marked cases of hyperpyraemia, the teeth and gums are in excellent condition and the digestive powers conspicuously strong.

§ 226. But digestion and absorption depend, as pointed out (Chapter II), *inter alia*, upon the supply of proteid: hence the proteid intake becomes an important factor of hyperpyraemia; and, as we shall see later, a diminution of the proteid intake may render less frequent and severe, an increase may render more frequent and severe, some of the manifestations of hyperpyraemia (§ 343).

§ 227. Further, the efficiency of digestion and absorption depend, to a large extent, inversely upon the degree of glycogenic distension, and this, *inter alia*, upon the efficiency of hepatic glycogenesis. Hence deficient hepatic regulation, as pointed out in the succeeding paragraph, may be an important factor in hyperpyraemia.

DEFICIENT HEPATIC REGULATION.—It has been argued that the glycogenic function of the liver acts as a safeguard against hyperglycaemia, as a regulator of the general nutritious income from the alimentary canal, and probably also as a regulator of the food intake, through its influence upon the appetite (§ 67). Now it is obvious that, if this function acted as a perfect regulator in all these respects in all cases, hyperpyraemia, any more than hyperglycaemia, could not arise. Hence we must postulate a certain deficiency of this regulating function as an essential factor in all cases of hyperpyraemia.

§ 228. The relation of increased glycaemia to hyperpyraemia must remain doubtful, since the chemistry of the latter is unknown. Clearly, hyperglycaemia is not identical with hyperpyraemia, since the former leads presumably in all cases to glycosuria; and we shall have to regard glycosuria, in most cases, as a means of dispersing hyperpyraemia, substitutive of pathological distension of the liver by glycogen, and of the various pathological conservative processes of which such hepatic distension is the instrument (§ 269). Nevertheless, these considerations do not preclude us from regarding sugar in the blood, in quantity less than the amount required to cause glycosuria, as a constituent of the hyperpyraemic accumulation.

As already pointed out on the authority of Pavy, the glycogenic capacity of the liver may be present in all grades, between that which pertains to the healthy state and the condition in severe diabetes. But, of the factors responsible for the deficiency, little seems to be known. These will be referred to in Chapter XVII.

§ 229. DEFICIENT KATABOLIC DECARBONIZATION OR COMBUSTION.—It has been argued in Chapter IV that combustion depends upon (1) a vital capacity of the nitrogenous tissues, in part inherent, in part dependent on nitrogenous nutrition, and probably in part on other conditions: (2) the supply and absorption of oxygen, which is dependent on many conditions, such as the intake of fresh air, the integrity of the respiratory and circulatory mechanisms, the amount of haemoglobin in the blood cells, the number of the blood cells, etc.: (3) the necessity for force and heat-production, which is dependent upon muscular activity, external temperature, etc.: and (4) the necessity for decarbonization. The last of these does not concern us here, since its absence cannot of course lead to

hyperpyraemia. But, in the case of all the rest, the absence or inadequacy of any of the contained factors may contribute materially to hyperpyraemia, should compensation in other directions be inadequate.

§ 230. An *inherently deficient* combustion capacity on the part of the tissues is probably present in some cases; but it is obviously impossible to dilate upon its causation or to measure its influence in conducing to hyperpyraemia. Deficient combustion capacity, dependent on malnutrition, probably arises in many ways. In so far as it depends upon deficiency of proteid in the diet, it has already been sufficiently considered (§ 103). But it may depend (as pointed out in § 104) upon the exaggerated nitrogenous disintegration of pyrexia: hence it is to be anticipated that hyperpyraemia will be peculiarly liable to arise during the convalescent stage of fever; and we shall find indeed that many of the clinical manifestations of hyperpyraemia date from this period.

§ 231. One of the most important, because commonest, causes of deficiency of combustion is simply age. It is probable that, with advancing years, the combustion capacity of the tissues, in common with other capacities of the organism, tends to wane progressively: such doubtless is largely inevitable. But some of the deficiency of combustion, which is so potent a cause of disease in middle and old age, is largely avoidable and depends merely on insufficient physical exercise. Hence the commencement of hyperpyraemic ill-health (for example, some of the manifestations of so-called irregular gout) is not infrequently contemporaneous with retirement from business, an event in male life which has aptly been compared to the menopause in women.

Consistent with waning combustion is the clinical observation that a healthy old age demands great moderation, not only in drink, but in food. Though probably more necessary now than ever, this advice can hardly be considered new. Hippocrates said: ¹—‘In old persons the heat is feeble, and therefore they require little fuel, as it were, to the flame, for it would be extinguished by much. On this account also fevers in old persons are not equally acute because their bodies are cold.’ The ancient physician perceived very clearly that heat-production depended fundamentally on two factors, namely,

¹ *The Genuine Works of Hippocrates*, Adams, Section I, Aphorism 14, p. 197.

capacity for combustion on the part of the organism (function) and fuel (supply). Can the same be said of us modern physicians in all cases? Are we not at times open to the charge of overlooking the former?

§ 232. It seems highly probable that chronic lead-poisoning acts by damaging the metabolic capacities of the tissues. Oliver says: ¹—‘Whatever view we take of the pathology of plumbism, it must be admitted that lead rapidly deranges metabolism.’ If we are permitted to assume that the metabolic derangement is of the nature of retardation, we shall be enabled to account for many of the phenomena of plumbism. For any retardation of metabolism, whether of katabolism, of anabolism, or of both, will tend, other things equal, to an accumulation in the blood of material, of which a part will be carbonaceous; and thus will be established, *inter alia*, hyperpyraemia.

The mechanism of the retardation of metabolism is doubtless complex. Broadbent says: ²—‘Probably the formation of compounds of organic matter with lead salts, albuminates of lead too stable to undergo readily dissociation and oxidation, is the cause of accumulation of imperfectly oxidized products in the blood.’ But plumbism probably leads also in a less direct manner to hyperpyraemia. Ewing says: ³—‘In cases of chronic lead poisoning the blood commonly shows a moderate grade of secondary chlorotic anaemia. . . . This anaemia is commonly attributed to gastro-intestinal disturbance, but Hayem referred it to destruction of cells from direct action of lead.’ But, however induced, anaemia, as I shall argue presently, tends to retarded combustion or katabolic decarbonization, and so to hyperpyraemia.

Conformably, we shall find that many, if not most, of the clinical manifestations of plumbism resemble very closely, if they are not identical with, the clinical manifestations of hyperpyraemia.

§ 233. The influence of a deficiency in the supply of oxygen to retard combustion is seen in a variety of circumstances. Many sufferers from chronic bronchitis and emphysema, and even from very chronic non-pyrexial phthisis, show the signs of deficient combustion; and they are all liable to high pressure in

¹ Clifford Allbutt's *System of Medicine*, vol. ii. p. 984.

² *The Pulse*, W. H. Broadbent, 1890, p. 159.

³ *Clinical Pathology of the Blood*, James Ewing, p. 97.

the arterial system (Broadbent),¹ a phenomenon to be ascribed later to hyperpyraemia. For similar reasons, persons suffering from chronic cardiac affections are liable to develop hyperpyraemia: this may be inferred from the benefit which accrues sometimes in such cases from restriction of the carbonaceous intake (Case LXXXIII).

A deficiency of haemoglobin, the oxygen carrier of the blood, involves a deficient supply of oxygen to the tissues: this will lead to deficient combustion, through deficient 'draught' so to speak; and the result may be hyperpyraemia. Hence in chlorosis and anaemia, however induced, many of the clinical manifestations of hyperpyraemia, such as paroxysmal sick headache, may arise, and they may be dispersed by the cure of the anaemia by iron or other appropriate remedies; and Broadbent² has called attention to the high pulse-tension of many anaemias. Though haemorrhage is a decarbonizing process and gives immediate relief from most of the manifestations of hyperpyraemia, yet profuse or repeated haemorrhage leads to anaemia, and thereby possibly to hyperpyraemia. Accordingly we shall find that some of the recurrent manifestations of hyperpyraemia are apt to commence or become intensified, after the occurrence of exhausting haemorrhage; for example, some cases of migraine date from severe post-partum haemorrhage (Anstie).

§ 234. It has been argued that civilization tends on the average to increase the carbonaceous intake. Were this accompanied by a corresponding increase in the organism's demand for fuel, probably but little harm would result; but the opposite is true. As all will admit, civilization tends towards the substitution of mental for physical energy. Manual labour is daily being replaced by machinery; and out-door industries are giving way to employments entailing more sedentary employment in heated workshops. Thus is diminished the demand for fuel for both force and heat-production; and thus are increased the chances of hyperpyraemia.

The influence of deficient muscular activity is very conspicuous clinically: many of the manifestations of hyperpyraemia, we shall see, date from the sudden cessation of an accustomed exercise.

§ 235. The influence of deficient exposure to cold may

¹ *The Pulse*, p. 161.

² *Ib.* p. 160.

be inferred from the not infrequent development of hyperpyraemic disorders in persons who have removed to the tropics from cooler climates in which they had enjoyed perfect health, and from the highly beneficial effect upon such disorders of the opposite climatic change.

It cannot be maintained, however, that thermic variations are the only active factors in climatic influence: the amount of aqueous vapour in the atmosphere will have an important action. If, as most physiologists are inclined to assume, there is a direct relation between heat-loss and heat-production, then any circumstance which interferes in any way with the former will tend to reduce the latter. Evaporation of the water of respiration and perspiration is one important means of heat-loss: the rate of evaporation will depend, *inter alia*, upon the dryness of the air: hence humidity will tend to retard heat-loss. Usually, perhaps, such diminished loss is compensated by increased loss in other ways, such as conduction and radiation; but it is conceivable that such compensation may be inadequate; and then, for the maintenance of a constant temperature, a diminution of heat-production will be demanded. Diminished heat-production means diminished combustion, and this, in some circumstances, may determine hyperpyraemia. Whether this argument is valid or not, there can be no doubt that, of two equally warm climates, the more humid conduces more frequently to many hyperpyraemic disorders, such as bilious attacks, migraine, etc.

§ 236. Bouchard has raised deficient combustion to the rank of a diathesis—the ‘*diathèse bradytrophique*.’ This he regards as the underlying factor in a long list of morbid affections, a list which is, for the most part, identical with the list of affections which are here ascribed to hyperpyraemia. But to ascribe all these to deficient combustion alone is, according to my view, an incomplete generalization; for hyperpyraemia may arise through excessive income or through deficient expenditure; and deficient combustion, though a very important, is but one, variety of deficient expenditure.

§ 237. DEFICIENT ANABOLIC DECARBONIZATION, ESPECIALLY FAT-FORMATION.—The anabolic deficiency, wholly or partly responsible for hyperpyraemia, concerns mainly the fat-forming capacity. Every physician is acquainted with the individual who lacks the capacity to form fat in any appreciable degree.

Murchison says :¹—‘Some persons . . . consuming much fat as well as saccharine and starchy matter remain permanently thin.’ Other physicians refer to such cases, but seem to regard them in the light of physiological curiosities. Robert Hutchinson,² one of the most recent writers on dietetics, says :—‘One does seem to meet with cases in which, owing probably to some failure of assimilative power, it is found to be very difficult to achieve the laying on of fat, even although a considerable surplus of food is supplied.’

The failure of fat-formation in such cases is not always ascribed, as in the above quotation, to a failure of assimilative power. In too many cases, I think, we are apt to assume that the carbonaceous excess is unabsorbed and merely passed through the alimentary canal—that the failure is one of supply. This is doubtless true of many, especially of those who manifest dyspeptic symptoms ; but that it is true of all is highly improbable.

Many habitually lean persons have excellent appetites and powerful digestions: of them it is commonly remarked that ‘their food does not do them any good.’ Amongst them are to be found the individuals (referred to in § 140) who are constantly restless and active, and who thus avert hyperpyraemia and maintain their health by substituting exaggerated katabolic for deficient anabolic decarbonization. But other lean persons take little exercise ; and such, if not endowed with an inherently high combustion rate, will be especially liable to develop hyperpyraemia through slight carbonaceous excess.

Since we are ignorant in great part of the conditions which influence the power to construct fat, it will be impossible to enumerate fully the factors which conduce to a deficiency of this capacity. It would seem that the deficiency is often inherent, if not hereditary, but it is certainly ascribable in many cases to malnutrition of the active nitrogenous tissues. Hence it may be due to a deficiency of proteid in the dietary, and it may be dispersed by an increase thereof. And it is highly probable that the special tendency to hyperpyraemia, characterizing the convalescent stages of fever and hitherto ascribed to deficient combustion capacity, is due in part to deficient fat-forming capacity, depending on the same

¹ *Functional Derangements of the Liver*, 1874, p. 47.

² *Food and the Principles of Dietetics*, 1900, p. 489.

condition, namely malnutrition, of the fixed nitrogenous tissues. At any rate, I have never yet observed the post-pyrexial slow high-tension pulse in cases which were rapidly accumulating fat.

In most cases, however, I think it must be admitted that the fat-forming capacity of the nitrogenous tissues is less damaged by pyrexia than the capacity for combustion; and that during convalescence the former usually takes a relatively larger share in decarbonization than the latter. Hence quite commonly there arises at this period a considerable degree of obesity; and this may then be regarded as an indirect result of retarded combustion.

§ 238. We have now to face a difficulty which we shall frequently encounter hereafter. Why does not the exaggerated nitrogenous disintegration of pyrexia, responsible for the reduction of the decarbonizing capacities, katabolic and anabolic, reduce proportionately the carbonizing capacities of the digestive organs? Probably in the majority of cases it does so: hence the fact that convalescence is usually uncomplicated by the manifestations of hyperpyraemia. And we can only assume that in the minority, in which such complications arise, unknown factors have intervened and determined the disproportionate reduction of the decarbonizing capacities.

Conformably with the decarbonizing influence of fat-formation, we shall find that the disorders of hyperpyraemia are far more easily dispersable by reducing the carbonaceous intake, or by increasing the carbonaceous expenditure, in persons with a tendency to corpulence, than in those who are lean. This is a general rule to which there seem to be few, if any, exceptions.

§ 239. DEFICIENT HAEMORRHAGIC DECARBONIZATION OR MENSTRUATION.—It has been argued sufficiently already that absent or deficient menstruation, dependent upon any cause other than the absence of the carbonaceous surplus, may be a factor in hyperpyraemia, since it will intensify the tendency to carbonaceous accumulation which is normally recurrent towards the end of each intermenstrual period; and that hyperpyraemia, so arising, is especially frequent at puberty and the menopause (§§ 174 to 177). Hence the pathological phenomena so often observed at these and other periods, whenever the menstrual flow is suppressed or becomes inadequate—phenomena which

may for the most part be explained by hyperpyraemia or by subordinate pathological distension of the liver by glycogen or pathological vaso-motor action (§§ 458 to 460).

§ 240. A full knowledge of the protean manifestations of hyperpyraemia is of the greatest practical utility in clearing up the diagnosis in cases of suspected pregnancy. The absence of hyperpyraemic manifestations associated with one or two missed menstruations is probably not of very great value, since there are so many alternative means in the domain of pathology which reduce pyraemia; but the presence of hyperpyraemic manifestations, *especially if these have arisen simultaneously with the amenorrhoea*, must be regarded as strong evidence against pregnancy. And generally, hyperpyraemic manifestations if present will serve to distinguish amenorrhoea due to imperfect discharging capacity from amenorrhoea due to absence of the carbonaceous surplus.

§ 241. MENTAL STRAIN AND PSYCHICAL FACTORS.—It will be pointed out on many occasions later, that conditions, such as prolonged study or continued overwork of the brain, are notoriously efficacious in precipitating the manifestations of hyperpyraemia, especially migraine and headaches generally; and I shall argue that such conditions operate, in great part, indirectly through diminished physical exercise and consequent diminished katabolic decarbonization. But we shall be by no means justified thereby in excluding more direct influences.

Carpenter says:¹—‘That the secretion of gastric juice is affected in a very marked manner by conditions of the nervous system, is indicated by the effect of mental emotions in putting an immediate stop to the digestive process, when it is going on in full vigour.’ As a result, dyspepsia, vomiting, or diarrhoea may arise. The influence of emotion upon the secretion of the gastric juice has recently been demonstrated by Pawlow. Sudden emotion, such as fear, has long been known to cause marked and sudden modifications in the menstrual flow and in the secretion of the saliva, sweat, urine, and milk. Fright has caused jaundice and mental shocks have induced diabetes. On the other hand, relief from grief or anxiety, the confident expectation of cure, and faith in treatment, are therapeutic factors, the value of which there is no tendency to under-estimate.

Hence it seems by no means improbable that the more

¹ Quoted by J. M. Fothergill, *Indigestion and Bilioussness*, 1881, p. 85.

important of the physiological decarbonizing processes, combustion and fat-formation, are also susceptible of direct modification by various psychical conditions, especially those that are of a depressing nature ; and if so, then such psychical conditions will have an important place amongst the factors of hyperpyraemia.

Prolonged study, and other occupations involving the use of the eyes at close range, may also, as I shall argue (§§ 545 to 568), conduce to many of the manifestations of hyperpyraemia through eye-strain in those who suffer from ametropia. But eye-strain determines a mere 'relative hyperpyraemia,' which may, indeed, amount to no more than an actual hypopyraemia. Consequently, its real influence is in the direction of acarbonization, not of over-carbonization.

THE PRINCIPLES OF TREATMENT OF HYPER-PYRAEMIA

§ 242. On the view that hyperpyraemia arises through an imperfection in the balance between the carbonaceous income and the carbonaceous expenditure of the blood whereby the former exceeds the latter, the aim of treatment will be the restoration of the balance. This might be achieved by increasing the expenditure, by restricting the income, or by both methods in combination. In practice, we shall find it expedient to use various combinations of these methods. Meanwhile, they may be considered separately.

§ 243. TREATMENT OF HYPERPYRAEMIA THROUGH INCREASED EXPENDITURE.—In order to increase the expenditure of carbonaceous material by the blood, it will be essential in the first place to maintain at a high level the decarbonizing capacities, both katabolic and anabolic, of the nitrogenous tissues. Such high functional capacity will imply due nutrition, and due nutrition will involve a due supply of digestible, absorbable, and assimilable proteid in the food. Hence meat, fish, and eggs are essential articles of diet. The proteid food-stuffs not only increase the capacity of the tissues for combustion, but directly increase the rate of combustion.

Katabolic decarbonization or combustion may further be greatly increased by systematic physical exercise, by due exposure to external cold, and by a due supply of oxygen in the

form of a maximum allowance of fresh air, day and night. In short, the modern open-air treatment of consumption, minus over-feeding, may be taken to embody most of the leading principles which should govern the attempt to increase the expenditure of carbonaceous material by the blood. Certain drugs, for example, arsenic and thyroid extract, are also probably useful in certain cases, and operate by stimulating the decarbonizing tissues.

In addition to katabolic and anabolic decarbonization, haemorrhagic decarbonization or menstruation will require attention during non-pregnant adult female life: conditions interfering with the due discharge of this function will have to be combated.

§ 244. TREATMENT OF HYPERPYRAEMIA THROUGH RESTRICTION OF INCOME.—We might seek to restrict the carbonaceous income to the general blood-stream by augmenting the regulating function of the liver, since, as has been argued (§ 65), the former depends inversely upon the latter. And this might well be the ideal treatment for hyperpyraemia in certain cases. But, unfortunately, we are for the most part ignorant of the factors which together constitute this regulating function. Therefore this method of restricting the carbonaceous income remains a future possibility and will not again be referred to in these pages.

§ 245. B. Moore says: ¹—‘Absorption of some substances begins in the stomach, but the main part takes place in the intestine.’ And since both the complete digestion and the absorption of carbonaceous material in the intestinal canal depend, other things equal, inversely upon the rate at which the chyme travels over the intestinal mucosae, it will obviously be possible to restrict the carbonaceous income by hastening the alimentary current. Now Lauder Brunton points out that ‘purgatives act both by increasing peristaltic action and intestinal secretion.’ ² Hence purgatives will hasten the alimentary current and so restrict the carbonaceous income. And, since the nutritive value of the intestinal contents diminishes progressively from above downwards, the greatest restriction of carbonaceous income from purgatives will follow such as act mainly upon the higher portions of the canal.

¹ *Text-book of Physiology*, Schäfer, 1898, vol. i. p. 482.

² *Pharmacology, Therapeutics and Materia Medica*, L. Brunton, 1885, p. 341.

Such a purgative is calomel, which, according to Lauder Brunton, has a 'peculiar stimulant action on the duodenum and ileum.'¹ Thus, in so far as concerns the carbon contents of the blood, a smart calomel purge will have an influence similar to that of abstention from food; but its action will obviously be more rapid. Conformably, we shall find that many sufferers from common hyperpyraemic affections, such as bilious attacks, recurrent headaches, asthma, etc., come to rely largely on purgatives, especially calomel, for relief; and that calomel is the purgative especially selected by Broadbent for the treatment of persistent high blood-pressure and its complications, conditions which will be ascribed later to unrelieved hyperpyraemia (§§ 727 to 753).

§ 246. Since the carbonaceous income to the general bloodstream depends primarily upon the efficiency of the carbonizing functions of digestion and absorption in the alimentary canal, we may seek to restrict the income by weakening these functions. We may proceed to this end in many ways. Dyspepsia is often an index of impairment of these functions; and dyspepsia might be deliberately induced in numerous ways. But I shall refer to one method only. We have seen that the efficiency of the functions of digestion and absorption depend largely and fundamentally, as indeed do all other functions, upon the supply of proteid in the food (§§ 55 to 60). It is open for us, therefore, to weaken these functions by restricting the proteid intake.

This method of dietetic treatment has been arrived at empirically, or, at least, upon hypotheses which we must regard as incorrect. Haig, on the hypothesis that most of the disorders here ascribed to hyperpyraemia depend upon uricaemia, cuts off the supply of meat, fish, and eggs, and relies for nitrogen mainly upon milk and cheese, which however he reduces to what he regards as the *physiological minimum*. Lauder Brunton, on the hypothesis that periodic headaches (migraine) depend upon toxic nitrogenous substances derived from flesh foods, reduces very largely the supply of meat. And many other medical writers, not to mention a large section of the general public, influenced by a diversity of motives, have inveighed strongly against the 'vice' of meat eating and advised generally a vegetarian dietary.

¹ *Pharmacology, Therapeutics and Materia Medica*, L. Brunton, 1885, p. 355.

Now there can be little doubt that, when such vegetarian or modified vegetarian diets are successful against hyperpyraemic disorders, they act by weakening the carbonizing functions of the digestive organs, and that the essential factor is the reduction in the proteid intake. Evidence in favour of this view will be adduced hereafter (§§ 342 to 345).

§ 247. But the most natural and least complex method of restricting the carbonaceous income to the general bloodstream is simply to reduce the carbonaceous intake. It is easy to over-stoke an engine, and the obvious remedy is to reduce the supply of fuel. Reduction of the carbonaceous intake is attained by cutting off or reducing the purely carbonaceous food-stuffs, the carbohydrates and fats, and throwing the onus of nutrition to a larger extent upon proteid—of which a portion only is carbonaceous—and upon green non-starchy vegetables—which contribute but slightly to the nutritious income, nitrogenous or carbonaceous.

§ 248. Reduction of the carbonaceous intake is the essential factor in several plans of dietetic treatment which have been arrived at empirically or upon various hypotheses. For gout, one of the affections to be ascribed to hyperpyraemia, Cantani¹ advises a moderate amount of nitrogenous foods, such as fish, eggs, and broth, with the free use of green vegetables and water; but he forbids all starchy and saccharine foods, alcoholic drinks, acid foods, milk and cheese. The dietetic plan pursued at Carlsbad, referred to already (§ 85), is not essentially dissimilar from Cantani's plan. And in the Salisbury treatment, which consists in limiting the dietary practically to lean meat, white of egg, and hot water, the purely carbonaceous intake is abolished.

§ 249. THE TWO DIETETIC METHODS, THAT BY REDUCTION OF THE PROTEID, AND THAT BY REDUCTION OF THE CARBONACEOUS, INTAKE, COMPARED.—I have little doubt that both these methods of dietetic treatment succeed in different cases in dispersing hyperpyraemia; but it is clear that they act in fundamentally different ways, the former by *weakening the carbonizing functions*, the latter by *diminishing the carbonaceous supply*.

The two methods may be compared from a theoretical standpoint. To the first there is a serious objection. A

¹ *Food in Health and Disease*, B. Yeo, 1897, p. 437.

reduction of proteid, which is capable of weakening the carbonizing functions of the digestive organs, will presumably, as already suggested, be capable of weakening the decarbonizing functions of the tissues. Hence we may have at least three possible results from such a line of treatment:—1. The carbonizing functions may be weakened preponderatingly: in this case hyperpyraemia will be relieved. 2. The carbonizing and decarbonizing functions may be weakened proportionately: in this case hyperpyraemia will be unaffected. 3. The decarbonizing functions may be weakened preponderatingly: in this case hyperpyraemia will be exaggerated. Manifestly there would be factors determining the different result in each case; but these seem quite obscure.

Parallel with these theoretical deductions, may be placed the following clinical observations:—The manifestations of hyperpyraemia, such for example as migraine, treated by reduction of proteid, are (1) in some cases relieved: (2) in others unaffected; and (3) in others again exaggerated. And, since the factors which determine these varying results are unknown, we shall be unable to foresee the effect of this method of treatment in any individual case. In effect, the grave disadvantage of the method is that the physician who uses it is largely at the mercy of these unknown factors.

§ 250. To the second method of treatment—the treatment by reduction of the carbonaceous intake—there are no such obvious theoretical objections. Here there is no question of weakened function in any direction. Indeed, if, as usually happens in this dietetic plan, the amount of nitrogenous food is somewhat increased, function of all kinds, and therefore both the carbonizing and the decarbonizing functions, will be strengthened. Increased decarbonization will directly reduce hyperpyraemia; while the increase of the carbonizing functions, which, under a diet containing a carbonaceous excess, would tend to increase hyperpyraemia, will, under vigorous restriction of the carbonaceous supply, be immaterial; and so, too, will any associated nitrogenous excess, since, as pointed out (§ 5), nitrogenous excretion is largely determined by supply.

The theoretical superiority of the treatment of hyperpyraemia by reduction of the carbonaceous intake is not more striking, in my opinion, than is its practical superiority (see Chapter XXVI and Appendix).

DIATHESES

§ 251. It has long been indistinctly perceived that a vast number of morbid conditions have mutual affinities and are banded together in some obscure manner ; and it is reasonable to believe that their bonds of union consist in some common factor in their etiology. Murchison, as we have seen, sought this common factor in functional derangements of the liver : others have sought it in dyspeptic conditions, or in toxic products resulting from dyspeptic conditions ; but more commonly it has been sought in some diathetic tendency of the individual, inherent or acquired. So we have the 'arthritic,' 'herpetic,' 'uric acid,' and 'gouty' diatheses, and many more. But the absence of any marked predilection for any particular type has always proved a stumbling-block in the correlation of these diseased states by the aid of diathetic theories. Ewart says : ¹—'The supposed gouty diathesis cannot without strain be made to fit such opposites as the over-fed, full-blooded, and plethoric, and the thin, half-starved subject, the scrofulous and the nerve-ridden patient' ; and he concludes that the attempt to find a common factor in diatheses of any sort leads only to chaos.

But if, as is proposed in this work, we substitute the humoral condition hyperpyraemia as the common factor, the difficulties of correlation will largely disappear. For the co-operating factors responsible for hyperpyraemia are, as we have seen, numerous and varied, and may be combined in groups of various sizes and great diversity : the condition may affect persons of the most diverse pathological proclivities, living in the most diverse environments. Therefore, we shall be prepared to find that the clinical manifestations of the condition are extremely varied, and observable in individuals of the most different types, habits, and constitutions.

Obviously, under diathetic theories, the common factor concerns *function* : under the hyperpyraemic theory, the common factor concerns *supply*. Under the latter, the functional factors are individual, determining and differentiating.

¹ *Gout and Goutiness*, 1896, p. 9.

SUMMARY

§ 252. The present chapter is mainly an *à priori* argument intended to show that, in health, temporary variations in the carbon or fuel contents of the blood (pyraemic variations) are constantly occurring : that such variations are prevented from exceeding physiological limits by the capacities possessed by the organism for regulating supply by function and function by supply : that such capacities are limited and vary with the individual, and that, consequently, in certain circumstances, the carbon contents of the blood may exceed physiological limits and constitute hyperpyraemia : that hyperpyraemia may be regarded as due to a faulty relation between supply and function : that the primary fault may concern either supply or function ; and that hyperpyraemia may be treated successfully either by modifying supply, that is, by reducing the carbonaceous supply in many ways, or by modifying function, that is, by reducing the carbonizing functions or increasing the decarbonizing functions.

CHAPTER VIII

§§ 253-283

Pathological acarbonization—Bilious attacks—The paroxysmal neuroses : migraine or sick-headache : gastralgia : major epilepsy : asthma : catarrhal croup : angina pectoris : acute mania—Haemorrhage—Diarrhoea and lymphorrhoea—Glycosuria—Pyrexia : phthisis : acute gout : cyclic vomiting—Pathological anabolism—Summary.

§ 253. The conception that hyperpyraemia may be due to an inadequacy of physiological function suggests the further conception that pathological action, or *pathological function* (so to speak), may come to the aid of, and reinforce, physiological function. This we shall find to be true ; and we shall also find that the pathological reinforcements referred to are, generally speaking, modelled upon the plan of the physiological processes which they supplement.

We have seen that, in health, the carbon contents of the blood are restrained within physiological limits by processes which restrict the income and by processes which increase the expenditure. So it will be found to be in disease. Hyperpyraemia may be dispersed by pathological processes which operate by restricting the income, by increasing the expenditure, or by both means combined. And, just as pathological hyperpyraemia may be presumably an exaggeration of physiological pyraemia, so the pathological processes referred to may be regarded *for the most part* as exaggerations of the physiological processes which normally reduce the carbon contents of the blood. Here, as elsewhere, strained physiological action graduates into pathological action.

§ 254. But, even in physiological processes, we have found it difficult to discriminate sharply between restriction of income and increase of expenditure : for example, in the menstrual process there are indications that income is restricted as well as expenditure increased. And in pathological processes, we shall find the difficulty accentuated, since, quite frequently,

both means are in operation simultaneously. Consequently, it will be convenient henceforth to be able to refer to all processes, physiological and pathological, which in any way tend to reduce the carbon contents of the blood, under the more comprehensive terms, '*acarbonization*,' and '*acarbonizing processes*.' Physiological acarbonization will include the normal regulation of the carbonaceous income, through physiological distension of the liver by glycogen, together with katabolic, anabolic, and haemorrhagic decarbonization within physiological limits. Pathological acarbonization will include a long and heterogeneous list of more complex processes, which are ultra-physiological and which operate by restriction of income, by increase of expenditure (either of these in several ways), or by some combination of these means. Some of these pathological acarbonizing processes will now be considered.

BILIOUS ATTACKS

§ 255. In considering their mechanism, bilious attacks were regarded as due to a pathological degree of glycogenic distension of the liver (§ 73). But if, as assumed, such a degree of glycogenic distension is an index of excessive carbon contents of the blood—or hyperpyraemia (§ 95), then we must believe that bilious attacks are adapted to reduce the humoral, not less than the hepatic, condition. And it is easy to see how a bilious attack is capable of reducing the carbon contents of the blood. Later, I shall argue that the proximate factor responsible for the climax of the glycogenic distension of the liver is a sudden stoppage of the reconversion of glycogen into sugar, brought about by vaso-motor action (§§ 442 to 453). Thus a bilious attack would imply cessation of the saccharine income to the general blood-stream; and, at the same time, the mechanical block in the portal circulation, introduced by the hepatic distension, would, as already argued, cause a material retardation, if not the complete stoppage, of the nutritious income of all kinds from the alimentary canal. But the mere continuance of life implies the continuance of combustion, and so the carbonaceous excess in the blood will, in the absence of fresh supplies, be steadily burnt off and eliminated as carbonic acid. The carbonaceous load being removed, the condition of the blood responsible for the glycogenic distension will have

been removed; and the liver will recommence to unload as under normal conditions.

THE PAROXYSMAL NEUROSES

§ 256. In many of these, acarbonization is achieved in the main by restriction of income: such are the disorders termed migraine or sick-headache and gastralgia (some cases).

§ 257. MIGRAINE.—In typical cases, anorexia is present from the commencement to the end of the paroxysm. The anorexia is indicative of the fact that digestion and absorption are in complete abeyance. Lauder Brunton says:¹—‘The changes in the nervous system associated with migraine appear to cause stoppage of the secretion of the gastric juice, so that the food taken at the onset of the headache is not digested. But if the headache has not begun until the digestive processes have taken place, the food, although partially digested, is still brought up. The reason for this appears to be partly that the process of absorption has been arrested and partly because the movements of the stomach itself appear to have ceased during the migraine, so that the food is not ejected from the stomach into the intestine.’ It would appear, indeed, that during migraine the stomach suffers temporary paralysis. Conformably, ‘Mangelsdorf’ (‘Berlin. Klin. Woch.,” November 2, p. 1004) in 1892 found that the stomach of a patient was much larger during an attack of megrim than it was the day before, and has since examined the stomach in every case of megrim he has seen both during and between the attacks. His observations show that in every case of megrim the stomach enlarges considerably during an attack and contracts again to its normal size in the intervals. But if the attacks are frequent the alternate relaxation and contraction leads in the course of years to loss of muscular tone and atony. . . . Megrim is a common *cause* of gastric atony.’ (Italics mine.) Mangelsdorf’s observations are of peculiar interest because many physicians have regarded gastric atony as an important *cause* of migraine. Haig³ points out the defective circulation in the glands and mucous membrane of the digestive system; also the fact that, in severe migraine, ‘drugs⁴ introduced into the stomach pro-

¹ *Actions of Medicines*, p. 394.

² *Medical Review*, January 1904, p. 35.

³ *Uric Acid in Disease*, 1897, p. 330.

⁴ *Ib.* p. 235.

duce absolutely no physiological effect and do not appear in the urine until the headache is passing off.'

Now, since many migraines commence in the early morning and abate only towards evening, during the succeeding night, or even later, it is clear that the diminution in the accustomed income may be considerable: indeed it may be that, for one or even more days, no food at all is taken. The hepatic mechanism, whereby the digestion and absorption of food is interrupted, has been considered in the case of bilious attacks (§ 73); and there can be little doubt that, in migraine, the more prominently nervous disorder, it is essentially similar.

§ 258. While income is thus restricted or inhibited, expenditure (katabolic expenditure or combustion, at any rate) proceeds probably at nearly its usual rate. This will be, in the first place, at the expense of the carbonaceous material which has already passed beyond the hepatic barrier, and at the expense, therefore, of the carbonaceous material accumulated in the general circulation. Thus the 'arrears of expenditure' are made up. Later, as pyraemia becomes reduced, the liver commences to unload and the glycogenic block is dispersed.

In children, it may be that combustion is increased, since pyrexia not infrequently accompanies the attack (Gowers);¹ and in a case (seen by me in consultation with Dr. Lilian Cooper of Brisbane) of nearly lifelong recurrent migraine, which underwent transformation into recurrent major epilepsy at the age of 62, each paroxysmal seizure (migrainous originally, epileptic ultimately) was accompanied by pyrexia, the temperature in the mouth usually registering 102° F. for a short time.

§ 259. It has been suggested that there is an increased bile-formation in the migrainous attack, since cases are recorded in which jaundice,² occurring at no other time, regularly followed attacks; and, since bile is a carbonaceous, no less than a nitrogenous, secretion, the withdrawal of its chemical antecedents in amounts above the average would aid in securing acarbonization. But exaggerated bile-formation seems highly improbable; and the bilious phenomena of migraine are fully explicable by a retention of bile in the ducts, brought about as in the ordinary bilious attack and succeeded by sudden evacua-

¹ *Diseases of the Nervous System*, Gowers, 1893, vol. ii. p. 845.

² Labarraque, quoted by Liveing, *Migraine and Sick-headache*, 1873, p. 232.

tion into the duodenum. Jaundice in some slight degree is, as Harley points out, an occasional sequel in subacute or recurrent biliousness (§ 75).

§ 260. That the anorexia is the chief salutary factor in migraine cannot, I think, be disputed. Cases of migraine are not rare in which anorexia is absent. These are usually old-standing cases, which have gradually ceased to be complicated with digestive symptoms; but in some cases these symptoms are absent from the outset. And it is significant that in neither instance are such attacks followed, as a rule, by the marked sense of well-being or by so definite a period of immunity as (we shall see later) characterize migraines associated with complete anorexia and nausea. Moreover, such cases tend to become increasingly frequent.

In one of my cases of this kind, headache had recurred every morning for several weeks, lasting till the late afternoon. The patient had an excellent appetite and digestion, and had been encouraged to live well. That the absence of anorexia was the element responsible for the continuance of the condition was shown by the effect of two days' starvation, which completely removed all pain.

§ 261. GASTRALGIA.—In this affection, complete anorexia and vomiting may occur: these insure restriction of the carbonaceous income. In one of my cases, the attacks lasted forty-eight hours, and were associated with violent and almost constant vomiting. There are other cases which are lacking in the symptoms of anorexia and vomiting, and, in some of these, food may give relief. But these, like migraine without digestive symptoms, are self-curative in much less degree, and consequently the paroxysms tend to recur more frequently. In the typical cases, food causes an aggravation of the pain, and is immediately succeeded by vomiting.

It must be remembered that, in all cases (migrainous or gastralgic) associated with vomiting, especially of course when violent, the muscular work involved materially increases combustion. This applies to many cases of cyclic or periodic vomiting.

§ 262. In others of the paroxysmal neuroses, acarbonization is effected mainly by exaggerated katabolism through pathologically induced muscular exertion: these may be regarded as pathological analogues of physiological muscular exercise.

MAJOR EPILEPSY.—Here a carbonization is achieved in the main by increased combustion. The powerful tonic and clonic convulsions, which are so conspicuous a feature of the seizure, increase the rate of combustion in the same manner as, and probably in a higher degree than, physiological muscular exertion. So rapid is combustion that sometimes heat-production outstrips heat-dissipation and a rise in the temperature of the body occurs. This is observable especially in the *status epilepticus*, in which many convulsions occur in rapid succession. In the most severe forms of this condition, 'the¹ intervals between the fits become shorter, the coma deepens, the pulse and respiration become very frequent, and the temperature rises, it may be to 105° or 107° (Bournsville)': in short all the phenomena of excessive heat-production, accompanied by overstrained yet inadequate heat loss, arise. Epileptic convulsions, especially when severe, are commonly succeeded by prolonged sleep, during which, of course, no aliment is taken. But that the exaggerated combustion of the convulsion is the main salutary factor, seems assured from the observation that fits tend to be infrequent in proportion to their severity, and conversely: the extreme frequency of attacks in some cases of *petit mal* is notorious.

§ 263. Nevertheless, restriction of income, achieved through distinctly pathological means, occurs in not a few cases of epilepsy. Many authors have called attention to the extreme frequency of dyspeptic conditions in epilepsy: Voisin and Petit point out that the dyspeptic conditions precede and accompany the fits, ceasing thereafter (§ 451); and Mangelsdorf² has found temporary gastric dilation in epilepsy similar to that which occurs in migraine (§ 257).

I have argued that hunger may be an index of reduced carbon contents of the blood. Gowers³ calls attention to the sense of hunger which may follow a fit, even if a hearty meal has immediately preceded it; and Dr. Hawkes tells me of a patient, who for seven years has suffered from severe nocturnal epilepsy, and who is made aware of the occurrence of a fit only by the distension of his bladder in the morning and by his ravenous appetite for breakfast. This patient has taken heavy

¹ *Diseases of the Nervous System*, Gowers, 1893, vol. ii. p. 751.

² *Medical Review*, January 1904, p. 36.

³ *Diseases of the Nervous System*, 1893, p. 744.

suppers just before going to bed, to reduce his morning hunger, but without result. The same increased sense of hunger may follow, in less degree, migraine, gastralgia, and other allied disorders; and in all it seems reasonable to ascribe it primarily to the pathologically increased acarbonization of the blood, secondarily and proximately to the reduction in the amount of glycogen in the liver.

§ 264. ASTHMA.—The muscular exertion involved in asthma may be extreme. Salter¹ says:—‘On stripping an asthmatic in the height of a paroxysm, an admirable example is seen of the immense array of muscles that become, on an emergency, accessory to respiration, and some idea is formed of the toil of the asthmatic, and the extremity of those sufferings that necessitate for their relief such intense labour.’ But, in addition to the increased expenditure so induced, it is probable—nay, almost certain—that, in all asthmatic paroxysms, fresh intake is greatly restricted, if not for a time abolished; and that for several reasons. 1. The pre-occupation of the air-hunger may be absorbing. 2. Sometimes distinct anorexia is present: more than one asthmatic has told me that during an attack the mere thought of food is revolting, and that not until several hours after the paroxysm is over can they raise the semblance of an appetite. 3. Experience teaches the asthmatic that food increases the severity and prolongs the duration of the paroxysm.

Salter did not observe anorexia in asthma: indeed, he expressly states that ‘asthma in no degree interferes with appetite.’² Yet he strongly asserts that the paroxysm involves a period of enforced starvation. He points out that nothing is so certain as food to cause exacerbations, and he says³ of the asthmatic:—‘Fainting with hunger he dares not let a particle of food pass his lips, and so long as his paroxysm continues, so long must he starve.’ He mentions cases in which each attack involved from thirty-six to forty-eight hours of total abstinence from food. ‘In one,⁴ for example, the patient habitually ate nothing after an early dinner; on his asthmatic days, he took nothing whatever, went to bed exhausted, but with his asthma gone, and awoke the next morning very weak, but perfectly well. If he yielded to the temptation of taking any food his

¹ *On Asthma*, 1868, p. 74.

² *Ib.* p. 82.

³ *Ib.* p. 82.

⁴ *Ib.* p. 83.

asthma got worse instead of better towards the evening, the night was sleepless, and the second day as bad as the first, so that, on the occasion of each attack, he took nothing from dinner on one day to the breakfast of the next day but one, an interval of forty-two hours. . . . The more inane and exhausted the asthmatic is, the more disposed is his paroxysm to give way—it seems starved out, as it were.’ Thus the influence of the asthmatic paroxysm is to increase carbon expenditure and to restrict carbon intake, whether it effects the latter through pre-occupation, directly through anorexia, or indirectly through the experience gained by the patient on previous occasions.

CATARRHAL CROUP.—It is obvious that the paroxysms of this affection, which, there are reasons for believing, is often a juvenile representative of asthma (§ 650), operate to promote decarbonization of the blood: the muscular exertion involved in the obstructive dyspnoea must increase combustion; and so, too, probably does the pyrexia so often associated with the paroxysm (§ 273).

§ 265. ANGINA PECTORIS.—The affection termed functional or vaso-motory angina pectoris—doubtless the same affection which Trousseau had in mind, when he stated emphatically that angina pectoris is a neurosis, sometimes quite independent of organic cardiac lesion and indeed of all organic lesion—can hardly be regarded in the majority of cases as an efficient acarbonizing process. Yet there can be little doubt that it is so in some. In one of my cases (a lady of 25) each attack was accompanied by severe tonic spasm of apparently all the voluntary muscles of the body other than those of respiration. She would lie upon her back in bed, the hands grasping the head-rail of the bedstead above her head; and the vigour of the muscular contraction, as estimated by palpation of the forearm, was I think greater than she was capable of at any other time. The muscular spasm was similar to that which occurs at the onset of any severe anticipated pain, such as a tooth extraction: it was voluntary in the sense that, by a strong effort of will, she was able to relax the muscles. The spasm lasted continuously throughout each attack, that is, from ten to fifteen minutes, and left her hot, very tired, and not infrequently hungry. Clearly such voluntary, or semi-voluntary, persistent muscular spasm involves a material increase of combustion and carbon expenditure.

§ 266. ACUTE MANIA.—In this affection, acarbonization is effected both by increased expenditure and by restriction of income. There is constant excitement, incessant motion and sometimes pyrexia, associated with complete indifference to, if not distaste for, food.

HAEMORRHAGE

§ 267. It has been already argued that one of the immediate effects of haemorrhage is acarbonization of the blood (§ 154). The only physiological form of haemorrhage is menstruation; and we have seen that the human female comes to depend in part for acarbonization upon this recurrent loss. But later I shall argue that certain individuals, affected with pathological forms of recurrent haemorrhage, such as epistaxis, bleeding from piles, etc., likewise come to depend upon such losses, and that the interruption of these losses is prone to be followed by the manifestations of hyperpyraemia (§§ 668 *et seq.*).

Conformably with its direct acarbonizing influence, haemorrhage will be found to be inversely correlated with many other forms of acarbonization, physiological and pathological. After profuse haemorrhage, the menstrual flow may fail to appear or may be much reduced in quantity: the normal temperature falls from retarded combustion; and the elevated temperature of pyrexia may be reduced to the normal or lower, as may be frequently seen in typhoid fever. Acute gout and many of the paroxysmal neuroses may, as we shall see later, be abruptly dispersed by haemorrhage. On the other hand, the sudden cessation or reduction of any habitual acarbonizing process, haemorrhagic or other, physiological or pathological, may lead to haemorrhage in other directions. So will be explained the occurrence of vicarious and supplementary menstruation, and many other so-called idiopathic haemorrhages (§§ 668 to 675).

But the acarbonization which follows haemorrhage is not always merely temporary. When venesection was a routine treatment for most disorders, many persons submitted to it at regular intervals, not for the relief of any existing morbid condition, but as a general hygienic or prophylactic measure. No doubt it had been observed that often a number of trivial ailments and minor disabilities were in this way dispersed, and that the general improvement was maintained sometimes

for considerable periods. This is certainly the experience of many in the present day, who suffer from recurrent 'idiopathic' haemorrhages of many kinds.

DIARRHOEA AND LYMPHORRHOEA

§ 268. It has been argued that by purgatives, more especially such as operate upon the upper part of the small intestine, we may restrict the absorption by the blood and lymph vessels of nutrient material, and so attain a certain degree of acarbonization (§ 245). But, obviously, the same result may follow an attack of diarrhoea, arising through natural causes. It may follow, for example, the recurrent diarrhoea, which depends upon recurrent glycogenic distension of the liver, secondary to recurrent hyperpyraemia (§ 89). Hence we shall frequently find that diarrhoeal attacks alternate with, and replace, many of the pathological acarbonizing processes (§ 332).

The rather uncommon condition, lymphorrhoea, stands in much the same position as haemorrhage with regard to the carbon contents of the blood. It is a means of acarbonization through direct loss; and therefore it may have, as we shall see later (§ 332), inverse relations with other acarbonizing processes.

GLYCOSURIA

§ 269. Throughout this work, I shall regard glycosuria provisionally as an acarbonizing process. The grounds for taking up this position are in the main inductive. At the onset of glycosuria, it is found that physiological acarbonization of every kind tends to become retarded and that the manifestations of hyperpyraemia, whether acarbonizing process or other, almost invariably disappear. Thus in diabetes 'menstruation¹ is generally deficient or absent' (Saundby). Combustion is retarded: 'the temperature² in diabetics is usually normal or subnormal, and in some cases may be very low indeed . . . 93·6' (Saundby). Anabolism ceases or becomes retarded: 'pregnancy³ is very liable to be interrupted in its course, and probably always by the death of the foetus' (Duncan); and fat-

¹ *Lectures on Renal and Urinary Diseases*, Saundby, 1896, p. 285. ² *Ib.*

³ Matthews Duncan, quoted by Williamson, *Diabetes Mellitus*, 1898, p. 114.

formation, though in some cases excessive in the beginning, tends as a rule to progressive failure.

§ 270. So far as I know, practically all the manifestations of hyperpyraemia, whether acarbonizing processes, such as recurrent bilious attacks, migraine and sick-headache, asthma, epilepsy and acute gout, or other, such as chronic secondary dyspepsia, chronic biliousness, certain neuralgias, certain other nervous affections and psychical disorders, and certain skin diseases, tend to disappear, or to become markedly modified, at the onset of glycosuria: in many cases, the disappearance of the previous disorders is sudden and complete. These inverse relations will be frequently referred to throughout the remainder of this work.

§ 271. On the other hand, glycosuria may be dispersed by powerful acarbonization of other kinds, physiological and pathological. It is well known that hard physical exercise is capable of this effect in some of the milder cases of the disease; and the influence of pyrexia of many kinds has long been observed. Trousseau says: ¹—‘It is the remark of all observers, that when an acute disease supervenes in diabetes, sugar no longer appears in the urine.’ And glycosuria has ‘been ² observed to disappear in relapsing fever (Simon), small-pox (Rayer, Parry), febrile angina, dysentery (Andral), and pneumonia (Leube, Oliver)’: it may be greatly reduced by intercurrent phthisis (Williamson).³

§ 272. In claiming glycosuria as an acarbonizing process, all we are called upon to show is that in this disorder the organism has an additional outlet for the escape of carbonaceous material and that the blood shares in the loss. But here we are faced with serious difficulties. It will be at once objected that in glycosuria the blood may contain more sugar than in health, that glycosuria is commonly an index of hyperglycaemia. This must be admitted of some cases, but it does not hold of all. Saundby says: ⁴—‘According to Seengen the amount present in mild cases of diabetes does not exceed the normal.’ And in the artificial glycosuria produced by the injection, or ingestion, of phloridzin or phloretin, not only does the glycogen disappear from the liver and muscles, but

¹ *Clinical Medicine*, New Syd. Soc., vol. iii. pp. 509, 510.

² *Lectures on Renal and Urinary Diseases*, Saundby, 1896, p. 299.

³ *Diabetes Mellitus*, Williamson, 1898, p. 211.

⁴ *Lectures on Renal and Urinary Diseases*, 1896, p. 270.

‘according¹ to v. Mering and most other observers . . . there is no excess of sugar in the blood,—in fact the amount may be less than normal . . . This seems to point to the fact that phloridzin, besides any action it may have upon the metabolism of carbohydrate in the liver and muscles, increases the permeability of the kidney tubules to sugar, or causes the epithelium of the tubules to be more susceptible to the presence of sugar in the blood, so that the kidney removes sugar from that fluid more rapidly than under normal circumstances, and thus the percentage is even diminished below the normal’ (Schäfer). Moreover,² ‘it must be remembered that the existence of a renal diabetes in man has been considered possible by Klemperer and others.’ Now the onset of a glycosuria, depending largely on an increased permeability of the kidney to sugar, would explain very simply indeed the sudden cessation of hyperpyraemic manifestations.

But this idea hardly helps us out of our difficulties. For in many of the cases in which hyperpyraemic manifestations have given way before diabetes, this latter has been of a severe form,—a form in which it seems certain that hyperglycaemia was present.

It must be admitted that the conception of hyperglycaemic glycosuria as an acarbonizing process presents great difficulties—difficulties which are increased by the fact that, in some cases, there is also an excess of fat in the blood. Such difficulties are of course irremovable so long as we remain ignorant of the chemistry of hyperpyraemia. All it is possible now to affirm is that hyperglycaemia and hyperpyraemia are for the most part antagonistic in their clinical relationships.

PYREXIA

§ 273. It is still undecided whether pyrexia is in all cases *caused* by an increased production of heat: whether in some a mere decrease in the heat loss—a retention of heat—may not suffice. We are warned against accepting hastily the fact of increased combustion as evidence that pyrexia is so caused, since it has been shown that an actual rise in the body temperature, even if due to heat retention, may *lead to* increased

¹ *Text-book of Physiology*, Schäfer, 1898, vol. i. pp. 921, 922.

² *Progressive Medicine*, June 1903, p. 308.

combustion.¹ Fortunately this question does not affect us here: all we are concerned with is that pyrexia, however initiated, is, in practically all cases, *accompanied by* an increase of combustion, as shown by an increase in the absorption of oxygen and an increase in the excretion of carbonic acid.

After referring to the observations of Liebermeister and Ringer upon the increased excretion of urea in fever, Fagge says: ²—‘But it is now well known that the production of heat may be largely dependent upon the increased oxidation of various substances, such as sugar, which have never formed part of the substance of the body.’ Professor J. Bauer says: ³—‘Liebermeister first announced that in two cases of ague he had observed a marked increase in the production of carbonic acid during the paroxysm; and in reports of exhaustive experiments published recently, he shows that in intermittent attacks the greatest increase in the excretion of carbonic acid (30 to 43 per cent.) occurred during the pyrexial period, and in the so-called cold stage it reached even to two and a half times the normal.’ Professor Bauer is careful to point out that ‘a large share in the increased production of carbonic acid in the cold stage’ must be ascribed to the excessive muscular action involved in rigor. He continues:—‘At the acme of the fever, Liebermeister found the production of carbonic acid raised by from 19 to 31 per cent., and at the commencement of the sweating stage both normal and excessive amounts of carbonic acid were observed.’ Other investigators then took up this subject. ‘Leyden instituted a large number of observations on several forms of febrile diseases, which invariably showed an increase in the excretion of carbonic acid, as compared with what had been noticed under normal circumstances. In two patients with recurrent fever the increase in the carbonic acid was 30 to 44 per cent., in one case of typhus 38 per cent., and in one of pneumonia 70 per cent. . . . Quite recently Leyden and Fränkel have published a number of experiments on the excretion of carbonic acid in fever, which are of great value as having been carried out with the aid of the most exact appliances. From the results of these experiments it follows indisputably that the

¹ *Text-book of Physiology*, M. Foster, 1895, p. 856.

² *Text-book of Medicine*, 1891, vol. ii. p. 38.

³ Ziemssen's *Handbook of General Therapeutics*, 1885, vol. i. pp. 203, 204, 205.

fever induced by the injection of pus is in animals constantly followed by an increased elimination of carbonic acid' (Bauer).

The most recent investigations into the respiratory exchange in human fever seem to render necessary some modifications in these conclusions. F. Kraus¹ concludes 'that in all cases of acute fever there is increase of respiratory activity (that is, greater frequency and depth of respirations), and that whenever this is the case, the actual intake of oxygen is increased, but that, when the febrile state is prolonged, this effect soon subsides, notwithstanding the continued abnormal elimination of nitrogen.' Loewy found 'that,² although there was usually augmentation of the oxygen intake with or without increased depth or frequency of respiration, this was only observed when the temperature was actually rising' (Burdon-Sanderson). In any case, therefore, it seems to me we may assume during pyrexia some exaggeration of the continued katabolic decarbonization which is ever present throughout life in the muscles and other tissues of the body; and this, even if merely temporary, would, in all probability, be sufficient in most cases to clear the blood of any pre-existing excess of carbonaceous material.

§ 274. But exaggerated combustion is not the only means whereby the blood is acarbonized in pyrexia. Clinical observation shows that pyrexia almost invariably involves some degree of anorexia and dyspepsia: Hoppe-Seyler found no hydrochloric acid in the gastric juice during typhus; and Uffelmann found 'that the peptone-forming secretion of the stomach ceases entirely during fever' (H. A. Hare).³ Thus the carbonaceous income to the blood will be largely restricted. And it is a fact that, in many cases, such food as is ingested is more highly nitrogenous and less highly carbonaceous (beef-tea and milk, for example) than the dietary of health. Indeed, it is difficult to imagine an acarbonizing process of greater potency than pyrexia of any severity and duration.

§ 275. Consequently, we are not surprised to find that, during all pyrexias, many other kinds of expenditure, physiological and pathological, tend to be in abeyance. Dr. Helen McMurchy,⁴ in the paper already quoted, says:—'Typhoid

¹ Burdon-Sanderson in Clifford Allbutt's *System of Medicine*, vol. i. p. 145.

² *Ib.*

³ *Text-book of Practical Therapeutics*, H. A. Hare, eighth edition p. 611.

⁴ *Lancet*, October 5, 901.

fever precipitates menstruation, generally bringing it on within a few days after the onset of the fever.' This is doubtless true and could be explained by the tendency to general vasoconstriction of the cutaneous area, which is a feature of the early stages of probably all fevers. Such premature menstruation is probably analogous to the frequent epistaxis which occurs at the same stage, and which I believe could be shown to be more common in the male than in the female sex. But it is equally true that menstruation usually ceases or becomes extremely slight *after the initial period* during pyrexia if at all severe and prolonged. Of upwards of 800 female cases of typhoid treated by myself, the great majority were admitted to hospital later than the early stage; and in these menstruation was absent or very largely reduced during the fever. This applies to many mild pyrexias, provided they are sufficiently long in duration: even the slight septic pyrexia associated with the wearing of a tape seton is, as we shall see (Case LVI), sufficient to modify markedly the amount of the menstrual loss. The same is true, even more conspicuously, of some less physiological forms of habitual hæmorrhage, such as periodic hæmorrhage from piles; and epistaxis, as just stated, is common in typhoid, *but only during the early stages*.

§ 276. *Anabolism* of all kinds remains in abeyance during pyrexia of any intensity. The *saliva*, probably also the *gastric*, *pancreatic* and other *digestive juices* are not formed or are formed in far less quantity than usual. The same is true of *sebum*: sebaceous follicles, emptied by pressure, do not refill during sharp pyrexia, or do so comparatively slowly: the skin ceases to be greasy, and acne disappears. *Fat-formation* probably always ceases during pyrexia of any degree: indeed, the fat already stored is rapidly withdrawn, doubtless in response to a deficiency in the carbon contents of the blood. *Pregnancy* not infrequently comes to an end by the death and discharge of the foetus; and it is difficult to avoid the conclusion that abortion, occurring during pyrexia, is, from the maternal standpoint, a conservative event, adapted to economize formative and nutritive material, nitrogenous and carbonaceous, too much of which is being rapidly spent in exaggerated katabolism.

The *lacteal secretion* does not escape. Of puerperal pyrexia, Spiegelburg says: ¹—'In the majority of cases infection has

¹ *Text-book of Midwifery*, New Syd. Soc., vol. ii. p. 459.

occurred before the establishment of the lacteal secretion, and in not a few even the outbreak of the disease has preceded it. In many such, and they are the worst cases, the breasts do not become functional at all, or if they do, their activity ceases after a few days. In mild attacks, on the other hand, the secretion may come on and last for the normal period: so that its condition mainly depends on the gravity of the attack.' Even the *lochial discharge* is affected: as is well known, one of the earliest symptoms of puerperal septicaemia is cessation of this discharge.

§ 277. Finally, as we shall see later, pathological acarbonizing processes of many kinds, such as migraine, asthma, and even epilepsy, and many others (if not all) of the clinical manifestations of hyperpyraemia, are, as a general rule, during all pyrexias except the mildest, greatly modified, if not completely absent.

§ 278. PHTHISIS.—With regard to phthisis, an affection we shall have frequent occasion to refer to as a potent acarbonizing process, Robin and Binet¹ allude to experiments which demonstrate that 'while respiratory capacity is diminished, the total pulmonary ventilation is enormously increased, the CO₂ production increasing upward of 60 per cent., and the total amount of oxygen used increasing by some 70 per cent., while the quantity of oxygen absorbed by the tissues is sometimes increased 90 per cent. Consumption, then, is the correct word: the disease is an active consuming process.' It is of course quite inconceivable that a disease associated with such an enormous increase in the rate of combustion, which affects all the fixed tissues of the body, could long exist without dispersing any pre-existing carbonaceous accumulation in the blood; and therefore we are well prepared to find that practically all the immediate manifestations of hyperpyraemia tend to cease abruptly at the onset of tubercular consumption, *when this is at all pyrexial*.

This anticipation is fully borne out on appeal to facts; and the knowledge of such facts is of extreme importance from the standpoint of practical diagnosis. It is admittedly difficult to make a definite diagnosis, positive or negative, in the very early stage of consumption—that stage when, above all others, an accurate diagnosis is of the utmost practical value. This

¹ *Progressive Medicine*, September 1902, p. 51.

embarrassment may often be obviated by a knowledge of the clinical manifestations, and theory of, hyperpyraemia. The abrupt cessation—without apparent cause and without the intervention of any other substitutive acarbonizing process, such as glycosuria—of an accustomed hyperpyraemic affection, such as recurrent bilious attacks, migraine, angina, acne and many other skin affections, about the supposed time of infection, is highly suggestive of tubercle. On the other hand, the persistence *in unmodified degree* of hyperpyraemic manifestations is, so far as my experience goes, strong evidence against tuberculosis. It must be admitted, however, that a few consumptives, affected with extremely chronic forms of the disease, suffer from mild hyperpyraemic affections, such as slight headaches, asthmatic and neuralgic disorders, and a moderate degree of high blood-pressure.

§ 279. ACUTE GOUT.—Acute gout is a recurrent pyrexia lasting ‘from¹ two to seven, eight or ten days’ (Duckworth). It does not seem over-bold, therefore, to assume it to be a recurrent acarbonizing process. But such assumption is unnecessary, for the increase of combustion upon which its acarbonizing influence mainly depends, has been demonstrated experimentally. ‘During² the acute attacks, Magnus Levy has shown that the oxygen intake may be increased by 5 to 10 per cent.’ (I. Walker Hall). Nevertheless, acute gout, like other pyrexias, tends to promote acarbonization through diminishing income as well as through increasing income. Von Noorden³ points out that in gout the hydrochloric acid of the stomach is deficient, but that this is the case only in severe attacks, and has the same significance as it has in other acute febrile conditions.

The efficiency of acute gout as an acarbonizing process may be inferred from a large number of clinical observations recorded in medical literature. Some of these will be referred to in the succeeding pages of this work: a few may be conveniently mentioned here. Gout has been observed to replace bilious attacks, sick-headaches, migraine, gastralgia, asthma, epilepsy, mania and other affections, which, I have argued, are themselves acarbonizing processes: the works of Trousseau,

¹ *Treatise on Gout*, Duckworth, 1890, p. 329.

² ‘Metabolism in Gout,’ I. Walker Hall, *Practitioner*, July 1903, p. 63.

³ *Brit. Med. Journal*, September 24, 1904, p. 740.

Living, and earlier writers are full of illustrations. Van Swieten¹ related a case in which regular attacks of gout completely replaced recurrent epilepsy, which had followed recurrent gastralgia. Garrod saw similar occurrences and he quotes a remarkable case of Robert Wilson's.² 'A gentleman had suffered from epilepsy from the age of 20 to 52: the fits were frequent, sometimes occurring as often as once a week: he then had distinct articular gout in one great toe and afterwards experienced attacks of the same kind from time to time up to his death at the age of 72. From the first manifestation of decided gout, there was an entire cessation of the epileptic convulsions.' The same author refers to cases in which mania replaced acute articular gout and subsided on the reappearance of the former. The alternations of gout with neurosal affections will be referred to frequently.

§ 280. CYCLIC VOMITING.—Under this term, Dr. Bernard R. Le Roy³ describes a series of nine cases. The attacks tend to be periodic or regularly recurrent: they are associated with headache, complete anorexia, nausea and vomiting, together with marked pyrexia. Such attacks tend to promote acarbonization of the blood in many ways: the intake is cut off; and the expenditure is increased, (1) by pyrexial increase of combustion, and (2) by the increase of combustion, due to the muscular exertion of vomiting.

PATHOLOGICAL ANABOLISM

§ 281. Physiological acarbonization, I have argued, is attained through restriction of income or increased expenditure; and the latter is achieved mainly in three ways, namely, by katabolism, anabolism, and haemorrhage. The pathological acarbonizing processes operate similarly: we have considered pathological restriction of income, pathological haemorrhage, and pathological katabolism. We have yet to consider pathological anabolism.

Excessive obesity may be argued to be a process of pathological anabolism; and we have already regarded it in that light. But it is clear that tumour formation of all kinds

¹ *Clinical Medicine*, Trousseau, New Syd. Soc., vol. iv. p. 379.

² *Gout and Rheumatic Gout*, 1876, p. 460.

³ *Therapeutic Gazette*, June 15, 1902, p. 377.

must be, *inter alia*, a process of acarbonization; and this applies especially to tumours which are rapidly growing, and above all to the various forms of malignant tumour, whatever their pathogenesis.

It is not contended that cancer disperses hyperpyraemia *solely* by means of anabolic acarbonization: undoubtedly it operates in many other ways as well. The cancerous cachexia probably restricts the intake of food, and may retard digestion and absorption: this is of course especially true of the cachexia associated with gastric cancer. The appetite may be greatly inhibited through the mental anxiety attendant on the disease; and, when ulceration has occurred, haemorrhage, discharge, and septic pyrexia will all tend to promote acarbonization.

Consequently, we shall not be surprised to find later that during the growth and development of a malignant tumour the manifestations of hyperpyraemia for the most part disappear (§ 337).

The acarbonizing influence of cancer is also shown by the tendency to antagonism between this disease and glycosuria. J. Boas ('Berlin. Klin. Woch.' March 15, p. 243)¹ points out that Kappler collected sixty-three cases of diabetes and carcinoma in the same patient. The writer himself saw diabetes in twelve out of 366 cases of intestinal carcinoma. In seven cases the urine was free from sugar when seen. The percentage of sugar usually was not great: it varied from 1·2 to 5·3 per cent. The writer had seen no case in which diabetes appeared after the carcinoma. The diabetes is the primary, the cancer the secondary affection. Nevertheless, the two diseases appear to be connected. For occasionally old-standing diabetes disappears on the establishment of carcinoma, in spite of a carbohydrate diet. And in other cases, though the diabetes persists, the percentage of sugar diminishes *pari passu* with increasing cachexia.

§ 282. Dr. Hawkes calls my attention to the high value which a recognition of the possibility of hyperpyraemia and of the acarbonizing influence of malignant tumour formation possesses in practical diagnosis. He cites two cases in illustration, both of which occurred in elderly men.

In the first, the diagnosis seemed evenly balanced between

¹ Quoted by the *Medical Review*, August 1903, p. 485.

uncomplicated cholelithiasis and cholelithiasis complicated by malignant disease: some of the consultants favoured the latter view. One circumstance alone led finally to the adoption of the former. The patient had suffered from chronic pruritus for from thirteen to fourteen years—for many years, that is, before the occurrence of jaundice or hepatic symptoms of any kind—and this had persisted undiminished. Now there can be no doubt that pruritus often depends upon hyperpyraemia, it being a common expression of the so-called gouty diathesis (§ 836); and therefore its persistence was considered to weigh heavily against malignant disease. A completely and permanently successful cholelithotomy confirmed the diagnosis.

The second case was similar. Cholelithiasis had existed for fifteen years; but of late, the condition seemed to point to secondary malignant disease of the gall-bladder. There was, however, sufficient doubt to render an exploratory operation justifiable; and such would have been performed, except for one circumstance. In addition to the symptoms of gall-stones, the patient had suffered from asthma: this had completely ceased at about the time when the malignant complication was suspected of having arisen. Now asthma is one of the affections which may almost certainly depend upon hyperpyraemia (Chapter IX); and consequently, a diagnosis of malignant disease was made and operation abandoned. The further history of the case fully justified this course. The patient developed symptoms pointing to empyaema of the gall-bladder: this was opened and drained, and the existence of a large carcinomatous mass, as well as of gall-stones, demonstrated.

These cases seem to show that internal cancer may sometimes be excluded by the persistence of the manifestations of hyperpyraemia; and conversely.

SUMMARY

§ 283. Before referring to the subject-matter of this chapter, we have accepted provisionally the possibility of the pathological condition of the blood which has been termed hyperpyraemia. This being so, the arguments adduced herein go to show that many pathological conditions, differing in their causation and clinical aspects, are capable of promoting acar-

bonization of the blood and thus of reinforcing physiological acarbonization. Such pathological processes, it is further argued, may operate by restriction of the carbonaceous income, by increase of the carbonaceous expenditure, katabolic, haemorrhagic, and anabolic, or by any combination of these means.

CHAPTER IX

§§ 284-349

Recurrent hyperpyraemia; or hyperpyraemia interrupted by recurrent pathological acarbonizing processes depending on hyperpyraemia: the paroxysmal neuroses—Theories of the paroxysmal neuroses: primary neurosal theory or theory of accumulation and discharge of nerve-force: toxic and uric acid theories: hyperpyraemic theory—Evidence in support of the hyperpyraemic theory: food: external temperature: physical exercise: oxygen inhalation: daily fluctuations in the carbon contents of the blood: monthly fluctuations: utero-gestation and lactation: fat-formation: plumbism: pyrexia: haemorrhage: diarrhoea and lymphorrhoea: glycosuria: cancer: self-curative and mutually curative influence of the paroxysmal neuroses: dietetic treatment by reduction of proteid: dietetic treatment by reduction of the carbonaceous intake: a salt-free diet—Summary of evidence and conclusions.

§ 284. We have seen in physiology that acarbonization does not always depend upon the necessity for acarbonization, but may arise incidentally through the necessity for force and heat-production. So it will be found to be in pathology. Processes possessing the power of promoting acarbonization in high degree may arise incidentally, that is, independently of hyperpyraemia, the humoral condition which constitutes the necessity for exaggerated acarbonization. In this light we must probably view the specific fevers; in these, acarbonization may be regarded as incidental, even if sometimes fortunate. But, if it can be shown that many acarbonizing processes have for an essential factor hyperpyraemia, then we shall have to regard these as conservative processes adapted to disperse this pathological humoral condition. Such an argument has been already applied to the common bilious attack; it may now be extended to some members of the class of affections termed paroxysmal neuroses.

THEORIES OF THE PAROXYSMAL NEUROSES

§ 285. The term paroxysmal neuroses was applied by Edward Liveing to a large class of regularly or irregularly

recurrent affections which are among the commonest to which mankind is subject: these are typified by migraine, asthma, angina pectoris, epilepsy, gastralgia, mania and others. That all these disorders, together with many more as yet unmentioned, are closely correlated, has been long known; and the co-relation has usually been regarded as one of community of causation. Liveing says: '—The pathology of megrim is in the main the pathology of the whole group of disorders to which it belongs.' It will be unnecessary to recall the large accumulation of authenticated evidence which bears upon this subject. It will suffice for the present to state that migraine,² epilepsy, asthma, angina pectoris, spasmodic croup, neuralgias of various kinds and distributions, tic douloureux, gastralgia, pleurodynia, insanity, and many other named and unnamed nervous affections, have at different times been observed to be interchangeable or to alternate with each other, not only during the course of hereditary transmission, though that is sufficiently marked, but also in the same individual at different periods of his life; also, that transitional forms of all degrees and kinds between almost any pair in the group have been observed: all of which facts are attested by professional witnesses, whose powers of observation and integrity are beyond all question (Liveing).

§ 286. THE PRIMARY NEUROSAL THEORY, OR THEORY OF ACCUMULATION AND DISCHARGE OF NERVE-FORCE.—The common factor above foreshadowed was assumed by Liveing³ to be 'a primary and often hereditary vice or morbid disposition of the nervous system itself: this consists in a tendency on the part of the nervous centres to the irregular accumulation and discharge of nerve-force, to disruptive and inco-ordinated action in fact; and the concentration of this tendency in particular localities or about particular foci will mainly determine the character of the neurosis in question. The immediate antecedent of an attack is a condition of unstable equilibrium and gradually accumulating tension in the parts of the nervous system especially concerned, while the paroxysm itself may be likened to a storm, by which this condition is dispersed and equilibrium for the time restored.' In this view Liveing is, so

¹ *Megrin and Sick-headache*, 1873, p. 224.

² *Ib.* pp. 205, 212, 215, 217, 218, 219; also Clifford Allbutt in the *Lancet*, 1884, vol. i. p. 508.

³ *Ib.* 1873, p. 336.

far as I know, followed by most of the prominent neurologists of the present day.

The theory thus formulated implies a conception of nerve-force as a separate measurable entity distinct from all other varieties of force: it takes no notice of the origin of all vital force, the supply of combustible matter. Now the nervous system may be regarded as the machinery whereby the potential energy contained in the nutritive material apportioned by the blood is transmuted into the special variety of actual energy which it dispenses; and the possibility of the storage of such energy, apart from the fuel whence it is derived, has never been more than conjectured.

It is true, the immediate dependence of nerve-force upon food is not clinically conspicuous: mental activity remains unimpaired—it may even become unwontedly vigorous—during starvation, long after other varieties of force have dwindled materially. But this is fully explained by the power, conferred upon the nervous system, of drawing its food supply from all the other organs and tissues of the body: it need not be taken to mean that it is drawing upon a supply of ready-made nerve-force, stored up as such. Indeed, the infallibility of the provisions which assure, under the most exceptional conditions, a regular supply of nutriment to the nervous system—to the extent that this system has a preferential claim over every other tissue in the body—would seem to negative any capacity for storage such, for example, as is possessed by an electric accumulator: to indicate, on the other hand, that the nervous system manufactures its force as it is required, and lives, so to speak, from hand to mouth.

§ 287. But, be that as it may, the primary neurosal theory, if pushed, lands us in serious difficulties. The paroxysmal neuroses, it is well known, alternate, not only with the members of their own class, but with other affections which cannot be seriously regarded as primarily nervous in origin. Migraine and gout may replace each other: ‘M. Labarraque¹ gives the case of a professor at Besançon, who had been long subject to migraine: he submitted himself to a long course of mineral waters, when the migraine was replaced by severe gout, which in turn was cured by the reproduction of the migraine’ (Liveing); and similar cases are freely recorded. ‘Migraine,² however, is

¹ *Megrim and Sick-headache*, 1873, p. 400.

² *Ib.* p. 404.

far from being the only neurosis which is thus associated with gout : a similar connexion may be traced in the case of asthma, angina pectoris, gastralgic paroxysms, and certain forms of transient mental derangement' (Liveing). And later we shall see that the paroxysmal neuroses extend their affinities far beyond the confines of their own group, and have intimate relations with disorders variously regarded as humoral, toxic, or metabolic in origin.

§ 288. Restricting ourselves, however, for the present to gout, it seems obvious that gout is a primary neurosis, or migraine (together with many of its congeners) is not. Liveing recognized the difficulty, but it can hardly be said that he faced it boldly : instead, he attempted escape through compromise. Forced to admit the existence of a migraine not primarily nervous, he created a special class which he termed 'symptomatic or pseudo-megrim.'¹ Of this he says :—'The morbid material may be introduced from without, or generated within the system by imperfect assimilation or defective excretion.' In this class he included (1) the gouty or arthritic ; (2) the malarial ; and (3) migraine associated with organic disease of the brain. Of the third I have no knowledge, and the second does not concern us now. As regards the first, it is clear there is only one reason for its dissociation and separate classification, namely, the author's preconception that the common variety of migraine is a primary neurosis. But this remains an assumption : it cannot therefore be permitted as the premise of an argument except provisionally ; and it may be inferred that Liveing was somewhat dissatisfied with his own conclusions, for later he inclined to the view that gout is a primary neurosis. I submit it is more reasonable to infer, from the proved existence of a humoral migraine, a humoral causation for the whole group.

§ 289. TOXIC AND URIC ACID THEORIES.—The above considerations possibly led to the tendency to revival of humoral theories, which is noticeable throughout recent medical literature. The natural way out of the difficulties which surround the pathology of the paroxysmal neuroses is to abandon the primary neural theory and search behind the nervous system for the common primary factor.

Now the possible factor which stands immediately behind

¹ *Megrim and Sick-headache*, 1873, p. 309.

the nervous system is the blood; and it is reasonable to suppose that in morbid variations in the composition of the blood, qualitative or quantitative, we may find the common cause of many allied disorders—of those which are prominently nervous as well as those which are manifestly humoral. Living admits a toxic factor in the case of gouty migraine: Lauder Brunton and James Mackenzie are inclined to ascribe all migraine to toxins; and Haig blames uric acid for this, as well as many an allied, disorder. Fleury¹ believes in the auto-toxic nature of epilepsy and regards diet as an important element in treatment: James Adam holds similar views.² Both the last mentioned authors refer to the extreme frequency of gastro-intestinal affections in epileptics. Bonnet³ thinks the epileptic poison may be cumulative and the attack a natural discharge for its evacuation. James Adam⁴ regards the exciting cause of asthma as endogenous toxins. And Ewart⁵ suggests 'that the so-called neuroses are, like gout itself, connected with, if not dependent upon, faulty chemistry, and upon auto-toxis, whether by hyperproduction or by retention.'

The evidence in favour of the hypothesis which ascribes the paroxysmal neuroses to uric acid circulating in the blood consists for the most part of certain variations which have been observed in the excretion of this substance in connexion with the attacks of these disorders. These excretory variations, however, are capable of more than one interpretation: they will be considered in some detail in Chapter XV.

The evidence in favour of the toxic hypothesis consists in (1) the frequency with which dyspepsia and gastro-intestinal disorders generally are associated with the attacks of the paroxysmal neuroses; and (2) the fact that by the steady withdrawal of meat and other nitrogenous food-stuffs, the only known source of toxins, the intervals between the attacks of some of the paroxysmal neuroses, notably of periodic headache or migraine, may be greatly increased, if not prolonged indefinitely. Against the toxic hypothesis, however, is the fact that many of those who suffer most severely from the paroxysmal neuroses are habitually free from digestive disorders of all kinds, such often presenting, indeed, exceptionally

¹ *Journal de Méd.*, May 10, 1900. ² *Brit. Med. Journal*, May 9, 1903, p. 1080.

³ *Med. Annual*, 1900, p. 194; also *N. York Medical Journal*, August 27, 1898.

⁴ *Brit. Med. Journ.*, May 9, 1903, p. 1080. ⁵ *Gout and Goutiness*, 1896, p. 281.

powerful and tolerant digestions; and the fact, to be brought out later, that many cases of periodic headache may be treated successfully by a dietetic system which includes a considerably increased supply of nitrogenous food (§ 346).

§ 290. **HYPERPYRAEMIC THEORY.**—The introduction of toxicity into the pathology of the paroxysmal neuroses—if by toxicity we refer to definite chemical poisons not present in the blood of physiological health—is superfluous, if we believe in the possibility of hyperpyraemia. Accordingly I venture to submit the following proposition:—

That the paroxysmal neuroses are often due to a gradually increasing accumulation in the blood of unoxidized carbonaceous material derived from the food: that sooner or later, according to circumstances, the load becomes intolerable; and that then there occurs, through the medium of the nervous system, a more or less precipitate and complex conservative reaction on the part of the organism, resulting in some degree of temporary relief: in short, that the paroxysmal neuroses depend upon hyperpyraemia and constitute acarbonizing processes.

EVIDENCE IN SUPPORT OF THE HYPERPYRAEMIC THEORY

§ 291. The evidence which can be found in medical literature to support this theory is extensive and, to my mind, conclusive. From a comprehensive survey of this evidence we may make the following generalization:—Whatever tends to promote acarbonization of the blood tends to prevent, modify, or disperse, the attacks of the paroxysmal neuroses: whatever tends to promote hyperpyraemia tends to induce, intensify, or render more frequent, the recurring paroxysms. The details of evidence upon which this generalized statement rests will now be considered.

§ 292. **FOOD.**—Food is the primary source of the carbon contents of the blood: hence, other things being equal, food will have an important influence upon the paroxysmal neuroses, if these disorders depend upon hyperpyraemia. Liveing regarded the influence of food upon *migraine* as greatly overrated; but it is almost inevitable for those who hold the primary neurosal theory to take this view. But the general public, who are unprejudiced in favour of any theory, remain unshaken in their belief that migraine and improper food are closely connected.

It may be argued that, just as physiölogical loss of appetite graduates insensibly into anorexia, and anorexia into overt bilious attacks (§ 77), so overt bilious attacks, usually admitted to depend upon improper food, pass by insensible gradations into the most typical migraine, attended by complex nervous phenomena; and it is certain, to my mind at least, that no physician has yet succeeded in drawing any satisfactory line of demarcation between bilious attacks and migraine.

§ 293. Fothergill, who had some experience of migraine himself, gives a list of articles which he found particularly efficacious in producing migraine: 'melted butter,¹ fat meats, spices, meat-pies, hot buttered toast, and malt liquors when strong and hoppy'; and he adds concerning butter,² 'nothing more speedily and effectually gives the sick headache, and sometimes within a few hours.' Fagge says:—³ 'Certain persons at least can always bring on an attack . . . by eating particular articles of diet towards the end of the interval between one paroxysm and another.' Liveing⁴ refers to the case of a medical man who for thirty years could never take the smallest quantity of wine, nor eat a fragment of burnt pastry, without infallibly producing a headache; and a medical friend of mine can practically always, with the exception of the early days succeeding an attack, induce a typical hemicrania, by taking a little over four ounces of whisky in the evening. I has been already argued that alcohol, especially the saccharine alcoholic drinks, fats, pastry, etc., are all eminently capable of causing hyperpyraemia. Of juvenile migraine, Eustace Smith says, the commonest cause seems to be deficient exercise combined with over-eating.

§ 294. The influence of abstention from food is often conspicuous. A friend of mine has been a life-long sufferer from migraine. The attacks, originally accompanied by much anorexia and vomiting, have altered of late in this respect. They begin about 11 A.M. and it is possible for him to eat a fairly good meal at 1 P.M. If he does so, however, the attack is prolonged and severe, while, if he follows the dictates of his experience and abstains from all food, he succeeds as a rule in cutting short the attack.

¹ *Megrin and Sick-headache*, Liveing, 1873, p. 45.

² *Ib.* p. 45.

³ *Text-book of Medicine*, 1891, vol. i. p. 782.

⁴ *Megrin and Sick-headache*, 1873, p. 45.

§ 295. Salter held the opinion that *asthma* in some cases is humoral in origin: that the responsible materials in the blood 'have¹ nothing particular in them, but are the same as they would be in any non-asthmatic person'; and that the essence of the disease resides in the morbid sensitiveness of the patient. He argues that at least in these cases the substances induce asthma by their presence in the blood, and not by irritating the gastric terminations of the vagus. He points out that substances which rapidly undergo absorption by the blood-vessels, such as wine or alcohol of any kind, may produce asthma 'within a minute² or two': while in other cases 'in which the food producing the asthma is such as would furnish material for lacteal absorption, the asthma did not come on till about two hours after taking the food.' He also shows that the interval which elapses between the ingestion of food and the asthmatic attack is governed by the size of the meal: he 'once knew an asthmatic who was always awoken by his disease with an earliness proportionate to the size of the supper he had taken.'³ Salter's view that the humoral factor in some cases of asthma is not peculiar to asthma, and that the essence of the disease consists in the morbid sensitiveness of the organism to the humoral factor, is identical with, though perhaps less defined than, the view taken in this work of pathologically prepotent cases (compare Chapter XIII).

It is true Salter believes that the blood containing the offending material acts directly upon the lungs, but that is a belief which would tend to follow from his preconception that asthma consists in spasm of the bronchial tubes.

§ 296. Salter gives a list of articles of food which he found especially liable to induce asthma: 'such asthmatic articles of food are, cheese, nuts, almonds and raisins, and sweet things in general, salted meats, condiments, potted and preserved and highly seasoned things, fermented drinks, especially malt liquors and sweet wines.' He thinks 'malt liquor, especially the stronger sort, with a good deal of carbonic acid gas in it, is perhaps the most asthmatic thing of any'; and he is very emphatic in condemning steak and kidney pudding. Obviously the articles of diet especially likely to determine asthma are essentially similar to those which induce migraine: they are at least all highly carbonaceous, and most, through containing an

¹ *On Asthma*, 1868, p. 49.

² *Ib.* p. 48.

³ *Ib.* p. 67.

ample proportion of nitrogen, are well adapted for complete absorption. The condition of the blood most favourable to asthma is termed by Salter 'sanguis cibi,'¹ certainly a more euphonious term than hyperpyraemia, but differing in no essential respect.

§ 297. It is impossible to read Salter's account of the influence of food upon the asthmatic without feeling convinced that the absorption of food into the blood, and not its mere presence in the digestive organs, is the important point. Asthmatics are often dyspeptics, but Salter shows that asthma follows meals with equal, if not greater, certainty in those who present no sign of dyspepsia, and that some of the worst asthmatics have exceptionally strong digestions: ² this is in complete accord with my own experience. But the strongest proof of the influence of food in causing asthma is derived from the effect of starvation. I have already quoted Salter (§ 264) to the effect that the asthmatic paroxysm may be 'starved out': and I have known many asthmatics who have discovered this fact for themselves.

The influence of alcoholic drinks is well marked in the following case communicated to me by Dr. Hawkes. The patient has for years made a point of getting drunk on Saturday night. Of late, however, he has commenced to suffer from severe spasmodic asthma on each Monday following, commencing at 10 or 11 P.M. and becoming steadily worse throughout the night. If, as not rarely happens in his case, he gets drunk on any other evening, the same occurs and at exactly the same interval, namely, forty-eight hours. This patient now regards himself as in serious danger of becoming a sober man.

§ 298. There are not many recorded observations as to the influence of food upon *epilepsy*. Certain authors have advised vegetarianism, and others a purely milk diet. On the other hand, vegetarianism has been strongly condemned.

But there is some evidence to show that food is an important factor in starting infantile convulsions; and 'there ³ is . . . no purely symptomatic distinction between infantile convulsions and epilepsy. The typical and fully developed attacks of both

¹ *On Asthma*, 1868, p. 310.

² *Ib.* p. 46.

³ *Diseases of Childhood*, Donkin, 1893, p. 231.

are identical' (Donkin). Gowers¹ says of the cases of epilepsy 'that commence in infancy, at least three-fourths date from infantile convulsions.' Such have been ascribed to teething and other sources of reflex irritation; but teething and the commencement of artificial feeding are often concurrent, and there can be little doubt that the food which follows weaning is as a rule far more highly carbonaceous than breast-milk.

Gowers says:²—'All now perceive the truth of the opinion, long ago urged by Sir William Jenner, that almost all convulsions associated with dentition are really due to the constitutional condition of retarded development which we call rickets.' But it may fairly be argued that this constitutional condition is itself a result of improper food. Donkin³ says that rickets is especially prone to set in 'very soon after weaning time in cases which according to all available evidence were previously healthy.' Burney Yeo says⁴:—'The common error upon which the production of rickets often depends, is the too great reliance by the poorer classes on farinaceous foods. Infants fed almost entirely on farinaceous foods are pretty certain to become the subjects of rachitis.'

I have known many cases of juvenile convulsions distinctly brought on by a surfeit of confectionery or sweets. Of course in many such cases the attacks may fairly be ascribed to gastro-intestinal irritation. But in two in which the fits followed sweets, the stomach was quite empty at the time of onset, which was about 4 A.M., nor was there present any symptom of intestinal disorder. In one of these, a boy of 6, the patient had had three series of convulsive seizures, all following a glut of sugar. The fits commenced about twelve hours later, doubtless long after the sugar had undergone complete absorption. The mother informed me that several medical men, whom she consulted, discredited the view that sugar had any baneful influence in the case. So convinced, however, was she in her own mind as to the causal connexion, that she had almost excluded sugar from her child's dietary, with the apparent result that he remained quite well.

§ 299. The improvement which, in two cases of angina

¹ *Diseases of the Nervous System*, 1893, vol. ii., p. 731.

² *Epilepsy*, 1901, p. 21. ³ *Diseases of Childhood*, 1893, p. 125.

⁴ *Food in Health and Disease*, 1897, p. 474.

pectoris, followed the mere restriction of sugar in the diet led Vergeby¹ to believe that this food-stuff induced paroxysms through its direct action on the cardiac nerves. In a patient of mine who suffered from violent angina, severe paroxysms were induced on three occasions by indulgence in Turkish delight, chocolate creams, and honey, respectively. On all three occasions the onset of the paroxysms was deferred for several hours. Restriction of the carbonaceous intake combined with graduated physical exercise has been extremely successful in my hands in many cases of angina pectoris, unassociated with organic cardiac lesion (Cases XLI to XLIV).

§ 300. EXTERNAL TEMPERATURE.—So long as there is a supply of carbonaceous material which is undergoing absorption from the alimentary canal—and this is probably continuous, though not uniform, under the ordinary conditions of life—the carbon contents of the blood will tend to vary inversely with the rate of combustion. Hence conditions which accelerate combustion will tend to prevent, render less frequent or severe, or disperse, the paroxysmal neuroses, if these affections depend on hyperpyraemia; and conversely. The influence of external cold in increasing combustion has been referred to. Solly² has found that the cold dry air of mountainous districts is beneficial upon both migraine and epilepsy. Liveing³ mentions the case of a young clergyman, a sufferer from migraine, who remained free from attacks during a seven years' residence in a mountainous district, the complaint recurring on his return to his old locality; but the increased exertion entailed through a hill residence must be borne in mind.

Boucharde⁴ says migraine 'est fréquente surtout dans tout l'Orient'; and I have seen many cases of this disorder, sick-headaches and bilious attacks, and some of asthma and other neuroses, which commenced only on arrival in the tropics. Further, I know of many who enjoyed complete immunity from the recurring paroxysms during a change of residence to a cold climate. Most of my cases of migraine and asthma were distinctly worse during the Queensland summer than at other seasons; and both these affections are, I think, common in

¹ *American Year-book of Medicine and Surgery*, 1896, p. 113.

² *Handbook of Medical Climatology*, 1897, p. 164.

³ *Megrim and Sick-headache*, 1873, p. 435.

⁴ *Les Maladies par Ralentissement de la Nutrition*, 1890, p. 368.

Australia in proportion to the proximity of the equator. Trousseau says¹:—‘Asthma is a summer complaint in this sense, that sufferers from it are much more frequently subject to it in the warmer portion of the year from May to November, than in the colder, from November to May. Again asthma is more common in equatorial regions than in temperate zones or in cold climates.’ One of Salter’s patients said the fits of asthma ‘were² always worse and more frequent in summer than at any other season’; and another said ‘the³ hot season is the worst.’

§ 301. The influence of the summer season upon the number of fits in epileptics is perceptible in the records of the Craig Colony for Epileptics, New York. Dr. William Spratling, in his annual report for 1903, says:—‘During January, February and March last the men had respectively 5718, 5320 and 6363 seizures. In July, August and September they had 4735, 4922 and 4723, a difference of 3011 in favour of the latter period.’ This, however, is due, as Dr. Spratling points out, to the physical exercise of outdoor occupations which the summer season entails. In the case of the female colonists, whose occupation is mainly indoor all the year round, the un-antagonized influence of high external temperature is moderately conspicuous. ‘During January, February and March of the same year, the women had attacks as follows: 3250, 2929 and 3258, a total of 9437. During July, August and September they had respectively 3439, 3636 and 3429, a total of 10502,’ a difference against the summer months of 1065.

The beneficial influence of cold weather upon neurosal disorders would probably be much more marked, were it not for the stimulating influence of cold upon the appetite.

§ 302. Salter⁴ observed much benefit to accrue to asthmatics from the shock of the cold shower-bath and from sea-bathing: he regarded the *tone* of the nervous system as raised. But most probably the therapeutic effect is due to the decarbonizing action of reflex stimulation of the skin by cold water in either case, and in the latter, to physical exercise in addition.

§ 303. PHYSICAL EXERCISE.—Combustion is greatly increased by muscular exertion (§ 14): hence those whose occupations entail physical exercise in the open air are rarely

¹ *Clinical Medicine*, New Syd. Soc., vol. i. p. 631.

² *On Asthma*, 1868, p. 363.

³ *Ib.* p. 344.

⁴ *Ib.* p. 311.

attacked by migraine, or by any of its congeners : the immunity of the classes who earn their living by the sweat of their brow is proverbial. On the other hand, 'it'¹ is remarkable how many distinguished literary and scientific men have suffered severely from megrim' (Liveing). Many regard mental strain in these cases as the principal factor, but that in all probability is because they have already arrived at the conclusion that the affection is a primary neurosis : at least it is clear that mental strain usually involves deficient physical exercise. Liveing says :²—' We find the disorder not unfrequently making its first appearance among overworked students, literary men, artisans and sempstresses . . . and in such cases the malady often disappears again, when the causes which determined it are removed.' Change from a sedentary to an active life has often resulted in cure. The last quoted author says :³ —' We have already spoken of exercise in the treatment of megrim, as promoting the general health in various ways, favouring assimilation and excretion, diverting the mind and procuring sleep ; but *sustained bodily exercise* seems also to have a more specific power in controlling irregular nervous action in the manner now suggested. In many instances it has proved of signal service in reducing the number and severity of the megrim paroxysms and occasionally in preventing their return for a considerable period. Professor Du Bois-Reymond says of his attacks—" Auf Fussreisen bleiben sie ganz aus " ; . . . Dr. Parry relates a case of habitual periodical megrim in a military man " who found that his complaint had been constantly prevented, or its violence diminished, by strong bodily exertion." In another instance of sick-headache from childhood recorded by him, where the complaint was always supposed to originate in the stomach, and various remedies were, under that view, ineffectually employed, the most beneficial of all was bodily exercise.' Parry⁴ found that sometimes an already existing headache could be cut short by voluntary exercise ; and I have been able to demonstrate the same in a case of typical migraine. The influence of exercise upon migraine and headaches generally will be again referred to and the mechanism of its action discussed (§ 363).

The relief of eye-strain, which, in the case of literary and

¹ *Megrin and Sick-headache*, 1873, p. 433.

² *Ib.* p. 434.

³ *Ib.* pp. 451-2.

⁴ *Ib.* p. 281.

scientific men, is an incidental result of physical exercise and which has recently been claimed as the sole salutary feature of exercise, will be referred to again (§ 545 *et seq.*).

§ 304. Salter saw cases in which bodily exertion was the best remedy to which the asthmatic could resort. He says the treatment 'must¹ be taken in the intervals of the attacks; but when so taken, it seems to have a marvellous efficacy in keeping them off, and in giving to the asthmatic a lightness and freedom of respiration to which at other times he is a stranger.' Its rationale puzzled him. One of his patients writes:—'Of² all the remedies there is none for me so lasting as a day of severe walking exercise—five and twenty miles over hilly ground or across heath. . . . I begin *slowly, almost saunteringly*, and only increase my pace when it is pleasanter to do so than not. Towards the end of my day, I can usually climb a hundred feet of cliff as fast as I can plant my feet, or run a mile or two to catch a train. Habitually I can never run or go fast up hill. . . . This habit of severe walking exercise, I consider among the most valuable hints which my experience enables me to give asthmatics.' (The italics in the above quotation are mine.)

It is difficult to conceive of a better clinical proof of the theory of hyperpyraemia than the experience of this patient, especially as it was impossible for him to be biassed in his mind: he could not understand the reason for his improvement, nor could his physician assist him to do so. Now, however, it is easy to read between the lines. Habitually his blood was loaded (for him) with carbonaceous material: he lived always on the verge of an asthmatic explosion, which he could only stave off temporarily by constant care. Severe sudden exertion was therefore impossible; but *graduated* exercise enabled him to clear his blood of some carbonaceous material: as the carbon contents fell he increased his pace because 'it was pleasanter to do so than not'; and finally, the contents having fallen to *his* physiological mean or lower, he ceased for the time being to be an asthmatic. Salter³ refers to two other cases, who gave up all treatment except prolonged or violent muscular exercise, such as walking, boating, and gymnastics; and Marcet,⁴ on the theory that deficient oxygen with an

¹ *On Asthma*, 1868, p. 309.

² *Ib.* p. 310.

³ *Ib.* p. 311.

⁴ 'Croonian Lectures,' *Lancet*, 1895, vol. ii. p. 79.

excess of carbonic acid in the pulmonary capillaries is responsible for asthma, has prescribed cycling in one case with excellent results.

A medical friend of mine, once asthmatic but later a sufferer from diabetes, confirms in all details the experience of Salter's patient: he says he has frequently walked off an impending attack of asthma and returned home absolutely free from dyspnoea. Another medical friend gives me his very significant personal experiences as to the effect of exercise upon asthma. Exercise suddenly commenced, even if not violent, invariably brought on a certain degree of asthmatic dyspnoea. Consequently, whenever he contemplated undergoing some special exertion, he was accustomed to prepare himself beforehand by gradually increasing exercise. For example, if he drove down to the river with his friends in the drag, he would be quite unfit to row in a race; but, if he paddled himself gently down to the starting-place, the subsequent severe exertion would be powerless to cause the slightest degree of pathological respiration. Again, he was accustomed to visit and climb a rather steep hill distant from his residence four or five miles. Whenever he walked or even rode on horseback to the foot of the hill, he could climb it easily without dyspnoea; but, if he drove thither, the subsequent climb invariably induced a considerable amount of asthmatic breathlessness. On starting a bicycle ride, he would have to ride for the first hour at less than six miles an hour: later any pace would be easy and pleasant. On one occasion he went on a bicycle tour for four weeks, and averaged about sixty miles a day: towards the end of the tour the tendency to initial dyspnoea completely passed off and he could start straight away at full pace. After this tour he remained free from asthma for three or four months. He first became aware of the beneficial influence of gradually increasing exercise, when quite a boy and attending gymnasium. The gymnasium master used to set him to walk slowly round the room, gradually increasing his pace until any tendency to dyspnoea had ceased. After this, he was well able to undertake his special exercises, trapeze work, etc.

§ 305. I find that practically all asthmatics whom I have questioned can confirm these experiences in great degree; and it is interesting to note that, although he disclaims knowledge of the actions of food and exercise respectively upon asthmatic

paroxysms, Salter arrives at practically a hyperpyraemic view. Having pointed out that 'blood rich in nutrient material, what we may call the *sanguis cibi*, the blood after a meal, is peculiarly offensive' to asthmatics, he says:—'If, then,¹ a blood much charged with these recrementitious materials is the most provocative of asthma, that which is the freest from them must be the least so, and under no circumstances is the blood so free from them as after prolonged fasting and exercise,—the fasting shutting off the supply of raw material, and the exercise drafting away, to supply the muscular waste, any unappropriated plastic store already existing in the blood. Whether this is, or not, the true explanation of the beneficial influence on asthma of prolonged muscular exertion, I am unable to offer any other.'

We see clearly, in the above paragraph, the influence upon the author's mind of Liebig's theory of muscular waste, at that time doubtless unexploded. Had it been recognized then that the energy of muscular contraction was supplied by the carbonaceous and not by the nitrogenous portions of the food, I cannot doubt that Salter, with his wide experience of the disease and his marvellously keen clinical insight, would have adopted, without hesitation, the theory of hyperpyraemia: he was within one step of it, as it was.

§ 306. On the other hand, the commencement of asthma is very often contemporaneous with the abandonment of physical exercise: especially is this so when the change in the manner of life is sudden. When the athlete begins to give up his athletic pursuits, he usually falls into flesh: his nitrogenous tissues are all highly nourished, and possibly on that account anabolic readily takes the place of katabolic decarbonization. He does not, it may be noted, abandon exercise suddenly: he is fond of athleticism, he gives it up reluctantly, and fat-formation keeps pace with carbonaceous supply. But when, as in cases of accident, he is suddenly laid up, he may commence to suffer from headaches or other morbid phenomena due to hyperpyraemia. It is often otherwise with the working man, in whom usually muscular exertion has been from necessity rather than choice. Should an access of fortune, not uncommon on the goldfields, enable him to cease from labour, he not infrequently abandons all exercise at once; and as he continues,

¹ *On Asthma*, 1868, p. 310.

or perhaps increases, his carbonaceous intake, fat-formation may fail to keep pace with supply. In this case, he may suffer from some 'neurosis' or other pathological acarbonizing process dependent on hyperpyraemia. I know of many cases of asthma which have this history: such are not uncommon amongst the Australian parliamentary labour representatives. In one marked case of asthma, the loss of exercise which was the essential factor resulted from a mining accident leading to blindness.

Dr. James Adam calls attention to the fact that asthmatic attacks in working men occur most frequently on Sundays or Mondays. 'Of ten¹ men, eight showed this "week-end" periodicity . . . Further, a school-boy, whose attacks were irregular during his school days, developed asthma regularly on Sundays and Mondays after he started work as a bricklayer. This periodicity was obviously connected with the altered life of the "week-end," its rest and good feeding, and its frequent want of exercise.' The author points out that this 'regularity is rarely manifest in women, because their work is rarely periodic'; but he saw it in a young woman who worked a tailor's machine during the week; and he knew 'an iron-worker escape his week-end attack of asthma when he had to work on Sunday.' Migraine, angina and other neuroses are also frequently 'week-end.'

§ 307. In angina pectoris, unassociated with organic cardiac lesion, graduated physical exercise has been in my hands the most useful of all therapeutic measures (Cases XLII, XLIII).

§ 308. Concerning epilepsy, Reynolds² observes:—'Muscular exercise regularly taken and carried as far as possible short of fatiguing, has always been of some service in cases which have come under my care.' Here the increased katabolic decarbonization of voluntary exercise is substituted for that of the involuntary exercise of convulsions. The same authority adds: ³—'Brown-Sequard's guinea-pigs, when shut up in cages and abundantly fed, had forty or fifty fits in the day; but when allowed their liberty and another kind of regimen, the convulsive tendency disappeared in a few weeks.' Broadbent⁴ says:—'It is important to note that they' (epileptic fits) 'rarely come on during exertion . . . This has a practical . . . bearing. We need not forbid epileptics to take exercise, or to ride, or

¹ *British Medical Journal*, May 9, 1903, p. 1080. ² *On Epilepsy*, p. 335.

³ *Ib.* p. 335.

⁴ *British Medical Journal*, January 4, 1902.

even to cycle in moderation. In this conclusion I am glad to have the concurrence of my friend Dr. Buzzard.' Presently, however, we shall see that one reservation must be made from the general statement that fits do not occur during exertion (§ 309).

Dr. Spratling of Craig Colony, New York, regards labour as the greatest therapeutic agent in curing epilepsy and idleness as a powerful factor for evil. He points out that this is proved by the record of seizures (already quoted, § 301). 'On¹ rainy days, holidays and Sundays, when patients do no work, the fits are doubled or even trebled in number. Dr. Weeks, medical superintendent of the New Jersey State Village for Epileptics, says that when winter comes on and outdoor work ceases, there is a rapid increase in the number of convulsions and in the irritability and discontent of the patients.' He naturally suggests that systems of gymnastics should be instituted under trained instructors to replace and even to supplement other forms of labour.

Dr. James Adam refers to a case of 'week-end' epilepsy under the care of Dr. Alexander Morton of Glasgow. 'A² lad who worked as a builder during the week, and who loafed about and fed up on Sunday, usually had a fit during the Sunday night. Dr. Morton cut down his diet and increased his open-air exercise on Sundays, so that no more fits recurred for a month. Then Dr. Morton went on holiday: the patient got lax in his *régime* and had fits as before. The lad was then taken by another doctor to a consultant, who ordered rest in bed on Sundays and abundant feeding, with the result that the fits were worse than ever on Sunday nights.'

§ 309. But, as already hinted, the influence of muscular exertion upon neurosal patients is not invariably beneficial. Many authors—Liveing in the case of migraine, Esquirol, Radcliffe, Reynolds in that of epilepsy, Salter in asthma, Graves in gastralgia—have pointed out that muscular exertion may be an important *exciting* cause of neurosal paroxysms. This seems at first sight evidence against the theory I am attempting to substantiate; but on examination we shall see that such evidence is confirmatory rather than the reverse. On reading carefully the description of cases in which exercise

¹ *Brit. Med. Journal*, Apr. 11, 1903, p. 871; abstract from *American Medicine*.

² *Brit. Med. Journal*, May 9, 1903, p. 1080.

has been followed by neurosal outbreaks, they are found to resolve themselves into three rather clearly defined groups.

1. Cases in which the paroxysm follows immediately and is conspicuously due to the exertion. Here we may suppose that hyperpyraemia is already present, and that exertion by raising the general blood-pressure (§ 363) precipitates the paroxysm: these will be considered later.

2. Cases in which the effect is not 'instantaneous but delayed some hours—in fact until the customary hour of seizure in the night or early morning.' Concerning these Salter says: ¹—'Although the asthma was . . . pretty sure to follow such over-exertion, it never came on immediately, never till the next morning; the exertion might be followed at the time by a little shortness of breath, not much exceeding that of a healthy person, which would speedily and entirely disappear, and the patient would pass the rest of the day and go to bed in perfect health; but as surely as possible he would be awoke next morning at the usual time with his asthma.' It is clear that, with most persons, unusual exercise (such as a cricket match), which stops short of fatigue, is followed by a more than usually hearty appetite, and that, unless this is provided for, the advantage accruing from the increased katabolic decarbonization may be altogether forfeited through the ensuing increased carbonaceous intake. Of epilepsy, Broadbent says: ²—'Attacks rarely come on during exertion. . . . The fear with regard to games is not of an attack at the time but during the reaction afterwards and especially next morning.'

3. Cases in which exercise is associated with distinct fatigue. The medical man whose experiences were detailed in § 304 informs me that when he pushed exercise to the extent that he became thoroughly fatigued—when for example he bicycled 100 or more miles in a day—articles of food which, under ordinary conditions, were liable to lead to asthma but which he could take with impunity after moderate exercise, invariably led to an attack during the succeeding night or early morning. We have seen that combustion is a capacity of the nitrogenous tissues and pre-eminently of the muscles (§ 100); and it is reasonable to believe that excessive exertion, pushed

¹ Quoted by Living, *Megrin and Sick-headache*, 1873, p. 173.

² *British Medical Journal*, 1902, January 4.

to the extent of causing marked fatigue, would be associated with a diminution of the capacity for combustion, and so lead to hyperpyraemia.

I have a mass of evidence which goes to show, that, the daily food supply and other conditions remaining constant, the freedom from asthma (and indeed all paroxysmal neuroses and many other pathological acarbonizing processes and manifestations of hyperpyraemia) is in direct proportion to the amount of physical exercise, so long as this stops short of causing marked fatigue. *Ceteris paribus*, the salutary results of increased physical exercise follow with almost mathematical precision: to me there is no more certain rule in medicine. Conformably, Harry Campbell remarks:¹—‘Within proper limits exercise is one of the best safeguards against all neuroses . . . but sudden exertion in those unaccustomed to it, and exercise which produces fatigue, are common causes of headache.’

§ 310. OXYGEN INHALATION.—Whether superoxygenation of the blood is possible or not, there can be little doubt that the inhalation of pure oxygen in the place of air hastens combustion, especially where this is retarded. Hence we should expect oxygen inhalations to exert a favourable influence upon hyperpyraemia and hyperpyraemic affections generally.

Conformably, Demarquay² successfully treated *migraine* in this way: he says that M. de Lepasse extolled the method and that it is especially useful in the case of women who are more or less chloro-anaemic. Beddoes cured or relieved four cases of cephalalgia out of four. Dr. Samuel S. Wallian treated thirty-one cases of headache of all varieties: sixteen were cured or fully relieved: four sensibly relieved: eleven little or not at all relieved.

Demarquay found that ‘in³ twenty-two cases of asthma treated by oxygen, there were ten cures: in nine there was marked relief, and in the three others no amelioration.’ Some of these cases are detailed:⁴ they go to show that, while in some the inhalation during the paroxysm gave instant relief from dyspnoea, ‘as if by enchantment,’ in others the treatment caused the succeeding paroxysms to become less severe and

¹ *Headache*, 1894, p. 36.

² *Oxygen and other Gases in Medicine and Surgery*, Demarquay, Wallian. Pub. F. A. Davis, 1889, pp. 150, 151, 122.

³ *Ib.* p. 52.

⁴ *Ib.* pp. 126, 127, 128, 129.

finally to cease entirely, resulting in a temporary, sometimes an apparently permanent, cure. The latter mode of convalescence is consistent with the idea of progressive decarbonization of the blood through accelerated combustion. Dr. Samuel S. Wallian¹ treated thirty-four cases of asthma, humid and dry: twenty-one were cured or fully relieved: eleven sensibly relieved: two little or not at all relieved.

As regards epilepsy, Beddoes² treated six cases: one was cured: five not relieved. Dr. Samuel S. Wallian³ treated three cases: two were cured or fully relieved: one sensibly relieved.

Recurrent angina⁴ pectoris also has been markedly benefited by oxygen inhalations.

§ 311. DAILY FLUCTUATIONS IN THE CARBON CONTENTS OF THE BLOOD.—Reference has been made to the rhythmic fluctuations in combustion throughout the diurnal cycle (§ 110); and it has been assumed that, in ordinary circumstances, the carbon contents of the blood tend to vary inversely with the rate of combustion (§ 300). Hence, if the paroxysmal neuroses depend upon hyperpyraemia, we shall expect to find their onset timed frequently for the period during which combustion is falling or low: after the minimum has been passed and combustion is once more upon the up grade, the danger will presumably be over for the time being. We see by the chart (fig. 1) that from 6 P.M. to 5 or 6 A.M. combustion is continuously falling; and that, throughout the latter half or third of this period, it is practically at its lowest level. Now it is a fact, which has been noted by all observers but which I do not think has hitherto received any adequate explanation, that during this period—more especially during its latter part—all ‘neurosals’ paroxysms, asthma, angina pectoris, epileptic fits, laryngismus, gastralgia and many others—are peculiarly prone to occur: in some cases, they occur at no other time.

Salter gives an appendix of 226 cases of the ‘true spasmodic’ form of asthma. Of these the time of attack is noted in 192, and, in all but eleven of these, the time was fairly

¹ *Oxygen and other Gases in Medicine and Surgery*, Demarquay, Wallian. Pub. F. A. Davis, 1889, p. 240.

² *Ib.* p. 122.

³ *Ib.* p. 240.

⁴ *American Year-book of Medicine and Surgery*, ‘Medicine,’ 1902, pp. 188, 189.

constant: in these eleven, it varied somewhat. The times of onset in the 192 cases may be grouped as follows:—

6 A.M. to noon—8 cases,	mostly at the beginning of the period.
noon to 6 P.M.—9	”
6 P.M. to midnight—34	” mostly at the end of the period.
midnight to 6 A.M.—141	” mostly about 3 A.M.

Thus there obtains throughout the four quarters of the diurnal cycle an accurately marked inverse relation between the incidence of asthmatic paroxysms and the rate of combustion. This is unmistakable when the following chart (fig. 3) is read in conjunction with the chart in fig. 1:—

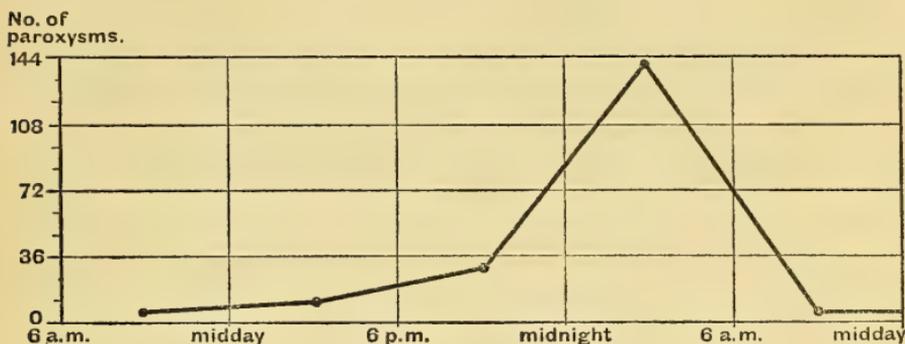


FIG. 3.

Chart showing the relative frequency of asthmatic paroxysms at different periods of the night and day.

Salter says: ¹—‘From 2 to 3 A.M. is the commonest time for asthma to appear’: this is the exact time when, according to Liebermeister’s chart, combustion stands at its lowest level. It is inconceivable that these coincidences should be merely fortuitous.

§ 312. Of migraine Bristowe says: ²—‘Not infrequently it comes on during the night, the patient waking from time to time with the consciousness of heaviness in the head, and getting up with the attack well developed.’ But more commonly migraine manifests itself on waking later in the morning at a time when combustion is rising. It is to be remembered that migraine is a neurosis of gradual development: its initial phenomena, sensory and visual disturbances and the like, are probably often insufficient to rouse the sleeping patient; and

¹ *On Asthma*, 1868, p. 408.

² *Theory and Practice of Medicine*, 1884, p. 1127.

thus they may be altogether missed or recognized only in dreams. Dr. Airy,¹ when his attacks occurred during the night, had an indistinct consciousness of having experienced the visual phenomena in his sleep, mixed up with his dreams; and one of my patients, in whom brilliant fortification spectra were well marked, dreamed invariably of thunder and lightning, whenever, as was most common, the attack commenced during sleep (§ 326). In a case described by Féré, the *true* commencement of the attack at the period of lowest combustion may safely be inferred. 'The² attacks occurred at various hours, often about 9 A.M., but the patient knew when an attack was coming on, as he always dreamed of fire, generally about 3 or 4 A.M. The dream might be of a tempest, a volcanic eruption, or a conflagration. . . . Since he began to suffer from migraine he never had the dream without an attack the following day, nor had he an attack unannounced by this dream.'

The frequency of morning headaches is proverbial. It is true these are not as a rule typically migrainous; but all gradations between them and typical migraine are to be observed; and they are common in sufferers from migraine, whenever circumstances have concurred to interrupt the recurrence of the more formal paroxysm. We may, therefore, reasonably refer the common variety of morning headache to the diminished combustion of the night. Headaches due to too much sleep are well recognized by the general public. 'I have overslept myself and got a headache' is a phrase very commonly heard. J. Kent Spender found that 'it was most fatal to have a good night, i.e. a long and deep slumber.' He adds:³—'And so my first preparation was to put off going to bed as long as possible, and if that ghostly thing rang, called the night-bell, I welcomed the peal as my truest friend. My invariable rule was to keep sleep at bay as much as possible, however tired I might be: an almost sleepless night would dash aside the coming headache.' Harry Campbell, who quotes the above, says:⁴—'I have frequently known simple, non-megrinous headaches result from excessive sleep—an extra hour in the morning for instance'; and we may suppose that, in such

¹ *Megrim and Sick-headache*, Liveing, 1873, p. 52.

² *Revue de Méd.*, February 10, p. 127; abstract in the *Medical Review*, April 1903, pp. 230, 231.

³ *Brit. Med. Journal*, 1884, vol. i. p. 1145.

⁴ *Headache*, 1894, p. 218.

cases, the postponement of the habitual stimuli to combustion—the activities called forth by rising, washing, dressing, etc.—allows the high carbon contents of the small hours to be prolonged unduly and to attain a pathological degree. The same explanation applies to some cases of epilepsy. Of this disorder, Dr. Alexander Francis has shown me a case which seems to have peculiar significance in this connexion. A lady had suffered from epilepsy for years. The fits occurred almost invariably in the morning just before rising. After a fit, she usually got up and dressed: on these occasions the first was the last fit of the series. But sometimes she fell asleep after the first fit: then she invariably had a second soon afterwards.

§ 313. We have seen that continuous work, or even watching without much work, throughout the night, practically reverses the daily fluctuations in combustion; and that sleep during the day causes a sharp fall, getting up in the evening a sharp rise, in the rate of combustion (§ 112). Accordingly, we shall expect to find that, in night workers, the paroxysmal neuroses commence most often in the evening, or in the time devoted to sleep. I have investigated this question in the case of journalists, hospital nurses, and policemen. The editor of a large Australian daily paper has been a life-long sufferer from migraine. In his career as a journalist, he worked during the night for eighteen years continuously. His hours of sleep were from noon till eight in the evening on six days of the week, but on Saturday he retired in the evening and slept through the night. His migraine recurred at fortnightly intervals and, as so often happens, Sunday was its chosen day. On these occasions, it was present on awaking in the morning. But whenever it occurred on other days (and this was not very infrequent), it was invariably present on awaking in the evening: *on no single occasion did it ever commence whilst engaged in work during the night.*

A hospital nurse, a life-long sufferer from intense migraine, was, when on day duty, always attacked before waking in the morning; but, when on night duty, the paroxysm commenced late in the afternoon when her sleeping hours were over. The headaches were then less severe: this she attributed to the fact that, when on night duty, her hours of sleep were considerably shorter and her fare considerably lighter. This case is but one of a series. I know of several policemen, whose sick

headaches alternated in exactly the same fashion, according as they were on day or night duty: in one the time of the attack often altered on the very day he changed his hours of duty.

Of asthma, the same is true in a marked degree. An elderly Hansard reporter has been asthmatic most of his life: he rarely suffers when at work during the night, and, when he does so, the attack is very slight; but for years he has been aroused by severe attacks towards the end of his daily sleep. During the Parliamentary recess he is unoccupied, and then his attacks are nocturnal. I have notes of several similar cases. Lemonnyer¹ ('Thèse de Paris, 1902') says of infantile asthma, that, instead of occurring during the night as in the adult, it most usually appears during the day: it is unnecessary to point out that not a few infants sleep peacefully during the greater part of the day and are active during the night. Salter, however, mentions a single exceptional case which, he says, went some way to shake his confidence in the influence of the sleeping state upon the asthmatic. 'The² case was that of a night porter whose duties compelled him to turn night into day. . . . But, though the ordinary times of sleeping and waking were . . . transposed, the asthma came on at the usual time, from five to six in the morning.' Nevertheless, it may be that the case was no exception: the duties of night porters are not commonly arduous; and I have known one night porter who slept very comfortably throughout the greater part of the night, although he strongly discountenanced the idea.

§ 314. Food late in the day, succeeded as it is by rapidly falling combustion, will, we can readily understand, greatly intensify the high carbon contents of the night, and be peculiarly liable to conduce to hyperpyraemia. Hence late dinners, and especially suppers, are proverbially harmful for 'neurosal' patients. Suppers lead to the formal neurosal paroxysms in those who are predisposed thereto, to night terrors in children, to nightmares and disturbing dreams in others, and to morning headaches. We are wont to smile, when a morning headache is attributed to the salmon rather than to the alcohol taken overnight, but I can have little doubt that the two are often equally responsible. The injurious

¹ *Brit. Med. Journal*, February 7, 1903, Epitome.

² *On Asthma*, 1868, p. 69.

influence of late meals is doubted by no asthmatic. Salter says :¹—‘The tendency of eating to induce asthma is in direct proportion to the lateness of the hour at which the food is taken : it is slight after luncheon, worse after a late dinner, worst of all after supper ; but breakfast seems entirely free from it.’ But mere lateness has little power for harm, unless it is succeeded by sleep ; one of Salter’s asthmatics, who ‘had² a very good digestion and a ravenous appetite,’ sometimes ‘yielded to temptation and ate supper . . . and if he did not go to sleep—as, for example, if he stayed up dancing half the night, or sat up reading, or took a very long walk—the asthma did not come on at all.’ The influence of sleep, following meals, is observable in the daytime also : in a patient of mine, even a short doze after his midday meal leads to an asthmatic paroxysm ; and many persons invariably wake with a headache when they fall asleep after meals. In all such cases, we may suppose that the conservative increase in combustion, which normally follows food (§ 108), is counterbalanced or defeated by sleep. All the above applies with equal force to anginal seizures and epilepsy.

In dwelling upon the influence of retarded combustion during sleep, we need not ignore factors more purely nervous. Epileptic paroxysms often appear to be peculiarly closely connected with the neural or neuro-vascular changes, which occur during the transitions between the waking and the sleeping states ; and the same may hold of other paroxysmal neuroses. Nor must we lose sight of the fact that cerebral inhibition is in abeyance during sleep ; and that, as will be argued later (§ 516), cerebral inhibition of the vaso-motor system is an important factor in the maintenance of purely physiological acarbonization.

§ 315. MONTHLY FLUCTUATION.—It is one of the oldest observations in medicine (one, however, upon which little stress is laid in modern text-books) that the attacks of the paroxysmal neuroses have a special tendency to group themselves about the imminence or onset of each menstrual epoch. In many cases, the incidence of attacks is limited for years to these periods. Yet the attempt to find any constant relation between the attacks and disease of the generative organs has always failed. Now it has been inferred that, before, and at the onset of, menstruation, there is a tendency to hyperpyraemia,

¹ *On Asthma*, 1868, p. 267.

² *Ib.* pp. 260, 261.

which tendency disappears towards the end of the period and thereafter (§ 156). And if, as I am arguing, the paroxysmal neuroses depend upon hyperpyraemia, it is easy to see why, other things being equal, they should be liable to occur most frequently in women at the menstrual period; and why they should occur in the majority just before, or at the outset of, menstruation; though there are rarer cases in which they occur during, or even after the termination of, the flow. Moreover, it is easy to see why the checking of the flow should have an aggravative effect.

Of *migraine*, Van der Linden says,¹ the patient 'was attacked every month generally when the flow was coming on': Fordyce says² 'in women who are subject to attacks of this malady at the catamenial period, the pain does not abate until the uterine discharge appears': 'when³ a suppression of the catamenia occurs . . . it of course aggravates the headache, and in many instances, it is the sole cause of it' (Graves). Bouchard says⁴ 'l'imminence ou le début d'une période menstruelle' is a common exciting cause. Harry Campbell finds from his notes that 'most cases of headache influenced by menstruation occur just before the flux.'⁵ In most of my cases of menstrual migraine, the commencement of the attack preceded the establishment of the flow: in a few it followed the cessation of the flow (i.e. a few days later): in one only did it commence during, that is, on the second or third day of, the flow. A very common history is that for some years the attacks are limited to the immediately premenstrual period, but that later intermenstrual attacks are superadded.

§ 316. ASTHMA has similar relations to the menstrual period. Salter says⁶ asthma occurring at monthly intervals is, so far as he has observed, 'due to the menstrual period': he never heard of it except in women. He refers to one case, in which the asthmatic paroxysm came on at varying intervals of three, four, five and six weeks. Inquiry in this case elicited the fact that the menstrual flow occurred concurrently at these irregular intervals and was 'pale and scanty.' Treatment directed to the faulty menstruation was successful

¹ *Megrin and Sick-headache*, Liveing, 1873, p. 47.

² *Ib.*

³ *Clinical Medicine*, Graves, New Syd. Soc., vol. ii. p. 351.

⁴ *Les Maladies par Ralentissement de la Nutrition*, 1890, p. 369.

⁵ *Headache*, 1894, p. 192.

⁶ *On Asthma*, 1868, p. 95.

in modifying the severity of the asthma: 'the¹ more freely menstruation took place, the less in almost exact proportion was the violence of the spasm.' Fagge also calls attention to these menstrual asthmatic paroxysms. My own observations tend to show that, in the great majority of cases, asthmatic women are worse just before menstruation, and obtain relief when the flow is well established: in some, the asthma is present throughout at this time only: in others, who are convalescing under treatment, the paroxysms, which were fairly constant, become restricted to the menstrual periods for some time before they finally cease. In one case, the following succession of events was repeated on several occasions: asthma, commencing on the day before menstruation, improved on the appearance of the flow, but got worse on the second and third days, improving again on the fourth. On each of these occasions, however, it was found that on the second and third days the flow had ceased and reappeared on the fourth, ending on the fifth; or this was approximately so.

All the above applies with equal force to recurrent anginal seizures occurring in non-pregnant adult women.

§ 317. *Of epilepsy* Gowers says:²—'In women attacks often occur at the menstrual period, although when closely investigated the relation is not found to obtain in more than about half the cases. The usual relation is for the attack to occur before, or (rather less frequently) during, the period, rarely after it. The relation does not seem to be connected with any abnormal state of the uterine organs.' That in 50 per cent. of all female epileptics the attacks are connected with the menstrual period, would seem to be ample for our purpose. That the attacks may occur during the flow might be explicable in many ways, especially remembering how often menstruation is scanty and irregular at the commencement of a period. In my own experience attacks occurring during the flow do so quite early and not towards the end, at any rate if the loss has been at all free.

§ 318. Gowers also says:³—'Retarded or absent menstruation coincided with the first fits in a large number of the cases which commenced in girls between fourteen and seventeen. . . When epilepsy is once set up in such cases, the subsequent

¹ *On Asthma*, 1868, p. 393.

² *Dis. Nerv. System*, 1893, vol. ii. p. 752.

³ *Epilepsy*, 1901, p. 34.

establishment of regular menstruation appears to exert very little influence upon the fits beyond the fact that they are rather more likely to occur at the menstrual period, however regular this may be in time or normal in its character. It has been already argued that retarded menstruation at puberty is a frequent cause of hyperpyraemia (§ 174).

The preponderating influence of puberty in the female sex as a cause of epilepsy is shown by the fact that it is in the second decennium, between 10 and 20, that the excess of females over males reaches its climax: ¹ during this period the female excess amounts to 20 per cent., whereas the average excess at all periods of life amounts to only 4 per cent. Gowers' statistics point with unflinching accuracy to the influence of puberty in girls upon epilepsy. Thus Whitehead ² of Manchester, from inquiries in 4000 cases, concludes that, in the English climate, menstruation commences, on the average, at the age of 15 years, six and three quarter months; and Gowers ³ finds that at the age of 16 the commencement of epilepsy in females attains the maximum for any year.

§ 319. The other epoch in women's life in which, as already argued, hyperpyraemia is especially prone to occur, and to occur severely, is the approach of the menopause (§ 174). Of migraine Liveing says: ⁴—'With women the seizures often become more frequent towards the period of the suppression of the catamenia, and diminish again when the critical period is passed.' Tilt ⁵ in a 'bead roll' of the disorders which 'occur for the first time, or recur with great aggravation,' at the change of life in 500 women, refers to 208 cases of headache, ninety-two of sick headache, seven of monthly headache, and three of hemicrania. He also found eight cases of hysterical asthma, three of epilepsy occurring for the first time, and five of epilepsy much aggravated.

What has been said of the influence of the menstrual function in determining migrainous, asthmatic and epileptic attacks, is applicable to very numerous other neurosal attacks, such as gastralgia, paroxysmal insanity, angina, various

¹ *Epilepsy*, Gowers, 1901, pp. 2, 15.

² *Dis. Women*, West and Duncan, 1879, p. 26.

⁴ *Megrin and Sick-headache*, 1873, p. 26.

⁵ *Change of Life*, 1882, pp. 71, 72, 158.

³ *Epilepsy*, 1901, p. 16.

neuralgias, and hysterical seizures. Dr. John Pollock¹ describes a case in which there occurred, on the third day of menstruation, a paroxysm of gastralgia so severe and acute as to lead at first to a diagnosis of perforating gastric ulcer. The paroxysm apparently abbreviated the menstrual period, since the flow ceased two days earlier than usual. Menstruation determines also the onset of many hyperpyraemic disorders not prominently nervous, such as bilious attacks and the minor digestive disorders, such as recurrent anorexia and dyspepsia (§§ 168, 169).

In maintaining that menstruation precipitates or intensifies neurosal paroxysms through its disturbing effect on carbonaceous metabolism, we are not called upon to exclude a more direct nervous influence.

§ 320. UTERO-GESTATION AND LACTATION.—It has been argued that both these physiological conditions are, *inter alia*, anabolic decarbonizing processes (§ 120); and some physiologists assert that, during the former, combustion (katabolic decarbonization) also is increased (§ 113). Hence we shall expect to find, throughout both periods, pathological acarbonizing processes more or less in abeyance; and this is found to be true in a marked degree. Liveing refers to the case of a lady who, throughout the whole reproductive period, suffered from severe menstrual migraine, except during her pregnancies, when she was ‘perfectly² free from the complaint, which . . . invariably returned after delivery.’ Heberden noticed the same thing. In a case of my own, intense migraine had recurred for thirty years: during her two pregnancies and during the periods of nursing which followed, a continuous period of thirty-seven months, she suffered from no attack: this was the only interval in the thirty years, during which she had been free for more than five weeks together (Case XII). I could add several similar cases.

Haig says:³—‘Asthma tends to be better during pregnancy’; and Salter⁴ refers to cases in which the attacks ceased at the commencement of child-bearing. Trousseau⁵ relates a case in which the paroxysms ‘disappeared entirely after she

¹ *Brit. Med. Journal*, August 15, 1903, p. 361.

² *Megrim and Sick-headache*, 1873, p. 47.

³ *Uric Acid in Disease*, 1897, p. 310.

⁴ *On Asthma*, 1868, p. 392.

⁵ *Clinical Medicine*, New. Syd. Soc., vol. i. p. 626.

began to nurse her children.' Dr. Robertson of Brisbane had an asthmatic patient in whom her third pregnancy was associated with complete freedom from attacks, which however returned a few days after delivery: during her first and second pregnancies she had remained asthmatic. Dr. W. J. Fearnley, resident medical officer at the Brisbane General Hospital, reports the following case:—

Mrs. M. S., aet. 31, has been subject to asthmatic attacks since girlhood: during her two pregnancies and while suckling she remained almost completely free.

I could add several similar cases of my own.

It is only fair to say, however, that Salter¹ saw asthma 'commencing at, and co-extensive with, pregnancy,' and other cases 'produced by parturition and occurring at no other time.' Such are possibly due to the high blood-pressure of pregnancy (compare § 736).

§ 321. Tissot and Fabre relate cases where pregnancy was accompanied by partial or complete immunity from pre-existing epilepsy, which returned immediately on delivery: in one case a subsequent pregnancy was accompanied by a return of the freedom.² Gowers says:³—'Pregnancy sometimes makes no difference to the disease, but on the other hand, in the majority of cases they are less frequent during gestation. In one case they occurred then in the night only, although at other times both in the sleeping and waking states. A considerable number of patients have almost or complete immunity during every pregnancy; in one of these a fit occurred three days after each confinement.'

But with epilepsy, as with asthma, cases are recorded in which the disorder commenced during pregnancy. Spiegelburg says:⁴—'In very rare cases . . . pregnancy appears to give rise to the first outbreak of convulsions . . . when pregnancy recurs, the disorder is apt to return.' As with asthma, it may be that such cases are due to the high blood-pressure of pregnancy (§ 736).

§ 322. On the other hand, the effect of prolonged lactation, especially in women who are feeble, will be to induce

¹ *On Asthma*, 1868, p. 392.

² *Megrin and Sick-headache*, 1873, p. 179.

³ *Epilepsy*, 1901, p. 212.

⁴ *Text-book of Midwifery*, New Syd. Soc., vol. i. p. 349.

exhaustion : milk is a highly nitrogenous, as well as a carbonaceous secretion, and its prolonged withdrawal, especially where the supply of new nitrogenous material is insufficient, may result in damage to the functional capacities of the nitrogenous tissues, amongst which are the decarbonizing capacities. Hence, as Liveing says,¹ migraine not infrequently makes its appearance in 'poor women exhausted from over-suckling.'

§ 323. FAT-FORMATION.—Fat-formation, as already argued, is probably the most important—it is at least the most unremitting—anabolic decarbonizing process: hence we shall expect to find that it has well-marked relations with the pathological acarbonizing processes, and with other manifestations of hyperpyraemia. An increased formation and deposit of fat may frequently be observed concurrently with the subsidence, partial or complete, of migrainous attacks, recurrent headaches, asthma, angina pectoris, and many other so-called neuroses. Of this I have seen many examples; and it is very common for corpulent persons to express fear of dietetic treatment directed to weight reduction, on the grounds that, before becoming stout, they suffered from frequently recurring headaches. I feel sure it is only necessary to call the reader's attention to this point of view, to enable him to recall from his own experience many similar coincidences; but it is not possible to extract from medical literature many illustrations; for, with few exceptions, we seem to have always regarded increasing fat-formation as a comparatively unimportant incident in the clinical history of disease—as a mere sign of improvement and not as a factor in the process.

Tilt, however, says:²—'I have seen sudden growth of fat coincide with great improvement in health,' but he thinks Dr. G. Bedford went too far when he stated 'that those who became fat-bellied were not troubled with nervous symptoms.'³ Berkhart has recorded some remarkable examples of the replacement of asthma by obesity: 'In⁴ three cases—two females and a male—an improvement of the asthma was followed by a rapid development of an enormous obesity. Both females were at the climacteric period . . . both had an hereditary disposition to corpulence . . . so long as they were subject to the dyspnoeal paroxysms, they were thin; but, on

¹ *Megrim and Sick-headache*, 1873, p. 27.

² *Change of Life*, 1882, p. 66.

³ *Ib.*

⁴ *Bronchial Asthma*, p. 147.

their recovery, the catamenial losses become very profuse, and in an *incredibly short time* afterwards an abundant deposition of fat took place all over the body. In the one male, the corpulence was preceded by a repeated and copious haemorrhoidal flux.' It is evident from the wording, that the author is inclined to regard the obesity as succeeding—that is to say, as permitted by—the abatement of the asthma; but a little consideration will show that it would be impossible to disprove the converse. For the actual commencement of the increased fat-formation would be clinically imperceptible; and the author points out that the deposition took place 'in an incredibly short time.' However, I am not concerned to dispute the author's view. All three cases may have been pathologically prepotent (see §§ 511 to 513). In this case, the recurrent asthmatic paroxysms would have been responsible for the previous failure of fat-formation, which would in fact have depended on absence of the necessary margin of carbonaceous material in the general blood-stream (§ 132). And quite possibly the antecedent haemorrhages were the initial step in the acarbonization which led to the cessation of the asthma. But even so, and whichever way we look at it, we must regard the rapidly increasing obesity as a process of acarbonization substitutive of the asthmatic acarbonizing paroxysms. The histories of many of Salter's¹ cases show that in all probability the cessation of the asthmatic paroxysms was the first step in improved nutrition: for instance, certain cases on arrival from the country in London ceased forthwith to suffer, and continued to gain in weight so long as they remained in the metropolis; and the same is most likely true of cases cured by the removal of some more obvious source of peripheral irritation.

In the past, before I was aware of the importance of food in asthma, I was fortunate enough to succeed in curing several cases by means of drugs, especially iodide of potassium and arsenic; but I was at a loss to understand my far more frequent failures. Now, however, on looking back, the reason seems clear: only those cases remained permanently well who managed to secure substitutive physiological acarbonization, whether by increased fat-formation (and these were in the majority), by increased physical exercise, or by both combined. In contrast to this, it may often be observed, under dietetic

¹ *On Asthma*, 1868, pp. 270, 272, 285.

treatment by reduction of the carbonaceous intake, that asthma and many allied disorders improve concurrently with a loss of weight and without increased exercise: under treatment which ignores diet, loss of weight is invariably, in my experience, of bad prognostic import.

It has been argued that a low grade of the capacity to form fat is, in many cases, the chief functional factor in hyperpyraemia (§§ 237, 238). The anabolic inadequacy may be inherent; and neurosal affections in the habitually lean are, as already stated, particularly resistant to treatment.

But the power to construct fat may be lost in various ways, for example, through dietetic errors. Hence asthma, migraine, angina pectoris, and other neurosal disorders, may arise, or rearise, after long intervals of health in patients who have become thin; and sometimes the loss of weight may have preceded for some considerable time the onset of the neurosis. This is especially true, in my experience, of migraine; but Dr. Hawkes informs me that it is true also of a high proportion of his asthmatic cases. The exaggerated nitrogenous disintegration of pyrexia has been dwelt on as a factor in deficient fat-formation capacity (§ 237); and the frequent commencement of neurosal disorders during the convalescent stage is a well-known clinical fact and will be again referred to (§ 328).

§ 324. We are now in a position to explain in part the long-observed relationship between obesity and many other disorders variously regarded as nervous, metabolic, toxic, etc. Amongst recent writers, Bouchard has especially insisted on the constancy of this relationship, not only in the family history of the patient, but in his personal history. Restricting ourselves to the two common paroxysmal neuroses, migraine and asthma, Bouchard¹ found that of 108 cases of obesity, forty-four had at some time suffered from migraine, and two from asthma. He infers a common factor in causation, but the prevalent conviction that civilized food habits are on the average physiological has led him, like most others, to search amongst the essential proclivities of the organism: he assumes a morbid temperament characterized by a retardation of metabolism and terms it 'diathèse bradytrophique.'

Our standpoint constrains us to regard the real common

¹ *Les Maladies par Ralentissement de la Nutrition*, 1890, p. 122.

factor as a food-fault, whereby the organism is supplied with fuel or carbonaceous material in excess of its requirements and in excess of its capacity for physiological disposal. This common food-fault leads, under varying personal proclivities, inherent or acquired, to varying morbid results: in other words, the common carbonaceous excess may be disposed of by various pathological processes, which are determined by various conditions, including the personal capacities and opportunities of the organism. Thus obesity, migraine, and asthma all depend upon a relatively excessive carbonaceous intake: they are all processes of acarbonization; and therefore they are interchangeable and capable of supplanting one another. It matters not from our present standpoint that the first is more or less physiological, the last two definitely pathological.

§ 325. PLUMBISM.—It has been argued that lead, through its influence on the tissues, probably retards metabolism, constructive, destructive, or both, and thus induces, *inter alia*, hyperpyraemia (§ 232); and it is a striking fact that many of the clinical manifestations of plumbism closely resemble, if they are not identical with, the clinical manifestations of hyperpyraemia: for example, cases typical of most of the paroxysmal neuroses are frequently met with.

Dr. A. J. Turner of Brisbane, who has made a special study of lead-poisoning in children and who was the first to point out the frequency of this affection in Queensland, writes:—‘I have been much struck by the periodicity of the attacks of complete anorexia with vomiting and abdominal pain, but not always attended by constipation in cases of lead-poisoning in children. These attacks, occurring at intervals of four to six weeks or longer, are often the earliest symptoms preceding the onset of the characteristic paralyses. In the intervals the appetite and digestion are good; and the child usually soon regains the weight and strength lost during the attack.’

The form of headache usually associated with plumbism is not typically migrainous; but I have seen one case in which it was so; and Gowers says,¹ ‘transient hemianopia or amaurosis has been met with.’

Samuel West says:²—‘Asthma has been described in cases of lead-poisoning. Thus Loewy records a case and Riegel

¹ *Dis. Nerv. System*, 1893, vol. ii. p. 954.

² *Diseases of the Organs of Respiration*, 1902, vol. ii. p. 575.

mentions two others but thinks both of them doubtful, so that if this form really exists, it must be very rare.'

'That ¹ epilepsy may be produced by . . . plumbism, there is no doubt' (Fagge). 'The ² convulsions are epileptiform in character, consisting of tonic and clonic spasm . . . Very rarely they may be hysteroid' (Gowers).

The ordinary lead colic is probably a true colic, but 'severe ³ paroxysms of epigastric pain have also occurred, associated with inaction of the intercostal muscles' (Gowers). These would correspond fairly with the ordinary form of recurrent gastralgia.

Though I have never seen or heard of a case, I can hardly doubt that plumbism may lead in some cases to symptoms indistinguishable from angina pectoris.

§ 326. PYREXIA.—We have seen that pyrexia is, from all points of view, an acarbonizing process of high potency (§ 273); and we have explained on these grounds the absence of some physiological acarbonizing processes during its continuance (§§ 273 to 277). Accordingly, we are prepared to learn that pyrexia overrides and disperses also many of the pathological acarbonizing processes and other manifestations of hyperpyraemia; and we find this to be true in a marked degree of the disorders termed paroxysmal neuroses.

Fagge says:⁴—'The conception of fever as having a salutary influence is indeed as old as Hippocrates and it can be traced all through the Middle Ages, and down to our own time; but our immediate predecessors recoiled from explanations teleological.' Thus it would appear that the conservative influence of pyrexia as regards other affections has received but scant attention during recent years. It is merely referred to incidentally in short paragraphs by most authors (even the paragraph just quoted is placed in a foot-note); and yet it is a clinical phenomenon which is most conspicuous, when once our attention has been called to it. One author, however, appears to accept pyrexia in a full and wide sense as a conservative, if not always salutary, process. Dr. George S. Keith, after speaking of the accumulated evil which results from prolonged

¹ *Text-book of Medicine*, 1891, vol. i. p. 759, Fagge.

² *Dis. Nerv. System*, 1893, vol. ii. p. 754, Gowers.

³ *Ib.* p. 947, Gowers.

⁴ *Text-book of Medicine*, 1891, vol. i. p. 34

over-eating, says:¹—‘ In these cases a long period of cleaning out is needed. . . . This may be done quickly by a fever or other acute illness, which, if it does not kill the patient, very soon burns off the offending matters. . . . If this rapid method of cure is not available, it may be reached much more slowly by failure of appetite coming on, or perhaps some of the more acute forms of dyspepsia.’

Acute gout is a recurrent pyrexia; and innumerable instances can be found in medical literature in which acute gout has replaced *migraine* for shorter or longer periods, or permanently. But I can find hardly any reference to the capacity of pyrexia, other than acute gout, to interrupt, during its continuance, the recurrence of migraine paroxysms: both Liveing and Trousseau appear to have overlooked the fact; and yet, so far as I know, such interruption occurs almost invariably.

In upwards of 2000 cases of typhoid treated by myself, I can call to mind no attack of migraine during the continuance of distinct pyrexia. Such a negative may be regarded as valueless: none of these patients may have been subject to migraine; and it may be that migraine occurred but was unrecorded mentally or in the notes. But I have much positive evidence bearing on the point. I have questioned a large number of migraine sufferers, most of whom had suffered in the past from pyrexia of some kind; and almost none can remember an attack of migraine concurrent with pyrexia: indeed, the great majority had themselves observed that the attacks ceased in these circumstances. Thus I recently met a clergyman, whom I had treated for a long attack of typhoid, fifteen years ago. He has been a sufferer from migraine all his life, and he reminded me that one of his few intervals of freedom was during his attack of typhoid: he added that the headaches recurred during early convalescence. In another case, migraine, occurring once a week, ceased during an attack of subacute bronchitis lasting two months, but recurred when the chest affection disappeared. Later, this patient contracted phthisis of a markedly pyrexial type, after which he finally ceased to suffer from headache.

These cases are mentioned merely as examples: with one important exception, namely, the pyrexia which is associated

¹ *Plea for a Simpler Life*, 1897, p. 131.

with vaso-constriction of the surface or rigors (an exception which will be considered later in § 375), the antagonism between migraine and pyrexia seems to me practically complete; and I could adduce numbers of cases in point, did space permit. But this is unnecessary; for I feel sure that most family practitioners will be able to recall numerous cases from their own experience—cases which, on account of their seeming meaninglessness, may have made but little impression on them at the time. Even the short and mild pyrexia, which accompanies a feverish cold, is sufficient in many cases to avert a migraine paroxysm which is impending; and the same is true of tonsillitis, erysipelas, septic and inflammatory fevers of any sort.

Quite recently Walter Whitehead has made the somewhat startling announcement that, during the last five and twenty years, he has 'never¹ failed to treat successfully the most inveterate and severe cases of migraine, by the introduction of an ordinary tape seton through the skin at the back of the neck': he advises that the seton be worn uninterruptedly for three months at least in the first instance, and repeated if the attacks recur. He advances no theory as to the rationale of this therapeutic procedure.

Others quickly made a trial of this treatment, and before many weeks had passed, several successful cases were reported in the 'British Medical Journal,' though not all can be regarded as typical migraine. Dr. Sydney Cornish reports:²—

'The patient, a labourer, aged 25, had suffered from headaches as long as he remembered. At first, vomiting used to accompany the attacks, but latterly the headaches had grown worse, but were less often associated with vomiting. In February 1901, he fell whilst carrying a pole and struck the back of his neck. Since then the headaches have practically incapacitated him from work. When he first came under treatment he was delirious for a fortnight and at times maniacal. His sole complaint was of his head, and he several times attempted to strangle himself in the paroxysms of pain. As he had no rise of temperature all this time, and no abnormal signs were discoverable, one was able to exclude meningitis, pneumonia, cerebral tumour, uraemia or typhoid. . . . Early in December he returned with the headaches as bad as ever. . . . He was so

¹ *British Medical Journal*, 1901, February 9, p. 335.

² *Ib.* 1902, April 26, p. 1025.

dejected about his condition that he now willingly allowed me to put the seton in. . . . From that day until now (more than four months) he has had but one slight headache (*on Christmas night after a particularly festive meal*), and from being gloomy and suicidal he has become bright and active, and has been back at his work for a month. . . . Although the three months are over, he refuses to have the tape removed. . . . This result in a man with almost daily headache . . . is I think wonderful. . . . A large blister was of no use' (Italics mine.)

Dr. Thomas Fentem reports :¹—

'I had under my care a young woman who had been suffering for a considerable time with paroxysmal hemicrania and pain referred to the lower jaw, neck and arm of the same side. She was of highly neurotic temperament. . . . Before coming under my care, many of the teeth had been removed, but I gathered from her history that this gave only temporary relief. . . . All manner of medicinal treatment had been resorted to without permanent benefit. On February 11, 1901, a seton was inserted. Shortly after its introduction the duration of the attacks and the severity of the pains began to diminish, and, after it had been worn for nine weeks, I removed it, the patient declaring herself well. . . . There being some return of the attacks of pain, I, at the request of the patient, introduced a second seton on August 22. . . . She has had no pain for upwards of three months, has improved in every way, and now does a share of the household work.'

Captain T. E. Watson, M.B., I.M.S., reports :²—

'The patient . . . had been given six months' leave on account of migraine. When he came under my care, he was in a very reduced state of health on account of the almost constant and severe pain which he suffered and from want of sleep. He had also lost all appetite and was very thin and weak. After the introduction of a seton in the back of his neck, improvement was most marked and decided, and in three weeks he was almost well, had lost all pain, was able to sleep at night, his appetite had returned, and he was a different man. The seton was then removed. . . . He has come back to report once since then, and at that time had had no return of the old pain, and was looking in excellent health.'

In discussing the subject with Dr. Hawkes, there seemed no room for doubt that the slight septic pyrexia, which follows

¹ *Brit. Med. Journal*, March 8, 1902, p. 587.

² *Ib.* 1902, April 19, p. 961.

the establishment of suppuration, is the active factor in the relief of migraine by seton. Accordingly, in the cases in which we have adopted this procedure, the question of site has been left altogether to the convenience of the patient. The following is an account of the first case in which we used the seton for migraine:—

A hospital nurse, aged 39, had suffered from recurrent migraine since she was a young girl. The paroxysms were severe and typical, being preceded by hemianopia and brilliant fortification spectra and accompanied by intense hemicranial pain, complete anorexia and vomiting. The result of the treatment by seton was eminently favourable: there occurred during the wearing of the seton, a period of 255 days, only eleven attacks, much modified in severity and duration, or less than one attack in twenty-three days, against one in seven or ten days previously: the rectal temperature, which previously ranged between 97°·8 F. and 99° F., ranged, under the influence of the seton, between 98° F. and 100°·6 F.: *the general health improved in all respects*: she continued to improve for three months after the removal of the seton, after which I lost sight of her. The seton was inserted in the left infra-mammary region.

The treatment of headache by seton is not new, though it has doubtless been forgotten. I have in my possession a MS. translation of the Practical Observations of Dr. Frederick Ruysch, who was practising in Holland in the year 1704. Observation XL is as follows:—

‘A head-Ach relieved by the application of a seton but on the removal of the seton returned, an Alternative that lasted some Time.

The daughter of a Merchant at Amsterdam aged about Eighteen of a sanguine Habit, had suffered for a long while a cruel and insupportable Head-ach. Mr. P. Adrian and myself unsuccessfully employed to cure this Head-ach, great quantity of medicines such as Purgatives, Cephalics, Alteratives, Bleeding in the foot and other places, Vesicatories, Sternutatories, Carminatives, &c. At length she consented to suffer a crucial incision upon the Bregma which was followed by a considerable Haemorrhage without procuring any relief. We had several consultations with the eminent Dr. M. Slade; at last finding no remedies successful we proposed to trepan the Scull but before we came to this Extremity I proposed to apply a Seton to her Neck which was approved of by the other two Consultants. The Seton had not been long made before the pains vanished, but what is worthy of remark is that the patient being

tired of this tedious Remedy Drew out the thread and the Seton dried up. The Disorder immediately returned in such a manner that we were obliged to renew the Seton, upon which it stopt. This event made us resolve that she should carry the second Seton 'till Nature dried it up. What happened then? The Seton being thus a second time stopt; the patient relapsed and the pain returned which obliged us to renew the operation; by this means she was again freed from her Complaint, Continues so still and enjoys perfect Health even to this Day.'

§ 327. The theory that the pyrexia is the salutary agent suggested the extension of the treatment by seton to many vaso-motor affections other than migraine, and indeed to all affections, whether vaso-motor or other, which depend upon hyperpyraemia. Accordingly, in addition to typical migraine, we have used the seton in atypical headaches of many kinds, in hay fever, asthma, epilepsy (major and minor), mental aberration, and other less definite pathological conditions. Some of the results are detailed in the appendix: many were favourable. We are in a position consequently to confirm very largely the original statement of Whitehead, and in addition to suggest the application of the method over a much wider territory; and our sentiments in recalling the days when setons were in daily use in every hospital ward are less disdainful than heretofore.

Although for the sake of convenience I have used in this connexion the term pyrexia, yet it will be clear that the real salutary factor does not consist in the increased temperature of the body, but in the increased combustion and output of carbon, associated therewith, assisted doubtless in most cases by diminished carbonaceous intake and absorption. It may happen, of course, that increased combustion or heat-production is fully compensated by increased heat-loss: in this case no rise of temperature will occur; and, indeed, some cases have occurred in which all the beneficial action of the seton was obtained without any material rise of temperature.

Migraine is practically always an intermittent affection, occurring at regular or irregular intervals; and these may be lengthened by various circumstances, such as change of air, increased exercise, etc. Hence the intercepting influence of short pyrexial attacks is often inconspicuous and overlooked by the patient, as well as by the physician. *Asthma*, on the

contrary, often tends to be continuous, or at least remittent or daily recurrent, for weeks together. Hence the intercepting influence of pyrexial attacks of all durations is conspicuous: it is rarely overlooked by the patient; and it has been noted by many eminent medical authorities. Trousseau relates a case in which an attack of broncho-pneumonia conferred, for the time being, complete freedom from orthopnoea upon an habitual asthmatic. He says of this case: ¹—‘Although he cannot even now sleep in a bed unless the mattresses be arranged so as to form a kind of arm-chair, he then slept flat on his back, during the whole of his inflammatory attack.’ Watson refers to two cases (one of which is quoted later in § 698) in which severe spasmodic asthma was completely and permanently replaced by acute phthisis. Dr. Hawkes tells me of three cases of asthma, treated by himself, in which the chest affection was in complete abeyance during rheumatic fever, typhoid, and influenza respectively. And, in my own experience, I have known asthma dispersed temporarily by typhoid, pneumonia, acute bronchitis, dengue, influenza, phthisis, febrile catarrh, septicaemia, and other pyrexial conditions. In most of these the asthma returned during convalescence: in a few, the return was long delayed; and in all the latter there was, I believe, a considerable increase in the deposit of fat.

As with migraine, so with asthma, there is one important exception to the general rule that the affection is inconsistent with pyrexia: this is the invasion stage of many pyrexias characterized by cutaneous vaso-constriction (§ 396).

Gout is a recurrent pyrexia, depending, as will be argued, upon hyperpyraemia; and the replacement of asthma by gout, and conversely, has been noticed for generations.

In the following case, this alternation was well marked:—

A gentleman, aged 54, from an early age, long before he can himself remember, suffered from spasmodic asthma occurring at frequent, but irregular, intervals which were much influenced by locality. At school, between the ages of 10 and 16, his asthma was at its worst. From the time he left school to the age of 32, the asthma slowly but steadily improved, both as regards frequency and severity. At that age he was seized for the first time with gout in the big toe. The gouty attacks at first recurred annually, during the Australian spring (September): then autumn attacks (April) were added; while of late

¹ *Clinical Medicine*, New Syd. Soc., vol. i. p. 625.

years he has suffered about every two months. *But from the onset of his first attack of gout, until the present time, a period of twenty-two years, he has never had a sign of asthma.*

As will be argued later (§ 591), it is not necessary to assume that the onset of gout is the first step in the cure of the asthma in cases such as the above. It is possible, on the other hand, that the cessation of the asthma leads to the development of gout. But even so, the recurring pyrexial acarbonization of gout is substitutive of the recurring neurosal acarbonization of asthma.

§ 328. Hippocrates 'stated¹ ("De morbo sacro") that intermittent fever replaced or mitigated *epilepsy*, at least temporarily, whence the adage: "Quartana epilepsiae vindex appellatur," and this view was also upheld by Van Swieten and Esquirol, the latter of whom said that epileptic attacks diminished and even ceased entirely, upon the intercurrent of febrile attacks (*accidents fébriles*). This was confirmed by Féré, Lannois, and Voisin.' Some authors have been so struck with the favourable influence exerted by infectious diseases 'over² a pre-existing epilepsy, that they have advocated the establishment of some of these different processes, such as malaria and erysipelas, to cure the epilepsy.' I have already referred to the replacement of periodic epilepsy by recurrent pyrexial gout (§ 279); and Hobart A. Hare says:³—'The influence of acute diseases on epilepsy has been quite recently studied by Bourneville and Bonnairè during an epidemic of measles in the epileptics and idiots at the Bicêtre, and they find that during the course of the intercurrent malady the fits are much decreased in force and frequency. Séglas has also made a series of observations at the Salpêtrière and the Bicêtre, and he reaches the following conclusions:—

'1. Intercurrent diseases have, in the greater number of cases, a favourable influence on epilepsy.

'2. In some cases this is only during the intercurrent disease.

'3. Febrile disorders modify it most commonly.'

West⁴ relates the following two remarkable cases:—

'A girl aged 10 years was admitted into the Children's Hospital suffering from epilepsy, fits of which occurred about seven times a

¹ *British Medical Journal*, 1901, July 27, Epitome.

² *Medical Annual*, 1901, p. 241.

³ *Epilepsy: its Pathology and Treatment*, H. A. Hare, p. 222, 1890.

⁴ *Diseases of Infancy and Childhood*, seventh edition, p. 221.

week. . . . After a month's stay in hospital, during which time twenty-four fits occurred, she was attacked by typhoid fever of a mild character . . . which ran its course in twenty-one days. . . . During the whole course of the fever, the fits completely ceased ; but, on the thirty-first day from the first complaint of frontal headache and first accession of fever, the fits returned, assumed their former severity, and returned afterwards with their former frequency. A boy, 10 years old, suffered from occasional attacks of *petit mal* in February. In the following August, the attacks became regular epileptic seizures which increased in frequency, and in the succeeding March returned several times a day, and were accompanied by marked impairment of his mental powers and by an unsteady and tottering gait. After a two months' trial of various remedies, and the insertion of a seton in the back of his neck, he left the hospital worse than on admission. On June 13, he fell in a fit and struck his occiput a violent blow. A large abscess formed there which burst of its own accord, continued discharging for a few days, and then healed up. I saw the boy again two years after this accident had happened, and there had been no return of fits ; but the boy had regained his power of walking, and had all the intelligence and cheerfulness that befitted his years.'

Manifestly in the last case the pyrexia induced by the seton was inadequate for acarboxylation, which was attained through the more powerful pyrexia—or better, the greater increase of combustion—attending the scalp abscess.

The treatment of epilepsy by the insertion of a seton in the back of the neck is referred to by Gowers, who says : '—That this occasionally does good is testified by strong though ancient evidence . . . In the few cases in which I have tried the seton, no effect on the attacks could be discerned.' Dr. Wilton Love of Brisbane recalls the following case under the care of Fraser at the Edinburgh Royal Infirmary :—

A man of 29 was suffering from epileptic fits amounting in number to between thirty and fifty a day. Bromide of potassium in dram doses proved useless. A seton was inserted into the back of the neck. As a result the number of fits fell to three in two days. The improvement was maintained while the patient remained under observation, a period of one month.

In the appendix will be found an account of a case of minor epilepsy, in which marked benefit attended the use of the seton. (Case LII.)

The marked success which follows the insertion of a seton, in many cases of the paroxysmal neuroses, fully confirms, to my mind, the truth of the ancient view that it is sometimes dangerous to promote the healing of old-standing sinuses, fistulas, and ulcers. Most such affections are associated with mild septic pyrexia; or if not, they may entail considerable purulent discharge. And the danger of healing them consists, not in the closure of an outlet for some poisonous humour or the removal of a salutary focus of counter-irritation, but mainly in the loss of an accustomed pathological reinforcement to physiological combustion, and, in lesser degree, in the loss of an accustomed additional means of acarbonization through direct loss. The physiological analogue to an apyrexial suppurative focus relieved by free discharge is found in lactation, a process which, we have seen, is capable of maintaining migraine in complete abeyance (§ 320). I have seen more than one case in which the development of varicose ulcers has intercepted long recurrent headaches, and in which the healing of the ulcers under hospital management has been promptly followed by return of the headaches. And Dr. Hawkes had occasion to perform abdominal section on an old migraine sufferer: some stitch-hole abscesses followed in the wound, and the migraine paroxysms returned only after the last of these had finally healed.

The cessation of anginal paroxysms on the supervention of acute articular gout has been noted by several authorities; and I have seen several cases in which recurrent angina ceased completely during other varieties of pyrexia. The cessation of recurrent epilepsy on the supervention of acute recurrent gout has already been referred to (§ 279).

It has been argued that pyrexia is peculiarly liable to be followed by hyperpyraemia (§ 230): hence we shall find that many pathological acarbonizing processes date from the occurrence of pyrexia, not, it is significant to note, from the pyrexial stage, but from the period of convalescence, or even later; and this is especially true of the paroxysmal neuroses.

Eustace Smith says:—'Exhausting illness, *e.g.* typhoid, seems to predispose to *migraine*'; and Donkin¹ points out that the tendency to this affection is sometimes latent and called forth by some form of 'nerve depression' such as that *which*

¹ *Diseases of Childhood*, 1893, p. 325.

results from severe illness. I have seen many migraines recur, some arise, during convalescence from typhoid.

Salter¹ says that 'whooping-cough, bronchitis and measles . . . are beyond a doubt the commonest of all the causes of asthma: a large proportion (as much as 80 per cent.) of cases of asthma in the young date from one or other of them.' Kingscote says: ²—'To these we must undoubtedly add influenza.' And, in so far as Queensland is concerned, we must further add dengue.

Now all these affections are pyrexial, and all of them, therefore, may, as already pointed out (§ 104), be regarded as capable of leading to hyperpyraemia during convalescence. But, on the other hand, all, with perhaps the exception of the last, are liable to be complicated with bronchial irritation or catarrh; and the local damage, so induced, is probably a most important factor in directing the ensuing pathological acarbonization into the respiratory channel (compare § 527). Thus pyrexias, associated with bronchial complications, probably favour asthma both generally and locally, by inducing the humoral condition hyperpyraemia, and by rendering facile morbid reaction of the bronchial mucosae. It may be contended that the latter means alone is worthy of consideration. But the importance of hyperpyraemia is shown by the fact that asthma not uncommonly follows pyrexia which has been, throughout its whole course, free from any bronchial complication. I have seen it follow typhoid, malaria, and, as already mentioned, dengue. Epidemics of dengue, during recent summers, have frequently swept the northern and central portions of Queensland, and many asthmas date approximately from the departure of the fever. And, though in some cases of this affection there is irritation of the mucous membranes of the eyes and nose, and in a few some bronchial irritation, yet, in comparison with influenza, respiratory symptoms are conspicuously absent.

§ 329. Gowers³ states that, excluding cases due to some sudden brain lesion, such as thrombosis and embolism, 'epilepsy is a sequel especially to scarlet fever, measles, and typhoid fever in that order of frequency, and more cases are consecutive to scarlet fever (apart from the influence of nephritis) than to all other acute diseases put together.'

¹ *On Asthma*, 1868, p. 148.

² *Asthma*, 1899, p. 98.

³ *Diseases of the Nervous System*, 1893, vol. ii. p. 733.

Hippocrates said:¹—‘It is better that a fever succeed to a convulsion than a convulsion to a fever’; and Galen and other commentators explain that, in the first event, ‘the succeeding fever removes the thick humours which occasioned the convulsion and in so far proves beneficial.’ Allowing for differences of phraseology, the conception here implied is practically identical with the view maintained in this work. The initial convulsion of a fever may, or may not, be associated with hyperpyraemia: it is at any rate due, in many cases, as will be argued later (§§ 421 to 432), to rapid widespread vaso-constriction and consequent sudden rise of blood-pressure. In any case it is not likely (any more than is the initial rigor) to be repeated, since pyrexia, after the initial stages, almost invariably involves acarbonization, general vascular relaxation and low blood-pressure. Conformably, Trousseau remarks:²—‘Convulsions at the beginning of an attack of measles, unless they recur frequently, are not of very serious import.’

On the other hand, it is highly probable that a convulsion, occurring for the first time in the convalescent stage of fever, depends upon post-pyrexial hyperpyraemia. And, since the exaggerated pyrexial acarbonization is then over, there is a strong probability that the epileptic acarbonizing process will become recurrent.

§ 330. HAEMORRHAGE.—Reference has been made to the acarbonizing influence of haemorrhage (§ 154). In virtue of this power, haemorrhage is found to disperse temporarily other acarbonizing processes, including the paroxysmal neuroses. Liveing³ quotes the following typical case of Tissot’s, in which epistaxis and migraine alternated:—

‘I once saw a youth who had several attacks between the ages of 12 and 16: then he began to suffer frequent bleedings from the nose, and the migraine disappeared. At 19 the bleeding ceased and the migraine returned; but after six months, the haemorrhages having returned, the migraines terminated.’

I have notes of several similar cases: in some the haemorrhage was from piles; and even physiological menstruation may

¹ *Genuine Works of Hippocrates*, Adams, Sec. II. Aphorism 26, p. 205.

² *Clinical Medicine*, New Syd. Soc., p. 219.

³ *Megrim and Sick-headache*, 1873, pp. 325, 326.

terminate, when the flow has become well established, those neural attacks which its onset precipitated.

It is true the relief afforded by haemorrhage is often so rapid, that we cannot ascribe it to decarbonization merely: we must attribute it to the reduction in the blood-pressure, which is admittedly the first result; but I shall argue later (§ 727) that increased blood-pressure is a factor intermediate in position between hyperpyraemia and the paroxysms of these neuroses.

But sometimes the relief is long persistent; and then its dependence upon acarbonization is clinically conspicuous. Graves¹ relates the case of a young lady on whom, after repeated attacks of headache, Stokes employed venesection, *ad deliquium*, during a violent paroxysm: the operation was followed by immediate relief *and the relief was permanent*. (Italics mine.)

The writer of these pages, when a schoolboy, suffered from irregularly recurrent attacks of intense headache: the pain was at first frontal, a day or so later it was vertical, later still it was occipital: the whole attack usually lasted a week. On one occasion, after the pain had endured for a few hours, profuse epistaxis occurred and was immediately followed by complete relief which lasted several months. At the onset of the next attack, he requested the visiting physician to bleed him, but a tonic was prescribed instead. However, a few self-administered taps on the nose brought on the wished-for epistaxis, and this was again followed by prolonged freedom from attacks. Several times subsequently, he treated himself in this way and always successfully.

Besides typical migraine, the less complex bilious attacks are often interrupted in their recurrent course by haemorrhages of various kinds; and asthma, as we shall see later, may be markedly relieved in the same way (§§ 400, 401).

§ 331. While haemorrhage is an acarbonizing process, profuse or repeated haemorrhage tends, as we have seen (§ 233), to anaemia, and so, to diminished combustion and hyperpyraemia. Hence, as a rule, very profuse or repeated haemorrhage reacts disastrously upon neural patients: this was fully recognized by the later physicians who continued to practise venesection. Of epilepsy, Graves says: ²—‘Detraction of blood

¹ *Clinical Medicine*, New Syd. Soc., vol. ii. p. 351.

² *Ib.* p. 358.

is sure to remove the violence and shorten the duration of the fit, but it is as sure to increase the subsequent tendency to their recurrence.' He goes on to describe the case of a lady, liable every third or fourth month for twenty-five years to violent epilepsy: on her, 'a young practitioner imprudently used the lancet,' and she became subject to an attack every third or fourth week. Anstie says: ¹—'It is very common for women to suffer severely from migraine and other forms of neuralgia, after a confinement in which they have lost much blood'; although he believes that, in most such cases, the affection was pre-existent. Many anaemic headaches may be explained by hyperpyraemia, secondary to anaemia; and their cure by iron is consistent.

§ 332. DIARRHOEA AND LYMPHORRHOEA.—It has been argued that both diarrhoea and lymphorrhoea tend to act as acarbonizing processes (§ 268). Hence we are prepared to find that both processes may alternate with, that is, replace, other pathological acarbonizing processes. In Cases XXVIII and XXXIX will be found examples of the alternation of diarrhoea with migraine and asthma, respectively; and in one case, the rupture of a lymph tumour (filarial) in the groin, and the establishment of a permanent fistula, completely dispersed a slight recurrent asthma of many years' standing.

§ 333. GLYCOSURIA.—On the view that it is a continuous acarbonizing process, glycosuria should tend to replace recurrent acarbonizing processes; and observation demonstrates that this occurs in a very conspicuous manner.

In two of my cases of diabetes, the patient had suffered from recurrent bilious attacks for years: these ceased a short time before the glycosuria was discovered and never recurred thereafter. Haig says: ²—'I have at present under my care a case in which periodical migraine of many years' standing has ended . . . in glycosuria and diabetes.' Dr. Hawkes contributes the following case:—

A dressmaker, aged 26, had suffered for most of her life from typical migraine occurring on an average once a week. At the age of 21, the attacks ceased suddenly and completely; nor have they ever recurred. At first she congratulated herself and gave up wearing glasses which had been prescribed for a low degree of hypermetropic astigmatism, supposed to be causative of the headaches. Soon,

¹ *Neuralgia and its Counterfeits*, 1871, p. 24.

² *Uric Acid in Disease*, 1897, p. 508.

however, she noticed definite loss of weight; and on seeking advice, she was found to be glycosuric.

Dr. W. J. Fearnley, resident medical officer at the Brisbane General Hospital, contributes the following two cases:—

A man of 47 had suffered at least once a month for about fifteen years from migraine, the severity of the attacks being such that on each occasion he could touch no food for three days. Eight months ago, he contracted diabetes, since when he has had no sign of migraine. A woman of 44 had suffered for twenty years from bilious attacks or migraine, averaging one a month and lasting three days. Two years ago, she became glycosuric: since then she has had no single attack.

A patient of mine, aged 36, had suffered from fairly regular periodic migraine, for as long as he can remember until the present year (1901): the pain was right hemicranial: began in the morning on awaking: was accompanied by vomiting in the late afternoon; and ceased during sleep at night. Eight months ago, he contracted typhoid; and ten days before the commencement of the fever, he had a particularly violent migraine, which turned out to be his final attack. At the commencement of the fever, he suffered from the usual frontal headache: the fever lasted many weeks. After its termination, he congratulated himself upon losing completely his 'bilious attacks.' Two months later, he consulted me for increasing obesity, and I discovered that his urine was loaded with sugar (sp. gr. 1045). He is otherwise apparently in perfect health.

The dispersion of recurrent migraine by glycosuria seems to be practically invariable. I have succeeded in finding only one case in which there remained any tendency to migraine after the onset of glycosuria. The patient had suffered from migraine once a month for many years. Three years ago, he became glycosuric. Since then, he has had three attacks of hemicranial pain; but it is worthy of note that these attacks are associated with no digestive symptoms, other than slight loss of appetite, whereas his old attacks were accompanied by complete anorexia and violent vomiting.

Since, as already argued, glycogenic distension of the liver is an essential factor in bilious attacks and migraine associated with anorexia; and since, on Pavy's hypothesis, which we have accepted, glycosuria implies an incapacity on the part of the liver for glycogenic distension: it might be contended that the cessation of the former, at the onset of the latter, is explicable

without assuming glycosuria to be an acarbonizing process. It is true that an inability for glycogenic distension would explain the cessation of bilious attacks and the cessation of the anorexia and digestive phenomena of migraine. But alone it would hardly explain the total cessation of the cranial pain of migraine; nor would it explain the cessation of angina pectoris (§ 335), asthma (§ 334), or recurrent gout (§ 590), all of which may be hyperpyraemic affections, having no necessary connection with glycogenic distension of the liver.

§ 334. The dispersion of asthma by glycosuria seems as invariable as that of migraine. Dr. W. J. Fearnley, resident medical officer of the Brisbane General Hospital, reports the following case:—

A man of 20 had suffered for three years from recurrent asthma, the attacks being always nocturnal and severe enough to cause him to leave his bed. Ten months ago he contracted diabetes, since when he has been completely free from asthma.

A personal friend of my own, a medical man, suffered for many years from irregularly recurrent asthma, usually induced by eating late in the evening. On the evening of his departure from Australia for a tour through the United States, he was entertained by his friends at a farewell dinner. At two o'clock on the following morning, he had a severe asthmatic paroxysm. This turned out to be the last from which he ever suffered; for shortly after his arrival in America, he contracted diabetes, to which affection he succumbed five years later.

§ 335. In two cases of irregularly recurrent angina pectoris, the paroxysms ceased permanently at the onset of diabetes.

§ 336. As to the influence of glycosuria upon old-standing epilepsy, I have no observations of my own; nor can I find any such recorded in medical literature. Williamson says: ¹— 'Diabetes and epilepsy are very rarely associated in the same subject, though epilepsy, diabetes, and mental disease are sometimes met with amongst the various members of the family of a diabetic patient. In only one case of diabetes which has come under my notice was the patient subject to fits . . . he had suffered from epilepsy for some years before the onset of diabetes.' The author quoted, however, did not state what was the influence, if any, of the onset of glycosuria upon the

¹ *Diabetes Mellitus*, 1893, p. 240.

recurrent disorder. *A priori*, a marked modification, whether in the number or severity of the attacks, or in both, was to be expected. But verification was urgently demanded, and the case plainly offered an exceptional opportunity for this. Accordingly, I wrote to Dr. Williamson, who responded most kindly and promptly. The subjoined is an extract from his letter :—

'The case was that of a man, aged 44, who had suffered from epileptic fits since the age of 19. When I saw him first, he had suffered from diabetes mellitus for three months. About one month before his diabetic symptoms were first noted, he had fallen into the fire during a fit and had burnt his left arm rather severely. . . . His diabetes was of a severe form: the sp. gr. of the urine was 1035. The urine was loaded with sugar: it contained a little acetone but no albumen. . . . He was a hospital patient, and I saw him for a few weeks only. He then left Manchester and I have never seen him since. Fortunately, I had his address in my notes, and I have written to his relatives and asked for the information you desired, as the time he was under my observation was too short for me to form any opinion as to the effect of the diabetes on the epileptic attacks. The patient's wife replies as follows :—

"1. Previous to the diabetes being diagnosed, he used to have one or two fits a week.

"2. After diabetes was diagnosed

"a. Had four fits in six months. He then died.

"b. The fits were much weaker and resembled a child's fit . . . "

The above is given in the words of the patient's wife. I think it is quite reliable. I had seen a good number of epileptic patients and diabetic patients before I wrote my book on diabetes; and I have seen a good number of sufferers from both diseases since, but I do not remember ever meeting with any patient, except the one just mentioned, who suffered from both diseases.'

Epilepsy is a particularly efficient acarbonizing process and one which does not usually tend to wane in efficiency as time passes: hence, probably, it tends to confer immunity against other disorders depending upon hyperpyraemia or upon some of the causes of hyperpyraemia; and of these, I shall argue, diabetes is probably one (§§ 683 to 689).

§ 337. CANCER.—It has been urged that cancer, or malignant tumour formation of other morphology, is capable of promoting acarbonization of the blood, (1) through diminished intake: (2) through increased anabolism; and (3 and 4) perhaps through

haemorrhage and pyrexia, the latter including suppuration (§ 281). Consequently, cancer should have inverse relations with the manifestations of hyperpyraemia, whether a carbonizing processes or other.

I have long recognized clinically the existence of such inverse relations, but I was unaware until recently that they had been observed and recorded. Gout, and gouty affections generally, will be ascribed to hyperpyraemia; and Bouchard¹ points out that cancer terminates gout. 'De même que la goutte disparaît, les autres maladies, telles que l'eczéma, l'urticaire, le psoriasis, qui peut accompagner la goutte, disparaissent aussi. L'asthme, que le gouteux peut avoir, s'éteint également.' I have seen cases in which cancer had dispersed recurrent bilious attacks, migrainous and anginal paroxysms; and I do not doubt that it is capable of dispersing most of the manifestations of hyperpyraemia.

Dr. Hawkes has notes of a series of cases in which the onset of cancer terminated abruptly long recurrent manifestations of hyperpyraemia. The following is an example, typical of such inverse relations:—

A man of 45 had suffered for most of his life from alternating migraine and diarrhoea. Ten months ago, both affections ceased to recur quite suddenly: this was the first thing he noticed. Next he noticed that he was rapidly losing weight and becoming dyspeptic. Later, vomiting supervened. An exploratory laparotomy disclosed rapidly growing carcinoma of the pylorus.

Such cases demonstrate the extreme importance of life histories of the individual from a practical standpoint: the sudden unexplained subsidence of any accustomed manifestation of hyperpyraemia should always lead to an exhaustive examination.

§ 338. THE SELF-CURATIVE AND MUTUALLY CURATIVE INFLUENCE OF THE PAROXYSMAL NEUROSES.—It has long been recognized by the medical profession that a frank attack of any of the paroxysmal neuroses is, in itself, a safeguard against an early recurrence, and all sufferers freely endorse this view. Niemeyer² knew a lady who 'had her guests invited the day she had migraine so that she might be certain of being able

¹ *Les Maladies par Ralentissement de la Nutrition*, 1890, p. 282.

² *Text-book of Medicine*, vol. ii. p. 297, Niemeyer.

to receive them on the following day.' This self-curative influence can hardly be expressed more clearly than in the oft-quoted words of Salter. He says of asthma—but his observations apply without modification, perhaps with even greater force, to the other 'paroxysmal neuroses' and, indeed, as we shall see later, to recurrent acarbonizing processes, not prominently neurosal, such as acute gout:—'There¹ is one curious circumstance about it that clearly shows that its periodicity is inherent—part of the disease. It is that each attack seems to impart, for a time, an immunity from a repetition of the fit. For some time after an attack, the time varying according to the interval characteristic of that particular case, the patient may expose himself to the ordinary exciting causes of the paroxysms, without the slightest fear of inducing one. As this period draws to a close, exposure to the provocatives of the attacks is attended with more and more risk; and, when it has transpired, the slightest imprudence is certain to bring on a fit. This curious feature, in which asthma so much resembles epilepsy, suggests to one's mind the idea that each attack is *a sort of clearing shower*.' Fagge says of epilepsy: ²—'Sometimes the temper is worse immediately before the epileptic attack: when a fit occurs it seems to afford temporary relief to the brain, and the patient afterwards feels lighter and more cheerful than for a long time before.'

All my patients suffering from recurrent bilious attacks, nearly all those suffering from migraine, several with epilepsy and asthma, and one with periodic gastralgia, have assured me that the few days following an attack are quite the most pleasurable of any. They may feel some disinclination for exertion, especially on the first day, but they are conscious of a sense of relief and sometimes of extreme comfort, comparable only with the sense of well-being experienced during the convalescent period of fever. On the other hand, Day says: ³—'For some days before the development of a nervous headache' (another term for migraine) 'patients will admit, on close examination, that they felt easily fatigued without any real cause: that they woke unrefreshed in the morning, with a feeling of weight over the eyes, which passed away after break-

¹ *On Asthma*, first edition, p. 97, Hyde Salter.

² *Text-book of Medicine*, 1891, vol. i. p. 754.

³ *Headaches*, Dr. Day, 1880, p. 12.

fast : that before the close of the day they were unusually tired, and felt on going to bed some flatulence and indigestion, with dryness of the mouth, and an extraordinary degree of depression and weariness. During the night or the following morning the nervous headache is developed, and after that the altered sensibility of the brain and the arrest of the powers of digestion proceed together.' Much the same is true of asthma and epilepsy ; Salter¹ refers to 'the drowsiness and languor of the preceding day by which the approach of the attack is fore-knownn' ; and increasing irritability or depression in many cases invariably leads up to an epileptic fit. But the inter-paroxysmal periods are not always absolutely regular. Other things—more especially the food supply—remaining constant, the severity of the paroxysm will be proportionate to the time which has elapsed since the previous paroxysm ; and again, the severity of the paroxysm will determine the duration of the succeeding interval. James W. Russell,² relating the history of a case of migraine which dated from birth, remarks :—'It has been noticed that the ensuing attack has always been worse after an unusually prolonged interval. On the other hand, a second headache occurring after a few days' interval has generally been mild, and of short duration.' This case may be taken as an example of the general rule that paroxysms tend to be severe in proportion to their infrequency, and conversely : as Sir Henry Holland³ said, 'there is clearly in . . . cases of lengthened periodicity some relation between the time of exemption and the violence of the succeeding attack.'

§ 339. It must, of course, be understood that, when speaking in this connexion of the severity of paroxysms, reference is made only to the severity (intensity and duration) of that feature of the paroxysms which secures acarbonization. In migraine and gastralgia, the acarbonizing feature is the anorexia or digestive revolt which precludes fresh carbonaceous income, although it may be that in most cases the pain is proportionately severe : in asthma, epilepsy, and some cases of angina pectoris, the acarbonizing feature is the involuntary or semi-voluntary physical exercise which promotes increased carbonaceous expenditure.

¹ *On Asthma*, 1868, p. 29.

² *British Medical Journal*, May 2, 1903, p. 1020.

³ *Megrim and Sick-headache*, Liveing, 1873, p. 169.

§ 340. The self-curative influence of neurosal paroxysms may be safely inferred from numerous observations. Therapeutic interference, which renders less acute the manifestations of the attack without removing the humoral cause, is liable to prolong the existing paroxysm or series of paroxysms. One of my patients volunteers the following statement :—

Every two or three months, he suffers from a series of asthmatic attacks : these are limited to the hours between 3 A.M. and 6 A.M. Himrod's cure gives almost instant relief ; and the attacks, so aborted, continue to recur each morning for a fortnight or perhaps three weeks. Usually when travelling he carries the drug with him ; but, on some occasions, he has been without it and unable to procure it. Then the attacks last from two to three hours, but they invariably cease to recur after the fourth or the fifth day at latest (Case XXX).

Any treatment which is successful in aborting or deferring paroxysms tends in many cases to intensify succeeding paroxysms, or to render their return more early. Later (§ 426) I shall refer to the observation that an epileptic fit, aborted and deferred by the inhalation of nitrite of amyl, is often unusually severe when it arrives ; but the working of this rule is observable in migraine and other paroxysmal neuroses.

But, to the general rule that the attacks of the paroxysmal neuroses are infrequent in proportion to their severity, and conversely, there are of course many exceptions, due no doubt to the fact that frequently other things are by no means equal.

§ 341. We are now provided with a simple and tangible explanation of the inter-relations of the paroxysmal neuroses—of the phenomena termed by Liveing ' neurosal transformations or metamorphoses,' and by other authors ' alternating neuroses.' Many such disorders are a carbonizing processes, depending on hyperpyraemia : consequently, each attack becomes for the time being an efficient preventive of further attacks of the same or of other neuroses : they are self-curative and mutually curative in the strict sense of these terms. And, since they are all adapted to the same end, the dispersion of the common blood-state, it can rarely happen that more than one variety is called for simultaneously : *their affinities are those of blood relations, their antagonisms, those of mutual rivalry.* Conformably, Harry Campbell considers that the evidence in favour of a connection between migraine and epilepsy is strong. But he

remarks: ¹—‘While, however, the two are probably related, there would seem to be a certain antagonism between them, so that the presence of one to a large extent confers immunity from the other. The child of insane parentage is much less liable to become insane or to develop epilepsy if megrinous than otherwise.’

It may be argued that the alternation of the neuroses is explicable as clearly on the theory of the accumulation and discharge of nerve-force, as on the theory of the accumulation and discharge of carbonaceous material. But the former theory covers only a small portion of the field: the alternations of the neuroses are not merely mutual: they occur, as we have seen, with other processes, physiological as well as pathological which never have been regarded as primarily, or essentially, nervous (§§ 287, 288).

§ 342. DIETETIC TREATMENT BY REDUCTION OF PROTEID.—It has been argued deductively that hyperpyraemia may be dispersed by two seemingly opposed methods of dietetic treatment—the treatment by reduction of proteid (§ 246), and the treatment by reduction of the carbonaceous intake (§ 247). If, then, the paroxysmal neuroses depend upon hyperpyraemia, they should be dispersable (though not necessarily in the same cases, nor with equal satisfaction) by either method.

We will consider first the *treatment by reduction of proteid*. Of periodic headache, Lauder Brunton says:—‘By putting a man upon a non-nitrogenous diet . . . you may increase the intervals between the headache more and more until you may make the interval indefinite and prevent the headache from recurring at all.’ Of his own migraine, Haig says: ²—‘My headaches diminished both in frequency and severity, and from an average of one a week, they fell steadily, as the diet was persevered in, down to one in a month, one in three, six, eight or twelve months, and eventually eighteen months elapsed without an attack of notable severity.’

We have seen that these methods of dietetic treatment reduce hyperpyraemia by weakening the carbonizing functions of the digestive organs (§ 246). Clearly the mode of convalescence described by Lauder Brunton and Haig is confirmatory of this view. The weakening of any function by the withdrawal of the nitrogen upon which it depends will necessarily

¹ *Headache*, 1894, p. 224.

² *Uric Acid in Disease*, 1897, p. 2.

be a gradual process : hence hyperpyraemia will subside only gradually ; and the clinical manifestation of hyperpyraemia will continue for a time to recur at widening intervals and with decreasing intensity.

§ 343. Consistently, Lauder Brunton asserts that the intervals between the attacks of periodic headache become less in the same person 'when he is on a more highly nitrogenous diet.' Haig says that, if he attempts to increase his fish and egg, he at once begins to suffer for it in the way of headache, catarrh, asthma or some other trouble connected with uricacid-aemia.¹ Dr. Brockway of Brisbane treated a gentleman aged 32, suffering from intermittent asthma, by means of Haig's diet. The result was satisfactory. The patient remained free from attacks for long periods, while he adhered to the dietetic restrictions. Occasionally, however, he became careless : now and then he indulged in some chicken, salmon, and meat ; and on each occasion he suffered thereafter from an asthmatic paroxysm. George S. Keith² described a case of angina pectoris, treated by reduction of proteid. The patient was a well-known Edinburgh literary man, past middle life, powerful alike in mind and body. He had enjoyed excellent health, was blessed with an excellent stomach, and had taken full advantage of it. When he came under treatment, he had given up all his outdoor pursuits and could scarcely walk across the floor without a threatening of an attack of angina : his only relief was from inhalation of amyl nitrite. Stimulants, beef and mutton were stopped, and great moderation in simple food enjoined. 'He soon began to improve, was able to resume his literary work, and even in moderate degree shooting and fishing . . . On three occasions only during a period of four years he partook of beef at dinner, and on all three he had one of his worst attacks.'

Such cases are clearly explicable on the theory of hyperpyraemia. The dietetic methods of Lauder Brunton and Haig involve a carbonaceous intake in excess of the necessities of the organism. But the reduction of proteid diminishes the functions of digestion and absorption (carbonization) and thus precludes, reduces, or disperses hyperpyraemia. Under such diets, there will be an excess of carbonaceous material in the alimentary canal, and, since any increase of proteid will increase

¹ *Fads of an Old Physician*, George Keith, p. 32.

² *Ib.* pp. 54, 55, 56.

the carbonizing functions, the result may be the development of hyperpyraemia.

To such facts must, I think, be ascribed the widespread prejudice against meat eating which exists in the medical profession at the present day. Assuming, as we do, that carbonaceous material in the blood is either rapidly oxidized or deposited as fat, etc., we, with few exceptions, have ignored most of the pathological potentialities of carbonaceous excess; and our eyes have been open only to the influence of increasing and decreasing the nitrogenous portion of a mixed diet. Hence various authors regard meat as an improper nutriment for migrainous, epileptic, asthmatic, bronchial, anginal, rheumatic, and other affections.

§ 344. That impairment of the carbonizing functions of the alimentary canal is the active salutary factor in Haig's diet, is further assured by an extremely important observation of this author. Speaking of epilepsy, Haig says: ¹—'It may be as well to point out, with regard to diet treatment, that in this disease just as in headache . . . the first effect of a strict diet may be an increase in the frequency and severity of the fits.' In Haig's ² diet 'all meat, fish, fowl, game and eggs' are cut off, and replaced by 'milk, cheese, pulses, bread and corn foods.' ³ The change plainly implies a reduction of the proteid intake and an increase of the carbonaceous intake. Now it is clear that the sudden enjoinder of such a diet will find the carbonizing functions of a person, who has lived habitually on the ordinary mixed diet containing an ample supply of proteid, in a condition of comparatively high activity, and that it will result in an immediate increase of the hyperpyraemia. It will not be until the scarcity of proteid has succeeded in reducing the activity of the carbonizing functions—and this will take time—that the hyperpyraemia and its manifestations will tend to subside.

§ 345. But it has been argued *à priori* that a reduction of proteid, which is capable of weakening the carbonizing functions of the digestive organs, will presumably be capable of weakening also the decarbonizing functions of the tissues: that consequently three different results are to be expected from this line of treatment, namely, (1) hyperpyraemia relieved; (2) hyperpyraemia unaffected; and (3) hyperpyraemia exaggerated;

¹ *Uric Acid in Disease*, 1897, p. 245.

² *Ib.* p. 615.

³ *Ib.*

and that the difference in each case is due to differences in the incidence of the resulting malnutrition (§ 249). Hence we shall not expect this dietetic treatment to be successful against hyperpyraemia in all cases, perhaps not even in the majority; and we shall expect, in some, to find evidence of impaired function generally, or of general deterioration of health. These expectations, I maintain, are fully borne out on appeal to clinical experience.

Suckling,¹ evidently referring to the dietetic plan by reduction of proteid, says:—‘I have never found any benefit from dieting patients suffering from migraine. I have met with several people who had been vegetarians for years on account of headaches, but the headaches were as bad as ever, and they were in worse health than when taking meat.’

My own experience of the treatment by reduction of proteid is not extensive. Such as it is, however, it is not so uniformly unfavourable as Suckling’s; and it conforms generally with the anticipations formulated. As regards bilious attacks, periodic headache, and migraine, I should say that in a certain rather small minority the attacks were reduced in frequency and severity: in the majority they were unaffected; and in a few, they were distinctly exaggerated, at any rate for some time after the initiation of the dietetic change. But, in the great majority, whatever the influence upon the recurring headaches, the general health, mental and physical energy and activity seemed to me less satisfactory than before: in some cases, there was no question as to the deterioration which occurred in these respects.

As regards asthma, my experience is still less favourable. There were the same objections on the score of the general health and well-being, while hardly ever have I seen diminution in the frequency, severity, or duration of the paroxysms; and the same remarks apply to epilepsy, angina pectoris, and other allied affections.

Haig,² however, refers to the case of a gentleman of 50 ‘who had suffered from fits all his life, and was cured by a severely vegetarian diet, with a purgative dose of calomel and colocynth, followed by haust. sennae co. twice a week.’ This patient lived twenty years more without any fits at all. ‘He

¹ *Periodical Headache or Migraine*, pp. 10, 11.

² *Uric Acid in Disease*, 1897, p. 220.

lost weight very decidedly and was considerably weakened by the treatment.' (Compare § 245.)

§ 346. DIETETIC TREATMENT BY REDUCTION OF THE CARBONACEOUS INTAKE.—This is the dietetic plan to which I have most frequently resorted for the relief of most of the affections which depend upon hyperpyraemia: it will be considered in some detail in §§ 943 to 950 and in the appendix of illustrative cases. Meanwhile, it may be stated that, though the different manifestations of hyperpyraemia, and the same manifestations in different individuals, respond to this plan in widely different degrees, the aggregate results seem to constitute ample evidence of the truth of the theory.

It has been argued that the theoretical objections, applicable to the treatment by reduction of proteid, do not apply to the treatment by reduction of carbonaceous food-stuffs. With this latter, there is no question of the impairment of any set of *functions*: the question is purely one of reduction of the carbonaceous or fuel *supply* (§ 247). Hence we shall expect, in successful cases, that the mode of convalescence under this treatment will differ widely from that under the alternative dietetic treatment described: we shall expect, at least in some cases, that the result will be immediate. This is borne out on appeal to clinical experience. In Case VI, recurrent bilious attacks (some would describe them as migraine) of probably thirty years' duration ceased absolutely from the day on which the dietetic change was instituted, and never recurred thereafter; and many other cases responded equally rapidly.

Results, as favourable and definite, were obtained in very numerous cases of recurrent headache, sick and other, in many cases of typical migraine, asthma, and angina pectoris vasomotoria.

The effect of the dietetic change in the ordinary varieties of recurrent headache, not amounting to formal migraine, points to the conclusion that the *great majority* of these affections are hyperpyraemic and dispersable with great facility by a moderate carbonaceous restriction, perhaps combined with some increase of physical exercise. Each word in the above sentence has been carefully weighed.

In epilepsy, the results have been as a rule much less definite; but it is only fair to say that the cases submitted

to treatment were almost uniformly unfavourable. Nevertheless, in one case of major epilepsy (Case XLIX), and in one case of juvenile convulsions (Case LV), extremely definite and happy results were obtained.

§ 347. Evidence, which to me seems conclusive as to the nature and meaning of the paroxysmal neuroses, may be obtained by simple experiments in dieting. In certain cases of recurrent bilious attacks, migraine, asthma, and angina, the attacks may be abolished indefinitely by simply reducing the carbonaceous intake to a certain level—this level varying within pretty wide limits with the individual: cases, responding so faithfully to restriction of the fuel supply, are by no means few or far between. Having by careful experiment, in a given case, determined the maximum carbonaceous intake compatible with entire freedom from attacks—with purely physiological a-carbonization, that is to say,—we are in a position to test the influence of slight increases in the carbonaceous intake. An example or two may be given here.

In a typical case of migraine (Case XI), I made a large number of such experiments; and it was astonishing to learn how small a daily addition to the carbonaceous intake is sufficient to reinduce attacks. On different occasions, one teaspoonful of glucose, two or three lumps of cane sugar, half an ounce of butter, one pint extra of milk, a very small plate of porridge, an extra ounce of bread or toast, six strawberries with cream but no sugar, were added to the daily diet: the result was the same on all occasions, namely, the development sooner or later of a typical migraine paroxysm. The time at which the attacks occurred after the carbonaceous addition varied with many circumstances, such as the amount of the addition, the temperature of the atmosphere, the amount of physical exercise, etc.: in general, however, an attack supervened in from three to seven days: it was never immediate.

In this case, there can have been no question of mere coincidence: an attack could always be induced, even after months of complete freedom.

In a girl of 17, violent paroxysmal asthma had become very frequent. For six weeks before her admission into hospital, she had had orthopnoea every night, from midnight to 4 A.M. On a diet comprising ten ounces of lean meat, two ounces of bread with a little butter, green non-starchy vegetables, and one and a half pint of milk per diem, the attacks ceased in thirty-six hours. For the

following ten days she remained free, with the exception of a very slight degree of wheezing on first waking in the morning, which passed off as she was dressing. At the end of this period, on Sunday at 4 P.M., she ate three cracknel biscuits, one scone, half an ounce of chocolate and two slices of pineapple. At 2 A.M. on Tuesday, that is exactly thirty-four hours later, she had a violent asthmatic paroxysm, which recurred with lessened severity on the following night.

The above two cases are merely isolated examples of a long series of similar observations, some of which concern angina pectoris and epilepsy.

Dr. Hawkes was treating two Catholic ladies for severe migraine by seton plus a mainly meat diet. In the first, the attacks, from having been severe and frequent, had become mild and premenstrual only. In the second, there had been no severe attacks for some months. In both cases, from February 20 to March 3, 1903, that is during Lent, severe paroxysms occurred. In the first, this was intermenstrual. On enquiry he found that, fish and eggs being difficult to procure, both patients had substituted a diet consisting of bread, jam, stewed fruit and puddings.

§ 348. A SALT-FREE DIET.—Quite recently good results in epilepsy have followed the use of a salt-free diet. It is claimed that, under this diet, bromide of potassium exerts a much more powerful inhibitory effect upon the attacks, than under the ordinary diet. Now it is not difficult to see that a salt-free dietary, if persisted in, would gradually tend in many ways to reduce hyperpyraemia. And it may be stated here as a fact, the truth of which can be substantiated by every medical practitioner for himself, that the inhibitory power over the fits of bromide of potassium is invariably greatly accentuated under acarbonizing treatment. This is so whatever the nature of the acarbonizing treatment: it is so under frequent purgation, restriction of proteid, restriction of carbonaceous foodstuffs, increased physical exercise, the septic pyrexia associated with the use of the seton, etc.

It may be that the omission of chloride of sodium leads to a deficiency of free hydrochloric acid in the gastric juice. Such would lead to deficiency in the digestion and absorption of proteid, and to a consequent deficiency of these carbonizing functions. As a result, we might attain reduction of hyperpyraemia and of its epileptic manifestations.

But a salt-free diet would operate otherwise to reduce hyperpyraemia. Pawlow has definitely proved, by experiments on dogs, that 'appetite is the first and mightiest exciter of the secretory nerves of the stomach'¹: that the 'secretory effect is due to the psychic stimulus, that is to say, to the keen desire on the part of the animal for food and to the satisfaction of enjoying it'²; and that 'the more eagerly the dog eats, the more juice will be secreted and the greater the digestive power which it possesses.'³ He has shown, by the experiment of 'sham feeding,' that food, for which the dog has no particular fancy, excites a relatively scanty secretion of juice of a relatively weak digestive power.⁴ Now no one, who has tried a salt-free diet for a few days continuously, will question the diminution of appetite and enjoyment of eating which follows. Several effects will follow: there will be a diminished intake of food: such food as is ingested will undergo less complete digestion and absorption; and if, as seems probable, the proteid food-stuffs, which depend largely upon salt for their sapidity, are reduced in greater proportion than the carbonaceous, then there may be for this reason also a progressive impairment of the carbonizing functions. Thus in many ways hyperpyraemia would be reduced. Of course, a deficiency of proteid might reduce proportionately the decarbonizing functions of the tissues; and such would serve to explain some of the numerous cases in which a salt-free dietary has no salutary influence on epilepsy.

Conformable with the view that a salt-free diet modifies epilepsy by weakening function, are the following observations. The diet does not act until it has been persisted in for some time;⁵ and, while the fits become less numerous, 'the body weight becomes less and the patient weak' (Heinrich Schlöss).⁶

SUMMARY OF EVIDENCE AND CONCLUSIONS

§ 349. I now submit that we have sufficient circumstantial evidence to show that some, at least, of the affections termed paroxysmal neuroses depend upon the humoral condition we have termed hyperpyraemia. Restricting our proposition for the

¹ *The Work of the Digestive Glands*, Pawlow and Thompson, 1902, p. 75.

² *Ib.* p. 73.

³ *Ib.* p. 74.

⁴ *Ib.*

⁵ Reference lost.

⁶ *Progressive Medicine*, September 1902, p. 308.

present, in order to be amply cautious, to the two varieties, migraine and asthma, we have seen both these affections prevented, dispersed, or markedly benefited by the conditions comprised in the following group :—

GROUP I.

1. Reduction of proteid in a mixed diet.
2. Reduction of the carbonaceous intake.
3. Cold weather.
4. Physical exercise.
5. Oxygen inhalation.
6. Diurnal accelerations of combustion.
7. The post-menstrual stage.
8. Utero-gestation.
9. Lactation.
10. Increase of fat-forming capacity.
11. Pyrexia.
12. Haemorrhage.
13. Glycosuria.
14. Intervention of other paroxysmal neuroses.

With some of these there is an increase, with others a decrease, of combustion : with some, there is apt to be an increase, with others, a decrease of the carbonaceous intake : with some, there is apt to be a gain, with others, a loss, of weight ; and each one has many effects peculiar to itself. But they all concur in causing one effect, namely, a tendency to acarbonization of the blood.

On the other hand, we have seen the two selected affections initiated, precipitated, or increased in severity, or frequency, by the conditions comprised in the following group :—

GROUP II.

1. Increase of proteid in a mixed diet.
2. Increase of carbonaceous intake, without reduction of proteid.
3. Hot weather.
4. Cessation of accustomed exercise, or habitual sedentariness.
5. Physical exercise to the extent of causing marked fatigue.

6. Diurnal retardations of combustion.
7. Sleep.
8. The pre-menstrual and early menstrual stage.
9. Prolonged lactation.
10. Decrease of fat-forming capacity.
11. The post-pyrexial stage of fever.
12. Profuse or repeated hæmorrhage.

Each of these has doubtless effects peculiar to itself : most of them are apt to be associated with retarded combustion : all of them tend to cause hyperpyraemia.

Thus, since everything which tends to promote acarbonization of the blood tends to prevent, disperse, or alleviate, whilst everything which tends to promote hyperpyraemia tends to initiate, precipitate, or render more severe or frequent, the paroxysms of migraine and asthma,—the humoral causation of these two affections, in some cases at least, can hardly remain doubtful ; and what is true of these two is certainly true of some others and probably of the majority, if not of all, of the paroxysmal neuroses.

Further, since the majority of the paroxysmal neuroses are acarbonizing processes and depend, as I think we may now fairly conclude of some cases, upon hyperpyraemia, we must regard them as conservative reactions on the part of the organism, adapted to relieve the circulating medium from an overburden of fuel or carbonaceous material.

We may regard such paroxysmal neuroses as pathological in the sense that they are special or additional acarbonizing processes, demanded in certain circumstances or in certain individuals by an inadequacy of physiological acarbonization—*we may regard them, in other words, as ultra-physiological (that is, pathological) reinforcements of inadequate physiological action.*

To this, it may naturally be objected that some of these affections are but ill adapted to the purpose : that no beneficial result accrues from the headache of migraine ; and that asthma, though it implies, through the violent exertion called forth, an increased combustion of carbon, renders difficult the output of carbonic acid and the intake of oxygen, then more urgently than at other times required : that, consequently, if the asthmatic paroxysm is 'protracted'¹ and intense, the heat of the

¹ *On Asthma*, Hyde Salter, 1868, p. 72.

body falls : the oxygenation of the blood is so imperfectly performed from the sparing supply of air, that it is inadequate to the maintenance of the normal temperature ' (Salter), and that the blood becomes intensely venous. It may further be objected that many of the paroxysmal neuroses (epilepsy for example), although they may succeed in dispersing a pathological condition of the blood, are expensive contrivances, in that they entail consequences to the organism in other directions which are more injurious than the fault they are adapted to correct.

The truth of both charges will have to be admitted. Many of the paroxysmal neuroses are most inefficient acarbonizing processes : indeed, in many instances we can only regard them as attempts at acarbonization ; and not a few are fraught with serious correlated injury to the organism. But even so, such arguments do not shake the theory herein set forth. For, if these affections were accurately adapted to the necessities of the organism from the standpoint of both efficiency and economy, it is obvious that we should be unable to regard them as pathological—they would be, on the contrary, physiological, and we should have no right to speak of them as disorders. Indeed, it seems to me that inefficiency or expensiveness or both combined are the leading characteristics which distinguish pathological action of all kinds from physiological action.

CHAPTER X

§§ 350–415

Mechanism of the paroxysmal neuroses : priority of vaso-motor action—Migraine : vaso-constriction : vaso-dilation : cardiac compensation : mechanism of the pain : clinical evidence confirmatory of the vaso-motor theory : some objections to the vaso-motor theory : relation of migraine to rigor : summary of pathology of headache, migrainous and other—Asthma : vaso-constriction : vaso-dilation : cardiac compensation : clinical evidence confirmatory of the vaso-motor theory : summary of pathology of asthmatic dyspnoea.—Angina pectoris : vaso-motor theory : confirmatory clinical evidence : angina and malaria : angina caused by flatulent distension of the stomach : summary of pathology of angina pectoris.

§ 350. If we adopt the humoral theory of hyperpyraemia, we shall be prompted to fall back upon vaso-motor action in order to explain the mechanism of neurosal paroxysms. Vaso-motor hypotheses have been advanced at various times by various authors for many of the paroxysmal neuroses ; and some of these, with slight modification and elaboration, will be found to fit without serious strain the humoral views preferred.

Impure or toxic conditions of the blood have been regarded by many as leading to defensive constriction of the systemic arterioles. George Johnson accounted for the vascular and cardiac phenomena associated with renal cirrhosis by assuming ‘an impediment to the circulation resulting from contraction of the systemic arterioles, excited by blood contamination.’ He regarded the arterial contraction as conservative, and described it as a ‘stop-cock action.’ Such a conception will fit the theory of hyperpyraemia. It is reasonable to believe that blood containing fuel in excess of the requirements of the tissues, and in excess of their capacities for decarbonization, will be less damaging if supplied in reduced amount ; and vaso-constriction will undoubtedly lessen the supply.

At any rate, during an attack of the paroxysmal neuroses, vaso-constriction of wide areas, conspicuously of the surface

and especially of the surface of the extremities, is, so far as I have observed or can infer from the writings of others, almost invariable. Such vaso-constriction will tend to cause a rise of blood-pressure. A rise of blood-pressure has been observed during these paroxysms in some instances; but such seems the exception rather than the rule. If there is an extensive area of vaso-constriction unassociated with a rise of blood-pressure, some compensating factor must be intervening. Such may be (1) a diminution of the quantity of blood in circulation: (2) an area of vaso-dilation; or (3) a modification of the heart-beat, whereby the work accomplished by this organ is reduced.

A diminution in the quantity of blood in circulation, to be effectual in preventing a rise of blood-pressure from following vaso-constriction, must be rapid; and such can only occur from haemorrhage. Sudden, and even profuse, haemorrhage is by no means unknown during neurosal paroxysms, but it is exceptional.

§ 351. Compensation for vaso-constriction by vaso-dilation, though apparently ignored for the most part in the domain of pathology, is a well-recognised physiological principle. Leonard Hill says: ¹—‘The maintenance of a mean arterial pressure of constant height is the object of the circulatory mechanism. On the one hand, we are convinced that this object is attained during life: on the other hand, we know that countless and ceaseless variations are occurring in all parts of the circulatory system. The system must therefore be so craftily built and so delicately balanced, that every variation in one part is compensated by a simultaneous and contrary variation in another part, and thus, throughout the wear and tear of life, the aortic pressure is kept at a constant mean height.’ The physiological principle involved is thus referred to by Stewart: ²—‘The blood supply of the organs is always shifting with the calls upon them. Now it is the actively digesting stomach and the actively secreting glands of the alimentary tract which must be fed with a full stream of blood. . . Again it is the working muscles of the legs or of the arms that need the chief blood supply. But wherever the call may be, the vaso-motor mechanism is able in health to answer it by bringing about a widening of the small arteries of the part which needs more

¹ *Text-book of Physiology*, E. A. Schäfer, vol. ii. pp. 81, 82.

² *Manual of Physiology*, Stewart, 1899, p. 162, 163.

blood, and a compensatory narrowing of the vessels of other parts whose needs are not so great.' In the last quotation, most stress is laid upon compensation for vaso-dilation by vaso-constriction; but the converse is, of course, equally true.

§ 352. In the absence or inadequacy of compensatory vaso-dilation, vaso-constriction will tend to cause a rise in the general blood-pressure; and, conversely, in the absence or inadequacy of compensatory vaso-constriction, vaso-dilation will tend to cause a fall in the general blood-pressure. In both cases, cardiac compensation will be called for. Leonard Hill says: ¹—'If all the cardiac nerves be intact, a rise of arterial pressure always slows the heart, and a fall accelerates it. This mechanism, first recognised by Marey, is of great importance, for by its means the constancy of the arterial pressure is maintained. So long as the vagi are intact, the arterial pressure cannot be *greatly* raised.' (Italics mine.)

Does not confusion sometimes arise through a tendency to infer, from a constricted radial, a rise of blood-pressure? I have seen it stated that Marey's law 'does not work in practice'; and Oliver says: ²—'Though I have made a large number of observations in which the pulse-rate was carefully recorded by the side of the measurements of the radial calibre, I have failed to discover any definite relation (direct or indirect) between the two.' To expect such definite relation seems to me to include the assumption that the calibre of the radial artery at any one time is an index of the tone of the arterial system generally—that vaso-constriction and vaso-dilation fluctuate proportionately and in the same direction throughout the body. But this, as we have seen, is untenable. Consequently, a definite or constant relation between the calibre of any artery and the rate of the pulse is to be expected only in the absence of the correlative vascular condition in other areas: until such has been excluded, it is premature to question the general applicability of Marey's law.

During the course of a most important epistolary discussion in the 'Lancet' on the mechanism of the rise of blood-pressure which tends to supervene in later life, it was inferred that hypertonus of the arterial system (as indicated presumably by constriction of the radial) without rise of general

¹ *Text-book of Physiology*, Schäfer, 1900, p. 56.

² *Pulse-gauging*, 1897, p. 28.

blood-pressure, occurs only in the presence of heart failure, 'when the heart has come to the very end of its tether.'¹ But William Russell¹ points out that hypertonus, without rise of general blood-pressure, is common under other conditions. He is here referring, I conceive, to cases in which a vaso-constriction of some portion of the surface of the body, as indicated perhaps by a perceptible tightening of the radial, is prevented from raising the general blood-pressure through the intervention of some compensating (no doubt internal, and therefore invisible) area of vaso-dilation.

Practically, it seems to me reasonable—I am sure it will be profitable—in cases where a constricted radial is unassociated with infrequency of the pulse, to assume provisionally the existence of some invisible area of vaso-dilation, and to search for the clinical manifestations of this compensatory vascular condition.² And as we proceed with investigation on these lines, we shall, I feel convinced, continue to gain confidence in the truth of the axiom that 'the pulse-rate is inversely as the blood-pressure,' not only in the physiological, but in the pathological, domain.

§ 353. I shall now attempt to show (1) that vaso-motor action is an essential factor in many of the commoner well-known paroxysmal neuroses: (2) that vaso-constriction occurs in all and is, perhaps, usually primary; and (3) that the phenomena peculiar to each neurosis are determined for the most part by the correlative vascular or cardiac condition, whether this consists of vaso-dilation, of cardiac inhibition, or of both.

For this generalization, it is not necessary to establish the nature of the impulse which determines the vaso-dilation. In all probability, arteries may be dilated (1) actively (*a*) through the direct action of vaso-dilator nerves, (*b*) through inhibition of vaso-constrictors: (2) passively, through a rise of general blood-pressure, due to vaso-constriction in other areas or other causes (for example, venous obstruction); and

¹ *Lancet*, February 21, 1903, pp. 550, 551.

² The above sentence was written in 1899. Since then I have been watching for indications that others held similar views, but without result until quite recently. Now, however, I am gratified to find, in the epistolary discussion above referred to, that Harry Campbell has arrived at an identical conclusion. This author says: 'Whenever with radial hypertonus, and a sound heart, the radial pressure is low, we should suspect hypotonus of some large vascular area.'—*Lancet*, March 21, 1903, p. 836.

(3) through some combination of these means. It may be that in many cases dilator impulses predominate or exert sole sway: that in others there is a mere inhibition of vaso-constriction; and that in some there is purely passive dilation (§ 406). In any case, however, these questions need not detain us: they may safely be left for further investigation.

MIGRAINE

§ 354. VASO-CONSTRICTION.—During a paroxysm of migraine, widespread vaso-constriction of the cutaneous area is commonly conspicuous: many writers have pointed out that the superficial arteries are palpably smaller than usual. Anstie says: ¹—‘The patient . . . lies quite helpless, intensely chilly and depressed, the pulse at first slow, small, and wiry, afterwards more rapid and larger, but very compressible. The feet are generally actually, as well as subjectively, cold.’ The large, compressible pulse is usually, in my experience, quite a late phenomenon, coming on in fact as the attack is commencing to abate; but I have seen one case in which both radials were dilated throughout the attack, the hands being hot and swollen: in this case, probably, vaso-constriction occupied some unusual position. Möllendorff noted ² ‘the icy coldness of the hands and feet, and shivering of the surface generally’: Haig says that he himself had shivering or slight rigors in his severe attacks of migraine; and in several of my cases rigor was distinct.

The vaso-constriction is usually most marked in the extremities; but the trunk and face are affected. Lauder Brunton ³ says the anterior branch of the superficial temporal artery is always firmly contracted, though the carotid is widely dilated. In Du Bois-Reymond’s own case, ⁴ the superficial temporal of the affected side was constricted: this led him to ascribe the disorder to tetanus of the corresponding sympathetic nerve, and to locate the pain in the nerves of the contracted vessel.

In headache not typically migrainous, the peripheral arteries

¹ *Neuralgia and its Counterfeits*, 1871, p. 29.

² *Megrim and Sick-headache*, Ed. Liveing, 1873, p. 311.

³ *Disorders of Assimilation, Digestion, &c.*, 1901, pp. 250, 251.

⁴ *Megrim and Sick-headache*, Liveing, 1873, pp. 295, 296.

are often constricted. William Russell¹ refers to the case of a man of 35, who came under treatment for headache, general weakness, and insomnia. 'The radial artery was markedly thick, the thickening being uniform and extending right up the arm.' But several considerations led the author to surmise that, though there was probably some sclerosis, the arterial thickening and the symptoms were largely due to exaggerated constriction or 'hypertonus,' or to the causes responsible for this functional condition. The administration of erythro-tetranitrate (a powerful vaso-dilator) showed this surmise to be correct. Under the use of this drug, the diameter of the radial artery, as measured by Oliver's arteriometer, rose from 2·3 to 2·7 mm.

§ 355. VASO-DILATION.—The vaso-constriction of migraine may be regarded as compensated, to some extent, if not always fully, by an area of intense vaso-dilation, affecting some part of the cranium, but not infrequently extending beyond this district. This vaso-dilation was pointed out by Möllendorff, who regarded it as due to a paralytic condition of the sympathetic, his theory thus becoming 'the converse of that of Du Bois-Reymond.'² In support of the view that this vaso-dilation is the proximate cause of the pain, Möllendorff adduces³ the throbbing character of the pain, the aggravation of the pain 'which follows stooping forward, and the measure of relief afforded by lying back.' He lays stress upon the fact that 'the⁴ pain and tension . . . are also felt deeply in the interior of the head, in the parts supplied by the internal carotid, and where, from their small extensibility and rigid surroundings, a trifling increase in their fluid contents would be felt as tension.' Finally, he points out that the vaso-dilation may often be seen. Of one case, he says:⁵—'During the attacks the background of the eye on the suffering side was of a bright scarlet-red, the optic papilla red and oedematous, the arteria and vena centralis retinae enlarged, the latter knotty and very tortuous.' Wilks, himself a sufferer, says⁶ that 'whilst the body is cold the head is hot, and that whilst the radial artery is small the carotid is full: in fact, if the

¹ *Lancet*, June 1, 1901, p. 1522.

² *Megrim and Sick-headache*, Liveing, 1873, p. 307.

³ *Ib.* p. 309.

⁴ *Ib.*

⁵ *Ib.* p. 310.

⁶ *Lectures on Diseases of the Nervous System*, Sir Samuel Wilks, 1878, p. 427.

term determination of the blood to the head is applicable to any malady, it is assuredly to this . . . the carotid on one side with its branches throbs inordinately, is apparently very full, and is sending too much blood to the brain and its coverings. This I knew when quite a boy, for when leaning my head upon my hand, I distinctly felt the increased size of the throbbing temporal artery on the side of the pain.'

We are by no means bound to assume that, in all cases of migraine, the vaso-dilation is secondary to vaso-constriction; but we are, I think, bound to assume that this is true of some cases—for example, of malarial cases (§ 374), of those cases in which the paroxysm is precipitated by chill to the surface, of those in which there is antecedent diuresis (§ 766), and of those which, we shall see later (§ 500), undergo transformation into, or replace, major epilepsy. In other cases, it seems probable that the vaso-dilation is not infrequently primary, the vaso-constriction secondary and adapted to prevent a serious fall in the general blood-pressure.

§ 356. CARDIAC COMPENSATION.—I am arguing of migraine that vaso-dilation of the cranial area tends to compensate for widespread vaso-constriction elsewhere; or conversely, that widespread vaso-constriction in other areas tends to compensate for the vaso-dilation of the cranial area. In either case, that is, whether the vaso-constriction or vaso-dilation is primary, these two opposite vascular conditions are correlative.

Now it may happen that these two vascular conditions are in accurate counterpoise: in this case, the blood-pressure will remain unaltered, and consequently the pulse-rate will tend to remain uniform. Hence, in some cases, the pulse-rate during a migraine paroxysm shows no deviation from that which is habitual.

But vaso-constriction may be in excess: in this case, the blood-pressure will tend to rise, and the only remaining mode of compensation will be a modification of the heart-beat. Hence cases occur in which the pulse-rate is reduced. Möllendorff says: ¹—'From the beginning and during the continuation of the hemicrania, the rate of the cardiac pulsations is considerably lowered, the normal pulse-rate of from 72 to 76 beats per minute sinking to from 56 to 48.'

¹ *Megrim and Sick-headache*, Ed. Liveing, 1873, p. 311.

Simple slowing, however, is by no means the only cardiac modification which may be adopted by the organism to reinforce inadequate vaso-dilation. The heart-beats may be weakened; and in two of my own cases, and in one which I saw in consultation, regular intermittence of the pulse, present at no other time, occurred during every migraine attack. As regards his own pulse, Haig looks 'upon a fluttering imperfect systole or a dropped beat . . . as conclusive evidence of high tension.'¹ And, in this connexion, it may be as well to recall the fact that, in vagus inhibition of the heart-beat, the action of the organ may be slowed or weakened or both: it is never increased in force (Foster).²

On the other hand, vaso-dilation may be in excess: in this case, the blood-pressure will tend to fall and the only remaining mode of compensation will be an increase of cardiac action. Hence cases occur in which the frequency of the pulse is increased. Labarraque says,³ the pulse 'becomes hard and frequent'; and Tissot says:⁴—'The pulse, when the suffering is severe, is always hard and quick: towards the close it subsides.'

None of these modifications of pulse-rate contravene Marey's law that 'the rate of the beat is in inverse ratio to the arterial pressure'; but some of them appear to do so, so long as we continue to ignore the meaning and influence of vaso-dilation in pathological conditions.

§ 357. MECHANISM OF THE PAIN.—If we thoroughly appreciate the general and local effects of vaso-motor action, it seems to me that it will be unnecessary to search further in order to elucidate the mechanism of the pain of migraine.

The following statement, a little altered in phraseology, is taken from Foster's 'Text-book of Physiology':⁵—The flow through any individual artery, in a state of normal tone, is determined by the resistance in the artery and in the vascular tract which it supplies, in relation to the mean arterial pressure, which again is dependent on the way in which the heart is beating and on the peripheral resistance of all the small arteries and capillaries including the artery in question. While the heart and the rest of the arteries remain un-

¹ *Uric Acid in Disease*, A. Haig, 1897, p. 177.

² *Text-book of Physiology*, M. Foster, 1898, pp. 184, 296.

³ *Megrim and Sick-headache*, Ed. Liveing, 1873, p. 329.

⁴ *Ib.* p. 330.

⁵ *Text-book of Physiology*, M. Foster, 1891, pp. 319, 320.

changed, the constriction of any individual artery will lead to (1) diminished flow through the artery itself: (2) increased general blood-pressure; and (3) consequent increased flow through other arteries. On the other hand, while the heart and the rest of the arteries remain unchanged, the dilation of any individual artery will lead to (1) increased flow through the artery itself: (2) diminished general blood-pressure; and (3) consequent diminished flow through other arteries.

Thus the mere dilation of an artery, even in spite of the fact that such dilation serves to reduce the general blood-pressure, increases the flow through the dilated artery: this will of course increase the distension of the capillary area supplied by the artery. But in migraine, there is not only a dilation of some artery or arteries supplying the cranium, but also an extensive constriction of arteries supplying other areas. The net result of this alteration of vascular balance may be a rise of general blood-pressure; but, even if this does not occur, the widespread arterial constriction will still further increase the already increased flow of blood through the dilated artery and, consequently, will still further increase the already increased distension of the capillary area supplied by the dilated artery: indeed, in such a combination of vaso-constriction and vaso-dilation, we have the essentials for the maximum of distension in the capillary area referred to.

The local effect of the vascular distension will vary with the nature and anatomical features of the tissue affected. As regards migraine, my observations lead me to place the distended area responsible for the pain usually in the scalp and pericranium, although it seems probable that the dura mater is often affected. Now all these structures are highly vascular: they are also inextensible; and the pericranium and dura mater are closely adherent to the subjacent bone. Hence vascular distension in these structures will inevitably result in extreme compression of the sensory nerves contained therein. The character of the pain of migraine is confirmatory of the view that it depends on nerve-pressure: more than one medical sufferer from this complaint assures me that the pain is identical in character with the pain of whitlow; and the latter is certainly due to nerve pressure.

§ 358. CONFIRMATORY CLINICAL EVIDENCE.—On the hypothesis that vascular distension caused by vaso-dilation com-

bined with widespread vaso-constriction is the proximate factor of the pain, we can correlate and explain many, if not most, of the isolated observations which have been made concerning migraine. Anything which could reduce the vascular distension would relieve the pain; and anything which could increase the vascular distension would increase the pain.

The vascular distension might be reduced: (1) by pressure on the main arterial trunk supplying the part: (2) by promoting vaso-constriction in the arterioles of the part: (3) by promoting vaso-dilation elsewhere or generally: (4) by reducing the force or frequency of the heart-beat; and (5) by reducing the total amount of blood in the circulation.

On the other hand, the vascular distension might be increased: (1) by pressure on arterial trunks supplying collateral areas: (2) by increasing vaso-dilation in the part: (3) by increasing vaso-constriction elsewhere: (4) by increasing the force or frequency of the heart-beat; and (5) by increasing the total amount of blood in the circulation.

Conformably with these theoretical anticipations, the following clinical observations may be arranged:—

§ 359. 1. In cases associated with dilation of the temporal artery on the affected side, pressure on this vessel always affords relief, which, however, may be complete or incomplete. When the relief is incomplete, we may assume that the temporal does not control the whole of the dilated area.

In cases associated with constriction of the temporal artery on the affected side, pressure on the vessel affords no relief: it may, on the contrary, increase the pain. Here we have only to assume that the dilated area lies within the distribution of some artery which arises behind the superficial temporal, such, for example, as the internal maxillary, the occipital, or the internal carotid. This assumption would fit such cases as Du Bois-Reymond's, in which the skin of the face remained pale and cold throughout the paroxysm, and regained its normal colour and temperature only when the pain abated.¹

Pressure on the common carotid of the affected side completely removes the pain in practically all cases: attention was called to this fact first by Parry,² later by Möllendorff and others.

On the other hand, pressure on the common carotid of the opposite side increases the pain.

¹ *Megrim and Sick-headache*, Living, 1873, p. 297.

² *Ib.* p. 309 *et seq.*

My own observations on the effects of compressing arteries during migraine paroxysms may be thus summarised. (*a*) In unilateral migraine, pressure on the common carotid of the corresponding side invariably, at once, and completely, removes the pain. (*b*) In bilateral migraine, pressure on either common carotid removes the pain on the corresponding side and increases the pain on the opposite side: by alternately compressing the right and left common carotid, the pain may be rendered hemi-cranial on the left and right side alternately. I have not tried the effect of compressing both common carotids simultaneously. (*c*) In a case of bilateral occipital migraine, immediate relief was afforded by compressing both occipital arteries; and the pain was rendered unilateral by compressing one occipital. (*d*) In a case of intense pan-cranial migraine, complete cessation of all pain followed simultaneous compression of both temporals and both occipitals: the pain was rendered unilateral by simultaneous pressure on the temporal and occipital of one side, or by pressure on one common carotid: it became limited to the posterior portion of the cranium by pressure on both temporals, and to the anterior portion of the cranium by pressure on both occipitals: finally, pressure on any one of the named arteries relieved the pain in the area of distribution of that artery. (*e*) In a case of severe frontal bilateral migraine the patient discovered for herself that pressure on both angular arteries (which were throbbing violently) gave very great, though not complete, relief: she would sit for hours compressing the root of the nose between her finger and thumb; and she had thought of devising a special padded clip for this purpose. (*f*) In many cases, general compression of the painful area of the scalp gave much relief: this has been noted by many writers: cases so relieved are doubtless pericranial.

Many of the observations here set down apply to the great majority of headaches, whether typically migrainous or other.

§ 360. 2. In some cases, the application of cold lotions or the ice-cap to the scalp affords great relief: here, presumably, the dilated area is in the scalp or pericranium, and the result is attained through direct vaso-constriction of the small arteries of the part. One of my patients, who for years had found marked relief from his violent migrainous pain by sitting in a hot bath up to his neck, discovered later that what little headache remained in these circumstances was absolutely dispersed

by swathing his head in cloths wrung out of iced water. One of Dr. Hawkes's patients, a sufferer from migraine of terrible severity, made an identical discovery. During his worst attacks, he is accustomed to sit in a hot bath up to his neck, while a cold shower plays upon his head. Then only does he obtain relief from pain.

On the other hand, cases are to be found in which the application of heat to the scalp materially increases the pain. Such too are doubtless pericranial.

§ 361. 3. Numerous observations testify to the relief afforded by promoting vaso-dilation in areas other than the seat of pain, or generally.

Liveing quotes M. Piorry to the effect that 'une vive stimulation des pieds par l'eau chaude ou par la proximité d'un brasier, a quelquefois arrêté brusquement la migraine.'¹ Graves found great relief in the headaches of young women to follow immersion of 'the legs as far as the knees in hot water.'² Haig found relief from his migraine by sitting over a fire. Immersing the arms in hot water will often give ease. Several of my cases of migraine take a full-length hot bath when attacked: they remain therein a considerable time, and enjoy for the most part almost complete temporary relief; but the pain recurs—one thinks it is actually worse—when the immersion is over.

Dry cupping over the nape of the neck is another means of relief in migraine and in headaches generally; and I have demonstrated, to my own satisfaction at least, that the relief so afforded is commensurate with the number, size, and degree of exhaustion, of the cups.

One of my patients obtains relief by drinking water as hot as she is able to swallow: part of the relief often afforded in headache from a cup of tea is doubtless due to the heat; for cold tea has a much less rapid effect. On the other hand, swallowing ice, we shall see (§ 365), is capable of causing headache.

Haig³ used to find that a good plate of roast beef and potatoes gave much temporary relief from his migraine. This seems at first sight inconsistent with the vaso-motor theory of migraine, for, as we shall see later (§ 728), the ingestion of a meal is always followed by a rise of general blood-pressure, in

¹ *Megrim and Sick-headache*, Liveing, 1873, p. 470.

² *Clinical Medicine*, New Syd. Soc., vol. ii. p. 350.

³ *Uric Acid in Disease*, 1897, p. 607.

spite of the large vaso-dilation which necessarily occurs in the splanchnic area. However, a part of the post-prandial rise of blood-pressure is due to peripheral vaso-constriction, and it is possible that the migrainous area shares in such vaso-constriction. Thus there would be a reduced vascular distension of this area, and a consequent relief from pain, in spite of a rise of general blood-pressure.

§ 362. Nitrite of amyl causes general vaso-dilation and great fall of blood-pressure; and Lauder Brunton says: '—As migraine is generally connected with vascular spasm, I employed the nitrite of amyl in headache, and found that frequently, though not invariably, it relieved the pain.' Nitro-glycerine is another well-known vaso-dilator; and Gowers² says that this is the drug which, in the majority of cases, has the most beneficial influence on migraine.³

§ 363. Leonard Hill says,⁴ violent exercise raises the arterial pressure by about 20 mm.: 'this lasts for about fifteen minutes and is then followed by a fall.' The secondary fall, which is more enduring than the primary rise, is doubtless in part due to the extensive vaso-dilation which soon supervenes. This vaso-dilation affects the muscular layer and is a necessary concomitant of increased functional activity; it affects also the cutaneous area, where it is necessitated by the increased demand for heat loss consequent upon the increased heat-production invariably associated with physical exercise. But the fall of blood-pressure is too prolonged to be thus fully accounted for: it continues after the cessation of exercise and after the cutaneous vaso-dilation has passed away; and, later, I shall argue that this more or less persistent fall is due in the main to a fall in the carbon contents of the blood occasioned by the increased combustion caused by muscular exertion (§§ 731, 732).

The influence of exercise upon migraine and upon numerous less typical forms of headache runs parallel for the most part with its influence upon blood-pressure. Exercise during an

¹ *Pharmacology, Therapeutics, and Materia Medica*, 1885, p. 711.

² *Diseases of the Nervous System*, 1893, vol. ii. p. 854.

³ When these drugs are administered to a person in perfect health, there is not infrequently the sudden development of headache, especially affecting the vertex; and, in some of the cases of migraine in which I have used them during the paroxysm, the result has been a distinct immediate increase of the pain. In explanation of these observations, it has occurred to me that the vaso-dilation induced by the nitrites, though general, is perhaps not uniform, and that the cranial area suffers primarily and preponderatingly.

⁴ *Text-book of Physiology*, E. A. Schäfer, 1900, vol. ii. p. 80.

attack causes at first great increase of pain. But, as already pointed out, some persons can walk off an existing headache or migraine (§ 303); and in *all* of the few cases in which I have known this experiment tried, the result has been an abbreviation of the attack, as compared with its duration on other occasions; though in most the pain did not cease during the continuance of the exercise, possibly because this was not sufficiently prolonged.

It seems clear, then, that vascular tone, one of the essential factors in blood-pressure, is in great part an index of the carbon contents of the blood; and that the salutary influence of exercise upon headaches, already ascribed to increased acarbonization of the blood, is attained through the mechanism of *general* vascular relaxation, a condition opposed to that which obtains in migraine and, as we shall see later, to that which obtains in the other paroxysmal neuroses. In general terms, we may conclude that the humoral conditions are primary, the vascular conditions secondary throughout.

§ 364. A similar argument explains the mechanism of the salutary influence of pyrexia upon migraine and, as we shall see later, upon other paroxysmal neuroses. Broadbent says:¹—‘Arterial relaxation is the condition of the vessels characteristic of pyrexia.’ Now, although this vaso-dilation may be in part due to the necessity for increased heat-loss demanded by the exaggerated combustion of pyrexia, yet we may ascribe it in the main to the low carbon contents of the blood, for as already argued pyrexia is an acarbonizing process of high potency (§ 274). Hence we may conclude that pyrexia disperses recurrent migraine, etc., by obviating the necessity for such pathological acarbonizing processes, and by inducing that vascular condition which is largely inconsistent therewith. An extremely important exception to the rule that pyrexia disperses migraine will be dealt with in considering the relation of migraine to malaria (§ 375).

§ 365. While it is true that conditions which promote vaso-dilation in non-migrainous areas, or generally, tend to prevent or modify migraine paroxysms and to relieve the pain of already existing attacks, it is equally true that conditions which promote vaso-constriction in non-migrainous areas tend to precipitate migraine paroxysms or to intensify the pain of

¹ *The Pulse*, 1890, p. 180.

already existing attacks. Exposure to cold has often precipitated an impending migraine; and the effect of cold air, general cold bathing, and cold applications, except when applied directly to the dilated area, is to intensify the suffering during an attack. The headaches which, Dr. Symonds¹ says, are due in some cases to ice in the stomach are doubtless explicable in this way.

Even in individuals not predisposed to migraine, headaches, hardly distinguishable from the headache of pan-cranial migraine may sometimes be induced by measures which promote sudden vaso-constriction in some extensive area. The most violent headache from which the writer ever suffered was caused through his slipping inadvertently into a rather cold swimming-bath feet foremost. Vertical pain commenced with the suddenness of a blow, synchronously with the closing of the water over his head, and persisted with diminishing intensity for several hours. The headache commonly associated with semi-asphyxial conditions may perhaps be ascribed in part to the vaso-constriction of the splanchnic area, which is probably always present.

§ 366. 4. Reduction in the force of the heart-beat may be accompanied by relief from the pain of migraine. In some persons, the onset of nausea and vomiting is the signal for the abatement of the paroxysm;² and both these conditions, it will be admitted, are commonly associated with reduction in the force of the systole. In one of my patients, an unusually severe migraine was apt to be associated with marked faintness: on one occasion, actual syncope supervened. The faintness always brought considerable relief from pain; and it is difficult, in such a case, not to sympathize with the conception of Parry³ that the cardiac weakness is conservative.

On the other hand, anything which increases the force of the heart-beat is liable to increase the pain: hence ammonia and alcohol are harmful as a rule. But alcohol has more than one action on the circulatory system: besides increasing the force of the heart-beat, it tends to cause peripheral vaso-dilatation;⁴ and it is reasonable to think that it produces these two

¹ *Megrin and Sick-headache*, Liveing, 1873, p. 244, foot-note.

² *Ib.* pp. 368, 369, 371.

³ *Ib.* p. 341, foot-note.

⁴ *Pharmacology, Therapeutics, and Materia Medica*, Lauder Brunton, 1885, p. 288.

different effects in different degrees in different individuals. Hence, probably, the seemingly inconsistent observations that alcohol may accentuate or may relieve headache. Such have led to misconception. Liveing says: ¹—‘ In what Dr. Parry says . . . of the aggravation of megrim by stimulants, he is not quite consistent, for he elsewhere advocates the use of stimulants under similar circumstances as tending to favour and *equalize* the circulation and so overcome any local determination; and this is the explanation which is usually given by most of those who, while they hold to a hyperaemic theory of megrim, cannot deny the rapid dispersion of an attack which occasionally follows a glass or two of wine or other stimulants.’ It is impossible also to deny that in many cases a glass or two of wine or other stimulants markedly accentuates the pain of a migraine paroxysm. But both observations are readily explicable, if allowance is made for the varying twofold action of alcohol upon the circulatory apparatus.

§ 367. 5. The effect of a reduction in the total amount of blood to disperse migraine is seen in haemorrhage of all kinds; and naturally the effect is most marked when, as frequently happens, the blood comes directly from the dilated area. I have already quoted (§ 330) from Liveing a case of Tissot’s, in which recurrent migraine and recurrent epistaxis alternated over long periods; and from Graves (§ 330) a case in which venesection dispersed severe headache. I have also referred to the writer’s own experience (§ 330). In all cases, the haemorrhage acts probably in the first place by reducing blood-pressure, and in the second by promoting acarbonization of the blood and thus maintaining the reduction of blood-pressure.

It is hardly possible to demonstrate the influence of an increase in the total amount of blood in the body upon migraine paroxysms; but I have seen one case (not at any time a sufferer from anaemia) who became worse as he became ‘plethoric.’ It is not, however, generally admitted that acquired plethora implies an increase in the amount of blood.

As regards the effect of an increase in the amount of blood upon an existing migraine paroxysm, this could only be investigated by transfusion, which would of course be unjustifiable.

§ 368. SOME OBJECTIONS TO THE VASO-MOTOR THEORY.—

¹ *Megrin and Sick-headache*, 1873, p. 279.

Liveing regarded vaso-dilation in migraine as only 'one among many phenomena of the paroxysm, and by no means as essential or the cause of the rest.'¹ He says: ²—'The vascular phenomena are themselves the most variable and inconstant of the series': that he has 'repeatedly watched the severest paroxysm of typical megrim without being able to detect any of those indications of hyperaemia to which Dr. Möllendorff refers': that he has 'carefully examined the fundus of the eye with the ophthalmoscope in a severe hemicranial case, where the visual phenomena were highly developed and where, if at all, we should expect to find the appearances Dr. Möllendorff describes';³ and all with negative results.

Now the whole of this argument succeeds in proving only that vaso-dilation is not always visible; and this may be freely admitted. But it does not follow that vaso-dilation is non-existent; and it is certainly not in cases where the visual phenomena are well developed, but rather in cases where tensile pain is felt in the globe of the eye, that we should expect to find vaso-dilation of the intra-ocular arteries. We have no right to deny the constancy of the vascular phenomena of migraine because they are variable in distribution and degree. In my experience, extensive areas of vaso-constriction, in paroxysms of any intensity, are amongst the most constant of all the manifestations of the disorder; and, when we consider the anatomical features of the cranium, it is clearly impossible to exclude all cranial areas of vaso-dilation.

In one of my cases, there was, during most paroxysms, no visible vaso-dilation: all over the exposed cutaneous area there was extreme anaemia and the superficial arteries were manifestly constricted. But, on some occasions, the hemicranial pain extended to the corresponding shoulder-blade; and, on all such occasions, this part was found to be the seat of marked hyperaemia. Surely, in such a case, it is reasonable to infer that the cranial pain is associated with a vaso-dilation which is concealed from observation.

§ 369. Liveing's view, and indeed all views which deny the priority of the vascular changes over the pain, not only fail to account for, but hopelessly contravene, the fact that the pain of migraine ceases when the artery supplying the painful area is compressed and recommences when the pressure is removed.

¹ *Megrim and Sick-headache*, Liveing, p. 317.

² *Ib.* p. 315.

³ *Ib.*

It is true, Liveing attempts to parry this objection to his view in the following manner. He says:¹—‘Since the ordinary pulsation of the arteries in cases where there is no obvious hyperaemia is painfully felt in consequence of the morbid sensibility of the parts, it is easy to understand that the relaxed and throbbing condition of the vessels described by Dr. Möllendorff, if present at the height of the paroxysm, might greatly aggravate the suffering; and, under the same circumstances, compression of the carotid might considerably relieve it.’

But this is no question of ‘aggravation’ and ‘considerable relief.’ Pressure on the common carotid of the affected side in hemicrania is associated with *instant and complete relief*, removal of the pressure, with *instant and complete return*, of the pain: this I have verified on numerous occasions. Möllendorff says:²—‘If the common carotid artery be forcibly compressed on the painful side at the level of the thyroid cartilage during the hemicranial paroxysm, so that the pulse in the temporal artery begins to fail, the headache vanishes as if by magic. The eye is livelily opened, the oppressed and suffering face brightens up and seems to inquire with an expression of delight, “What has become of the pain?” Unfortunately, however, with the intermission of the compression, with the first full pulse-wave, the pain begins afresh. . . . This experiment has infallibly succeeded with me in the case of all persons suffering from hemicrania whom I have had the opportunity of seeing in the attack.’ More than a century ago, Parry³ described his experience, which was identical, and he described it in equally forcible language.

§ 370. I submit that there is but one hypothesis which can explain these facts; and that is *that there is in all cases vascular distension at the seat of pain, and that the vascular distension is the proximate cause of the pain*. I am aware that cases have been described in which pressure on the common carotid of the affected side adds to the pain,⁴ although it is not pretended that such cases are common. For myself, I have searched for such cases in vain. Consequently, I would venture to suggest with deference the possibility of a mistake having

¹ *Megrim and Sick-headache*, Liveing, p. 317.

² *Ib.* pp. 309, 310.

³ *Ib.* p. 276.

⁴ Eulenburg, in Von Ziemssen’s *Cyclopedia of the Practice of Medicine*, vol. xiv. p. 12.

been made. It is evident that pressure directed to the carotid artery might, if inadequate or inaccurately applied, succeed only in blocking the venous return through the internal jugular vein, and so increase the vascular distension and the pain in the affected area.

§ 371. The evidence in favour of the view that the pain of migraine is due to vaso-motor action seems to me complete; and if so, it is highly probable that the other sensory symptoms, amongst them the initial symptoms, sometimes spoken of as the migrainous aura, own a similar mechanism. Gowers, in stating the case against the vaso-motor theory of migraine, says: '—The sensory symptoms must depend on deranged action of the sensory centres in some part of the brain. They indicate a combination of arrest of action and of over-action in the nerve-cells concerned. In the language of modern pathology, there is a combination of inhibition and discharge; the loss of sight, for instance, must be due to inhibitory arrest of action, the visual spectrum to discharge.' I see no insuperable difficulty in believing that such derangements of nervous action in the sensory centres depend upon derangements in the blood-supply. In general cerebral anaemia, however induced, there is general arrest of cerebral action or loss of consciousness: in the early stage of meningitis, in which we know there is general cerebral hyperaemia, the symptoms are characteristic of general cerebral over-action. And it is easy to conceive that the localized cerebral anaemia and the localized cerebral hyperaemia, which are due respectively to the presumed constriction and dilation of individual cerebral arteries in migraine, will result in manifestations of cerebral inhibition and discharge localized in the centres concerned. Contraction followed by dilation has been observed in the adjacent visible arteries: Benson² saw the inferior temporal artery of the retina undergoing slowly alternating dilations and contractions during an attack of migraine.

§ 372. Against the vaso-motor theory it has been argued that variations in the calibre of the cerebral arteries are passive and must be general; and this contention was supported by the fact that, until recently, observation had 'failed to demonstrate with certainty any special vaso-motor nerves or fibres

¹ *Diseases of the Nervous System*, 1893, vol. ii. p. 850.

² *Trans. Oph. Soc.* 1898.

directly governing cerebral vessels.’¹ But Foster,² writing in 1892, maintained that the existence of vaso-motor mechanisms would afford a more satisfactory explanation of many phenomena than was then available; and since then the gap has been filled. William Hunter³ reviews the work on this subject during recent years, and shows from his own microscopic observations that, while the vessels of the white matter are seemingly destitute of nerves, the vessels of the grey matter, whether of the cerebral convolutions or of the cerebellum, mid-brain, pons, medulla or cord, are surrounded by a dense network of delicate nerve-fibres, amounting in some cases to a continuous sheath: he refrains, however, from advancing any opinion as to the function of this nerve supply. But Ferrier speaks with no uncertain voice as to the existence of variations in the calibre of the cerebral arteries under the influence of the vaso-motor nerves. He says,⁴ the ‘negation of vaso-motor regulation of the cerebral blood-vessels seems to be in flagrant contradiction with the positive demonstration of nerves accompanying the vessels of the pia mater, as well as with other facts . . . and we can scarcely doubt that there must be some intrinsic mechanism which can secure a greater flush of blood in one part as compared with another in an organ in which there is proved localization of function.’ Again, he states:⁵—‘Brodie and I have . . . succeeded in rendering it more than probable that cerebral blood-vessels are under the influence of vaso-motor nerves, though so far we have not been able to determine their origin and course.’ Finally, Leonard Hill⁶ points out (September 1898) that recently ‘various observers, including Gulland himself (who originally failed), have been able to show the usual perivascular nerve-plexuses upon the cerebral vessels. (“Brit. Med. Journal,” London, 1898, vol. ii. p. 781.)’

Gowers, though strongly maintaining the subordinacy of the vascular changes in migraine, refers incidentally to a case which, so far as I can see, directly supports the opposite view. After pointing out that the vascular disturbance in the brain may lead at times to vascular degeneration, he adds:⁷—

¹ *Text-book of Physiology*, Foster, 1892, p. 1137.

² *Ib.* p. 1138.

³ *Journal of Physiology*, January 14, 1901.

⁴ ‘Harveian Oration on the Heart and Nervous System,’ *British Medical Journal*, October 25, 1902, p. 1340.

⁵ *Ib.*

⁶ *Text-book of Physiology*, E. A. Schäfer, 1900, vol. ii. p. 168.

⁷ Noyes in the *Journal of Nervous and Mental Diseases*, quoted by Gowers, *Diseases of the Nervous System*, 1893, vol. ii. p. 848.

'Hemianopia habitually preceded the headaches in a woman who, after reaching the degenerative period, found one day that the hemianopia persisted after the pain. It was permanent and due, as was subsequently ascertained, to a lesion in the opposite cuneus.' If the permanent hemianopia was caused, as is admitted, by the permanent vascular lesion, then it seems to me more than probable that the temporary hemianopia was caused by the temporary vascular changes which had been periodically recurrent and which led eventually to the permanent change.

§ 373. The importance of vaso-motor action, and especially of vaso-dilation, is further attested by the occurrence of sudden choroidal haemorrhage¹ (Liveing); and of oedema and even 'ecchymoses at the seat of the most intense pain'² (Gowers). Tissot refers to a case of migraine with hemianopia: 'it was no uncommon occurrence with her in the severer seizures for the violence of the spasm to occasion an extravasation of blood, rendering the skin of the forehead, eyelids, and even cheeks, black and blue.'³ Labarraque says:⁴—'The conjunctivae are . . . in certain cases ecchymosed'; and Fagge⁵ refers to the case of Dr. J. Phillips, in whom a fatal attack of apoplexy occurred during the course of a headache indistinguishable from migraine. 'Lauder Brunton draws attention to the fact that ocular tension may be increased during the headache of so-called biliousness' (Harry Campbell);⁶ and acute double glaucoma⁷ has occurred during an attack of migraine, which affection had been previously recurrent. Now, on the vaso-motor theory, it is easy to conceive that dilation of the central artery of the retina might determine this accident in an eye which is anatomically predisposed through hypermetropia.

§ 374. THE RELATION OF MIGRAINE TO RIGOR.—Liveing describes a malarial migraine,⁸ 'Hemicranialis intermittens' or 'Brow ague,' chiefly on the authority of MacCulloch; and Fagge refers,⁹ on the same authority, to a case of 'double tertian ague, in which the headache and the ague fit occurred

¹ *Megrin and Sick-headache*, Liveing, 1873, p. 328.

² *Diseases of the Nervous System*, Gowers, 1893, vol. ii. p. 844.

³ *Megrin and Sick-headache*, Liveing, 1873, p. 325.

⁴ *Ib.*

⁵ *Text-book of Medicine*, 1891, vol. i. p. 784.

⁶ *Headache*, 1894, p. 180.

⁷ *Brit. Med. Journal*, Epitome, March 24, 1900.

⁸ *Megrin and Sick-headache*, Liveing, 1873, p. 405 *et seq.*

⁹ *Text-book of Medicine*, 1891, vol. i. p. 782.

regularly on alternate days' throughout the whole of one relapse.

Now it is clear that rigors and migraine paroxysms have much in common as regards their mechanism. In both there is an extensive cutaneous area of vaso-constriction, and in both there is an internal area of vaso-dilation. The difference lies probably mainly in the site of the vaso-dilation; for, in rigors, this must affect the whole of the muscular layer of the body, which is, of course, at the time functionally active.

It has been argued that the cranial vaso-dilation of migraine tends to prevent a rise of general blood-pressure. The same may be argued of the muscular vaso-dilation of rigors. Broadbent says that, even in the cold stages of the ague fit, while the cutaneous arteries are constricted and the skin cold and pallid, 'the actual pressure within the vessel is not very great and the wave can be extinguished without much difficulty.'¹ And Lauder Brunton 'considers that the arterioles of the muscles . . . are so large that the blood is able to escape into the veins as rapidly as through the vessels of the splanchnic and skin areas together.'² It seems to me, then, that the affinity between migraine and malaria is of mechanism, not, of course, of humoral causation.

§ 375. This view receives strong support from the existence of cases, like the following, which demonstrate that migrainous paroxysms may be associated with rigors which do not depend upon malarial, but upon other kinds of, poisoning. The case is one of the very few I have heard of, in which recurrent migraine persisted throughout pyrexia of any degree of intensity. The patient was an habitual migraine sufferer and contracted puerperal pyaemia: during the fever migrainous attacks, indistinguishable from those from which she was accustomed to suffer, recurred with increased frequency; but they coincided with, and were limited to the times of, the irregularly recurring rigors of the disease (Dr. Hawkes). It is not difficult to conceive that the vaso-dilation, compensatory of the cutaneous vaso-constriction of rising temperature, might, in such a case, fall into its 'accustomed groove' wholly or in part, and so occasion headache in place of, or in addition to, rigor. Indeed, headache is a frequent associate of malarial rigor; and we

¹ *The Pulse*, p. 189.

² H. Oliphant Nicholson, *Lancet*, April 11, 1903, p. 1056.

have already seen that in some cases of migraine, non-malarial in origin, the cutaneous anaemia is excessive and graduates into rigor (§ 354). But, as we should anticipate, and as we have already seen in the case of malaria, headache and rigor may alternate: Parry¹ observed that many headaches and other 'head-attacks' may be cut short by shivering.

§ 376. Finally, if the mechanism of rigor is such as we are supposing, the administration of amyl nitrite should have a marked effect in this condition. Dr. W. J. Fearnley, resident medical officer of the General Hospital, Brisbane, kindly undertook to investigate this matter for me.

In the first case in which he tried the drug, the patient, a man of 41, was suffering from a compound septic Pott's fracture. The ankle was hot and swollen, his temperature 104°, pulse 110. At 5 P.M. he had a rigor, which had lasted two minutes when a capsule of amyl nitrite was administered. The rigor ceased completely in from twenty to thirty seconds. In a second case, a woman of 27 had felt ill for one day. She was suffering probably from influenza: temperature 102°: pulse 130. While awaiting admission in the out-patient department, she had a shivering fit. This was promptly stopped by amyl nitrite. In the third case, three severe rigors, occurring during the course of puerperal septicaemia, were instantaneously arrested by the same drug, the pulse improving simultaneously: the patient expressed herself as greatly relieved. Thus out of six rigors, the nitrite was followed by no failure.

The relief of rigor by amyl nitrite is naturally not so complete in all cases as in the above: much apparently depends upon the nature and intensity of the rigor.

Dr. Hawkes administered a capsule of the drug to a malarial patient just as the rigor had reached its point of greatest severity. The rigor was very distinctly lessened in severity and continued in its modified form, but it did not seem to be abbreviated: the pulse was markedly altered, and the patient expressed his sense of relief.

§ 377. SUMMARY OF THE PATHOLOGY OF HEADACHE, MIGRAINOUS AND OTHER.—The following propositions and admissions concerning the pathology of headache, migrainous and other, will serve to parry a charge of undue exclusiveness:

1. Headache may be due to peripheral nerve-pressure.

¹ *Megrim and Sick-headache*, Liveing, 1873, p. 281.

2. Such peripheral nerve-pressure may be due to vascular distension of the imbedding tissues.

3. Such vascular distension may be due to vaso-dilation of the supplying arteries.

4. Such vaso-dilation may be secondary to, and more or less compensatory of, some widespread vaso-constriction.

5. Such vaso-constriction may be due to hyperpyraemia.

Each of these propositions involves certain admissions, which, taken in inverse order, are as follows :

5. The vaso-constriction may be due to humoral factors other than hyperpyraemia, for example, to malarial and other toxæmias ; and to factors other than humoral, for example, exposure to cold.

4. The vaso-dilation may be primary, the vaso-constriction being secondary and compensatory.

3. The vascular distension may be due to causes other than vaso-dilation of the supplying arteries, for example, to venous obstruction.

2. The peripheral nerve-pressure may be due to factors other than vascular distension, for example, to tumour.

1. The headache may be due to causes other than peripheral nerve-pressure.

It is hardly necessary to add that, in my opinion, hyperpyraemia, actual or relative (compare Chapter XIII), is one of the commonest causes of headache. Even should it turn out that, in many cases of migraine, the vaso-dilation is primary, that would not of course exclude these humoral factors.

ASTHMA

§ 378. Although most modern writers hold to the theory that the phenomena of asthma—the distressing sensation and the demand for extraordinary respiratory efforts—immediately depend upon a spastic contraction of the fibre cells of organic muscle, which minute anatomy has demonstrated to exist in the bronchial tubes (Salter)¹—a theory which Salter regards as so well established as to render its further defence almost superfluous—yet not a few still prefer the hypothesis ‘ that the mucous membrane of the tubes becomes very rapidly swollen by what German writers term a fluxionary hyperaemia ’ or (as

¹ *On Asthma*, Hyde Salter, 1868, pp. 30, 31.

Weber put it) by a “dilatation of its blood-vessels through the influence of the vaso-motor nerves.”¹ (Fagge).

This is essentially the hypothesis of Sir Andrew Clark, who regarded asthma as an ‘internal urticaria’: it is the hypothesis of Osler, who regards asthma as ‘a neurotic affection characterized by hyperaemia and turgescence of the mucosa of the smaller bronchial tubes’;² and it is the hypothesis which we, from the views already expressed and on many grounds, shall find ourselves almost inevitably compelled to select. Under it, the vaso-dilation is, as in migraine, the compensation for vaso-constriction elsewhere; or it may be, as there are reasons to believe of some cases, that the vaso-dilation is primary, the vaso-constriction secondary and compensatory. In either case, however, these opposite vascular conditions are coexistent and correlative.

§ 379. As in migraine, the vaso-dilation will lead to vascular distension; but, in asthma, this will affect a tissue which diverges widely in its structure and anatomy from the tissue affected in migraine. By a process of exclusion and from clinical and circumstantial evidence, it has almost always been inferred that the asthmatic obstruction is localized in the smaller bronchi or bronchioles. But, quite recently, a demonstration of such localization has been made by Fraenkel, who had an opportunity of making a post-mortem examination on a case that had died during a paroxysm. The morbid appearances were consistent with what might result from vascular distension depending on vaso-dilation. Microscopically marked changes were found in the smallest bronchi (lumen $\cdot 15$ to $\cdot 03$ mm.) or bronchioles—*i.e.* tubes which still retain their stratified columnar epithelium, but which have lost their cartilages and glands, and which are about to break up into the alveolar passages and infundibula; and the changes were confined to tubes of this size.³ Now vascular distension of a membrane so situated could hardly occur without some swelling, and a very moderate degree of swelling would materially diminish the lumen and so induce obstructive dyspnoea.

§ 380. VASO-CONSTRICTION.—The widespread area of vaso-constriction is commonly found to occupy practically the same

¹ *Text-book of Medicine*, Fagge, 1891, vol. i. p. 1147.

² *Principles and Practice of Medicine*, 1894, p. 499.

³ J. J. Perkins in the *Practitioner*, 1900, p. 447.

regions in asthma as in migraine. The pallor, anaemia, and sense of coldness, subjective and objective, of the surface generally, and especially of the extremities, during severe asthmatic paroxysms, have been noted by most observers. Salter says: ¹—‘The pulse during severe asthma is always small, and small in proportion to the intensity of the dyspnoea: it is so feeble sometimes that it can hardly be felt . . . I have never known the small pulse absent in severe asthma.’ William Russell ² refers to the case of a man of 53, the subject of spasmodic asthma. ‘It was quite clear that when the asthmatic spasm supervened, his radial arteries became markedly tightened up. During the paroxysm the arteriometer measurement of the radial was 2·2 mm.: after the paroxysm was relieved by liquor trinitrini the diameter of the artery rose to 2·4 m.’ That the constriction of the radial is intimately bound up with the paroxysm, is shown by the fact that ‘immediately the paroxysm yields, the pulse resumes its normal volume’ ³ (Hyde Salter). Thus the issue is practically narrowed down to two alternatives: either the peripheral vaso-constriction results in some way from the dyspnoea, or it is an essential factor in the dyspnoea. In the first case, some further explanation of the meaning of the result is demanded: in the second, the mechanism of the whole process seems obvious.

§ 381. Many of the premonitory or initial symptoms of the asthmatic attack seem to depend upon the vaso-constriction. The premonitory drowsiness—common also in migraine and other paroxysmal neuroses—may be due to cerebral vaso-constriction and anaemia: ‘the paraesthesia of various kinds which Romberg happily called an asthmatic aura,’ ⁴ to localized vaso-constriction in the cerebral centres or at the periphery; and the polyuria, which, according to Salter, ⁵ may occur so early in the attack that the patient is awakened from his sleep by the distension of his bladder when the difficulty of breathing is but just commencing, is fully explicable by widespread cutaneous vaso-constriction, or by any sufficiently extensive vaso-constriction in which the renal arteries do not share. (Compare § 759.)

¹ *On Asthma*, 1868, p. 72.

² *Lancet*, 1901, June 1, p. 1522.

³ *On Asthma*, Hyde Salter, 1868, p. 73.

⁴ *Text-book of Medicine*, Fagge, 1891, vol. i. p. 1143.

⁵ *On Asthma*, 1868, p. 69.

§ 382. VASO-DILATION.—That vaso-dilation occurs in the bronchial area, is probable from many observations and on many grounds. During the asthmatic paroxysm, the patient breathes through the mouth. This, we are apt to assume, is due to the fact that the extraordinary respiratory efforts demand an aperture larger than the normal nostrils. But in a large number of paroxysms—I think in the majority—examination discloses that the nostrils are blocked by vascular distension of their mucosa. This condition may be traced further down. ‘Störck¹ actually observed with the laryngeal mirror, that, in certain instances of asthma, the whole length of the trachea and part of the right bronchus were deeply congested’ (Goodhart). In hay-fever there is ‘obvious swelling of the mucous membrane of the nose’;² and hay-fever and hay-asthma graduate imperceptibly into each other. The association of asthma with urticaria, especially, I think, the urticaria which affects the mucous membrane of the oral cavity, is extremely close; and urticaria, it will be admitted, implies vaso-dilation.

§ 383. In some cases of asthma, it has been observed that general enlargement of the chest, accompanied by descent of the diaphragm, precedes the onset of dyspnoea. Several lady patients inform me that the earliest warning they experience of an impending fit of asthma during the daytime is an increasing tightness of the corset: if this garment can be loosened immediately, the attack is deferred for a time: otherwise, the paroxysm quickly attains its climax. Now the smaller bronchial passages are devoid of cartilage,³ and, unlike those of larger size, are liable to close by collapse: increasing vascular distension of their mucous lining will, by narrowing their lumen, greatly increase this tendency; and the only conceivable means of compensation is an expansion of the whole chest cavity. The pre-dyspnoeal progressively increasing distension of the chest, which occurs in asthma, is consistent with a progressively increasing swelling of the mucous membrane, but less so with muscular spasm. During the height of the paroxysm, expiration to any marked extent would lead to lobular collapse: hence the chest is maintained in a state of almost full expan-

¹ Goodhart in Allbutt's *System of Medicine*, vol. v. p. 300.

² *Text-book of Medicine*, Fagge, 1891, vol. i. p. 1147.

³ *Text-book of Physiology*, Foster, fifth edition, p. 561.

sion and the movements of respiration are restricted to a narrow margin on either side of this point. Obviously, in this way only can a passage of communication between the outer atmosphere and the air-vesicles be maintained: the fixation of the chest-walls in the position of almost extreme inspiration and the strong diaphragmatic contraction are conservative measures, compensatory of the diminution of the bronchial lumina by vascular distension.

Starling says¹ the asthmatic 'type of breathing is often described as being marked by expiratory dyspnoea. This description is, however, erroneous. The muscles, which in these cases are contracted to their utmost, are the inspiratory muscles: the expiratory muscles, such as the abdominal, will be found to be quite flaccid during expiration.' I can myself confirm this statement in some considerable degree. The fact is that respiration during the asthmatic paroxysm is maintained by powerful inspiratory efforts alternating with extremely cautious, and therefore slow, relaxations of the inspiratory muscles: the patient *dare not suddenly* relax the inspiratory spasm, still less make any *serious* use of his expiratory muscles.

The theory of muscular spasm of the bronchial tubes did not assist Salter, imbued as he was with the conservative principle of disease, to understand the 'permanent distension' of the thoracic cavity. He says: ²—'I do not see that anything is gained by this distension of the thoracic cavity: the only difference is that the volume of air locked up in the chest is rather larger; but no more is changed at each inspiration, and it is the amount so changed, and not the quantity contained in the lungs, that relieves the demand of respiration.' Nevertheless, it must be admitted that the expansion of the chest is not inconsistent with the theory of muscular spasm; for such expansion would tend to antagonize the bronchial spasm, and so to maintain patent the lumina of the tubes.

§ 384. The suddenness of the onset and subsidence of the asthmatic paroxysm is often adduced as an argument in favour of the theory of muscular spasm of the bronchioles; but those who have watched a case of acute urticaria or angio-neurotic oedema will be able to realize that the onset of vaso-dilation,

¹ *Text-book of Physiology*, E. A. Schäfer, vol. ii. p. 312.

² *On Asthma*, 1868, p. 76.

as portrayed in the rise of the wheals,¹ is often sufficiently rapid to account for the phenomena of asthma; and swelling will take place more rapidly in mucous membrane than in skin. But the clearest illustration of the capacity of vascular distension to account fully for the phenomena of the most explosive asthmatic paroxysm is to be seen in the rapidity with which the nasal passages may become completely blocked by nervous erethism of their mucous membrane in many circumstances.

Brodie and Dixon consider it 'unsafe to argue that, because the nasal mucous membrane can rapidly become turgid and swollen and as rapidly recover, a similar thing can occur in the bronchi.'² These investigators point out that 'the nasal mucous membrane, especially over the inferior turbinate bone and lower nasal passages, is extremely vascular, and in many parts large venous plexuses are found encircled by bundles of muscular fibres, thus forming a sort of cavernous erectile tissue (Klein)';³ but that 'the bronchial mucous membrane, on the other hand, is thin and possesses what is, in comparison, a relatively insignificant blood-supply.'⁴ These anatomical differences between the two mucosae may be freely admitted; and the limited capacity for erection of the latter must be regarded as fortunate. For, it seems to me, were the mucosa of the bronchioles liable to become turgid and swollen in degree proportionate to that of the nasal mucosa, that many, if not most, asthmatic paroxysms would prove immediately fatal.

In discussing the relations between asthma and chronic bronchitis, it will be pointed out that, interposed between these two typical clinical conditions is an unbroken series of intermediate forms, which partake in many degrees of the characters of both. Such intermediate forms are difficult to understand on the theory of bronchial spasm; but they receive a ready explanation on the view that the anatomical cause of the dyspnoea is, in both affections, turgescence of the bronchial mucosa.

§ 385. We are by no means bound to assume of all cases of asthma that the vaso-dilation, responsible for the dyspnoea, is

¹ Malcolm Morris says:—'The wheal is simply a circumscribed oedema of the skin due to paralytic dilatation of the arterioles, followed by exudation of serum and migration of leucocytes.'—*Diseases of the Skin*, 1894, p. 63.

² *The Pathology of Asthma*, reprinted from the *Transactions of the Path. Soc. of London*, vol. liv. Part I. 1903, p. 21.

³ *Ib.* p. 12.

⁴ *Ib.*

secondary to vaso-constriction elsewhere; but we are bound to assume that this is true of some cases, for example, of the cases in which, as Salter points out, polyuria precedes the paroxysm, of those in which a paroxysm immediately follows exposure of the skin of the chest to cold air or cold bathing, and of those which, as we shall see later (§ 500), are prone to undergo transformation into major epilepsy. In others—and these may be in the majority for aught I know—it may be that the vaso-dilation is primary and that the vaso-constriction is secondary and adapted to prevent a serious fall in the general blood-pressure. On this latter view, it is of course easier to understand the dependence of many asthmatic paroxysms upon atmospheric conditions other than thermal, such as those which lead to hay-asthma, rose-asthma, etc.

§ 386. CARDIAC COMPENSATION.—It has been argued of asthma that vaso-dilation of the bronchial area tends to compensate for widespread vaso-constriction elsewhere; or conversely, that widespread vaso-constriction tends to compensate for vaso-dilation of the bronchial area. In either case, whether the vaso-constriction or vaso-dilation is primary, these two opposed vascular conditions are correlative.

Now it may happen that the two are in accurate counterpoise: in this case, the blood-pressure will remain unaltered, and consequently the pulse-rate will tend to remain uniform. But vaso-constriction may be in excess; in this case, the blood-pressure will tend to rise; and the only remaining mode of compensation will be a modification of the heart-beat. Hence cases occur in which the pulse-rate is slow: Liveing¹ quotes Sir John Floyer to this effect, and refers himself to a case in which the pulse-rate fell to 20. Salter, however, does not refer to retardation, and therefore we may infer that this phenomenon is, at any rate, infrequent.

On the other hand, vaso-dilation may be in excess: in this case, the blood-pressure will tend to fall; and the only remaining mode of compensation will be an increase of the heart-beat. Hence cases occur in which the pulse-rate is increased. M. Sihle² for three years has taken the blood-pressure measurements in all his cases of asthma, and he finds 'the low tension

¹ *Megrim and Sick-headache*, Ed. Liveing, 1873, pp. 331, 332.

² *Wien. Klin. Woch.* No. 4, 1903, referred to in *Brit. Med. Journal*, Epitome, August 29, 1903.

pulse (as a rule) with increased rapidity of the heart's action. In my experience, a low blood-pressure and a frequent pulse are more common than the opposite circulatory conditions during the asthmatic paroxysm. And I am strongly inclined to think that further experience with accurate instruments will show that the blood-pressure is low in proportion to the frequency and severity of the paroxysms. This refers, not so much to the blood-pressure during the paroxysms, as to that in the intervals. The point will be returned to hereafter (§§ 749, 750).

§ 387. CLINICAL EVIDENCE CONFIRMATORY OF THE VASO-MOTOR THEORY.—On the hypothesis that swelling of the mucous membrane, due to vaso-dilation correlative of vaso-constriction elsewhere, is the proximate cause of the dyspnoea, we can explain most of the observations which have been made concerning asthma. Anything which could reduce the vascular distension in the affected area would tend to relieve the dyspnoea; and anything which could increase the vascular distension would tend to increase the dyspnoea. The vascular distension might be reduced (1) by increase of the mucous secretion: (2) by vaso-constriction of the dilated area: (3) by vaso-dilation elsewhere, or generally: (4) by reduction in the force of the heart-beat; and (5) by reduction of the total amount of blood in the circulation. On the other hand, the vascular distension might be increased (1) by decrease of the mucous secretion: (2) by increase of vaso-dilation in the dilated area: (3) by increase of vaso-constriction elsewhere: (4) by increase in the force of the heart-beat; and (5) by increase in the total amount of blood in the circulation.

Conformably with these theoretical deductions, we may arrange the following series of clinical observations:—

§ 388. 1. The inverse relation between the amount of secretion and the intensity of the dyspnoea may often be observed, even in the purest varieties of 'spasmodic' asthma. Arthur Foxwell says: ¹—'It is hard to understand the numerous râles and profuse expectoration which usher in the later stages of many attacks of asthma, unless we admit a disturbance in the mucous membrane.' And Salter says: ²—'Expectoration never takes place without marked abatement of the dyspnoea.' The

¹ *Essays in Heart and Lung Disease*, Arthur Foxwell, 1895, p. 17.

² *On Asthma*, 1868, p. 10.

inverse relation, referred to, is most marked in the cases regarded as mixtures of bronchitis and asthma; but it is observable in bronchitis of all kinds, even in the bronchitis associated with pulmonary tuberculosis. The happy action of potassium iodide, well marked in both chronic bronchitis and asthma, may perhaps be in part (but only in part) explained by its effect in promoting secretion.

§ 389. 2. We have seen that in migraine the application of cold to the affected part may be followed by vaso-constriction and relief (§ 360): so it is with asthma. In asthma, cold can of course be applied to the dilated area only by means of *cold air*; and Demarquay¹ points out 'that paroxysms of asthma subside in certain individuals under the influence of keen air.' In others, the opposite occurs. It is clear that the salutary influence of the *inhalation* of cold air would be counter-balanced, if not overridden, were much of the surface of the body simultaneously exposed.

One of my patients suffered from extremely violent nocturnal asthma. He would wake about 4 A.M. in a semi-asphyxiated condition, tear open his pyjama jacket, open the window and stand there for hours. This gave him a certain measure of relief. It was explained to him, however, that the exposure of his skin to the cold night air tended to counterbalance the salutary influence of the inhalation of the cold night air. Thereafter, he kept ready to hand an eider down dressing-gown and woollen nightcap. These he assumed when attacked before opening the window; and he tells me that the relief he experiences is much greater than before. Indeed, on a really cold night, such as sometimes occurs in Queensland during the westerly wind, sitting at the open window under these conditions almost completely disperses all dyspnoea.

§ 390. It seems probable that much of the relief which follows the inhalation of certain fumes is attained by means of direct vaso-constriction in the dilated area. For it is not only the smoke of 'antispasmodic' herbs, such as stramonium, which is effectual in relieving the asthmatic paroxysm. The *fumes of burning nitre paper*, which are nothing if not irritating, afford, according to Salter,² in many cases, the most striking relief: in some they are the only effectual remedy.

¹ *Oxygen and other Gases in Medicine and Surgery*, Demarquay, Wallian, pub. F. A. Davis, 1889, p. 130.

² *On Asthma*, Hyde Salter, 1868, p. 244 *et seq.*; also p. 374.

And Trousseau¹ found the *vapour of ammonia* useful in some cases.

The action of both these remedies upon the bronchial mucous membrane seems similar in most respects to that of a pinch of snuff upon the swollen mucous membrane of the nose in nasal catarrh. Those who have tried this remedy know that immediate and complete, though temporary, relief from the obstruction commonly follows; and this is obviously effected through stimulation of the vaso-motor nerves and consequent vaso-constriction. The action of astringent solutions in gonorrhoea, conjunctivitis, etc., is parallel.

Such vaso-constriction, it would seem, is not invariably restricted to the stimulated part or to its immediate neighbourhood. I have seen the most violent paroxysm of asthma *cease instantaneously* upon the application of chromic acid to the inferior turbinated; and others have had similar experiences. Trousseau² states that the application of strong ammonia to the back of the pharynx sometimes affords relief, though occasionally it has the opposite effect; and I know of one asthmatic who often mitigates his dyspnoea with snuff. In such cases, the vaso-motor changes responsible for the relief are manifestly reflex, not direct.

There can, I think, be little doubt that, in some cases, the relief which follows the inhalation of *chloroform* is attained through direct vaso-constriction of the dilated area. It may be observed in some cases, though not in all, that chloroform vapour causes visible anaemia of the congested nasal mucosa; and Salter³ says of one case of asthma:—‘The first act of inspiration was accompanied with a sensible relief long before the blood charged with chloroform could have reached the nervous centres.’

§ 391. The newly discovered drug *adrenalin* is probably the most powerful of all local vaso-constrictors: this action has been taken advantage of in asthma. Dr. N. W. Jipson⁴ of the Lakeside Hospital, Chicago, relates the case of a lady who had suffered from paroxysms of asthma, increasing in severity since childhood. Solution of adrenalin chloride, 1 in 10,000, was administered by an atomizer, the patient being instructed

¹ *Clinical Medicine*, New Syd. Soc., vol. i. p. 651.

² *Ib.* vol. i. p. 650.

³ *On Asthma*, 1868, p. 217.

⁴ ‘Kansas City Medical Index,’ *Lancet*, September 1902.

to inspire deeply while using the spray. The relief was marked and immediate. The severity of the paroxysms was diminished, and, after three days' treatment, they ceased. Dr. F. J. Savage of Bowersville, Ohio, administered solution of adrenalin chloride, 1 in 1000, by means of an atomizer in an asthmatic paroxysm so severe as to have induced marked cyanosis. He threw the spray as far back into the fauces as possible, at the same time urging the patient to take as full respirations as he could. The spraying was continued for about half a minute, and, two minutes thereafter, the cyanosis had begun to disappear.

But adrenalin is also a powerful *general* vaso-constrictor. Administered by the mouth or hypodermically, it seems to cause constriction of all the arterioles throughout the body, thus raising the blood-pressure and slowing the heart. From the standpoint of the asthmatic paroxysm, such rise of blood-pressure would be immaterial provided only that the bronchial arterioles themselves underwent constriction. Hence we are prepared to find that the general, as well as the local, influence of adrenalin is capable of relieving the asthmatic paroxysm. Conformably, Drs. Jesse G. M. Bullowa and David M. Kaplin publish a series of five cases in each of which adrenalin chloride, given hypodermically, gave rapid and complete relief from the asthmatic paroxysm.¹ In Case 1, a girl of 17, 'three minutes after the injection, the dyspnoea was suddenly and completely relieved and the chest ceased to labour.' In Case 2, a man of 63, the full effect was delayed for about an hour. Case 3, a woman of 37, suffers from moderately severe attacks of asthmatic dyspnoea lasting a week or ten days. 'After an injection of five minims of adrenalin chloride the condition is promptly relieved in about three minutes and the patient feels better for several days.' In Case 4, a girl of 16, the attacks are nocturnal. 'During an attack . . . an injection of 7½ minims of adrenalin chloride solution cut it short in two minutes.' In Case 5, a man of 60, the attacks are nocturnal, and one of them was associated with wheezing and sonorous râles all over the chest. 'Five minutes after the injection of six minims of adrenalin chloride solution, the râles disappeared and the patient slept quietly.' Many other cases were treated similarly with equal success; but in no case, so far as I can make out, were the paroxysms rendered less frequent subsequently.

¹ *New York Medical News*, October 24, 1903.

§ 392. Many vapours regarded as stimulating do not cause vaso-constriction: some, conformably with the old aphorism 'ubi stimulus, ibi fluxus,' cause vaso-dilation. Hence some vapours (for example, the vapour of burning sulphur) may greatly intensify an asthmatic paroxysm. Personal idiosyncrasy comes in here very largely: some individuals are rendered worse by vapours which give instant relief in others. Salter¹ found chloroform inhalation one of the most certain means of relief, but he saw one case—and one case only—in which it added to the dyspnoea. In the following case, the different influence of vapours was well marked:—

Dr. Brockway of Brisbane was administering ether for Dr. Hawkes to an asthmatic girl, aged 21: the ether induced loud wheezing and some cyanosis: chloroform was substituted with instant relief: ether was then readministered and dyspnoea recommenced. Finally the operation had to be completed under chloroform.

It might be suggested of some of the cases in which exaggerated dyspnoea follows the inhalation of certain vapours, that the result is attained through constriction of the muscular fibres of the bronchioles acting defensively and superadded to the vaso-dilation: the suggestion cannot of course be disproved, but it seems to me an unnecessary one.

Though probably not an example of vaso-constriction in the ordinary sense, it will be convenient here to allude to the beneficial influence of compressed air inhalation on the asthmatic paroxysm. This has been found to afford much temporary relief; and its action would seem to be that of direct compression exerted on the swollen mucous membrane, and therefore analogous to general compression of the scalp in migraine.

§ 393. 3. Vaso-dilation in areas other than the area affected, or generally, is an important means of relief in asthma, as it is in migraine: many therapeutic remedies seem to act essentially in this manner. Those well-known vaso-dilators, amyl nitrite and nitro-glycerine, afford distinct immediate relief in some asthmatic paroxysms;² of the former, Hobart A. Hare says, it

¹ *On Asthma*, 1868, p. 217.

² *Pharmacology, Therapeutics, and Materia Medica*, Lauder Brunton, 1885, pp. 712, 713.

'is invaluable in many cases, and it rarely fails to relieve the spasm.'¹ This observation seems to me strongly opposed to the theory that the asthmatic dyspnoea depends upon constriction of the bronchioles by means of their own circular muscular fibres; for I can find no demonstration that the nitrites, in medicinal doses, have any paralyzing action upon muscular tissue,² other than that which is contained in the middle arterial tunic.

Part of the relief which sometimes follows the administration of chloroform may be due to cutaneous vaso-dilation. Alcohol is a powerful vaso-dilator; and Salter³ found it, in some cases, the only remedy which gave relief. Opium and morphia cause cutaneous vaso-dilation, and their immediate effect upon the asthmatic paroxysm is beneficial. But alcohol and opium, in some cases, induce asthma:⁴ here the effect is not immediate but delayed; and is attained, in all probability, through retarded combustion and consequent increase in the carbon contents of the blood. The influence of alcohol upon combustion is well known (§ 209); and Lauder Brunton and Cash⁵ have demonstrated by a number of experiments that morphia greatly lessens the oxidizing power of protoplasm.

Heat is probably one of the most efficient vaso-dilators; and I have never known a hot bath, water, vapour or other, fail to give some relief in an asthmatic paroxysm. The experience of one of my patients amounts practically to a demonstration.

During a severe paroxysm he entered a portable Turkish bath, the temperature of which was probably over 150° F. Quickly the paroxysm subsided; and the succeeding comfort was so enjoyable that he remained in the bath for about forty minutes. At the end of that time, he returned to his bed in an adjoining room. But on the way thither, he felt his skin becoming cold and the dyspnoea returning: the colder his skin became, the more violent became the dyspnoea. Everything was done to relieve his extreme sense of cold, hot bottles, blankets, etc., were applied, but for a time without success. Eventually, the warmth returned to the surface, and then only did the dyspnoea abate.

¹ *Practical Therapeutics*, eighth edition, p. 492.

² *Pharmacology, Therapeutics, and Materia Medica*, Lauder Brunton, 1885, p. 710.

³ *On Asthma*, 1868, p. 204 *et seq.*

⁴ *Ib.* p. 232.

⁵ *Pharmacology, Therapeutics, and Materia Medica*, Lauder Brunton, 1885, p. 55.

In this case, there was no question of the hot air causing relaxation of bronchial spasm through direct local action, since the head and face were excluded from the bath, and the air breathed was indeed distinctly chilly; and further, it can be readily demonstrated that the effect of breathing hot air is to aggravate the asthmatic dyspnoea.

Short of hot baths, heat to the surface gives relief. Graves says: '—It is often serviceable to stupe the whole chest during the fit with flannel wrung out of water as hot as can be borne.'

§ 394. On the grounds that cold locally applied is capable of promoting vaso-constriction, and that cutaneous vaso-dilation reduces vascular strain upon other areas, a most efficient means of relieving the asthmatic paroxysm would be the inhalation of cold air, combined with the simultaneous application of heat to the surface. This might be effected by means of an inhaler containing broken ice applied to the mouth and nose, while the patient sat in a hot-air or vapour bath from which the face is excluded. I have had no opportunity of deliberately trying this procedure so far, but I can hardly question the result:² the relief afforded would be attained by the same mechanism as in the case of the relief of migraine by means of the general hot bath, combined with cold to the scalp (§ 360). The nearest approach to such an experiment, which I can find in medical literature, is a statement by Frederick Roberts³ that 'a warm footbath with mustard, cold water being drunk at the same time,' is effectual in some asthmatic paroxysms.

As in migraine, so in asthma, the vaso-dilation induced by dry cupping often gives marked relief. Of one case Salter says⁴ that four small-sized glasses close together over the bifurcation of the trachea always gave immediate relief in the worst attacks. I have seen the same; but four large-sized glasses afforded greater relief.

§ 395. The influence, immediate and remote, of exercise and pyrexia upon asthmatic paroxysms has already been pointed out (§§ 304, 327), and all that has been said as to the rationale of the beneficial influence of these two conditions upon migraine (§§ 363, 364) applies with equal force to the case of asthma.

¹ *Clinical Medicine*, New Syd. Soc., vol. ii. p. 99.

² The value of this therapeutic procedure has long since ceased to be problematical. I have used it in many cases and always with success, which, however, is purely temporary; nor have I ever seen any compensating disadvantage.

³ *Theory and Practice of Medicine*, 1833, p. 417. ⁴ *On Asthma*, 1863, p. 393.

Exercise, however, influences asthma so strictly in accordance with what might be anticipated from its action upon blood-pressure (§ 363), it is capable in some forms of such exact dosage, and it is so essential an item in therapeutics, that it may be well to introduce here an illustrative case.

A girl of 17 had suffered for two years from violent paroxysmal asthma. For six weeks before coming under my care, she had been unable to lie down at night. Under strict dieting, the paroxysms rapidly abated, so that in twenty-four hours she was able to lie in any position throughout the night. She remained, however, somewhat wheezy, especially after meals and at night. She was then ordered skipping every evening before bedtime. The subjoined are the records of the first two skipping bouts.

FIRST EVENING

Before beginning, chest quite free from wheeziness.

After 49 skips, began to get wheezy.

„ 95 „ still wheezy.

„ 141 „ wheeziness less ; 3 minutes' rest.

„ 184 „ still improving ; 3 minutes' rest.

„ 233 „ chest quite clear ; 10 minutes' rest.

„ 282 „ a little wheezing ; 1 minute rest.

„ 325 „ wheezing hardly perceptible ; 1 minute rest.

„ 368 „ chest quite clear thenceforward.

She slept soundly through the succeeding night, waking about 5 A.M. with slight wheeziness.

SECOND EVENING

Before beginning, quite free from wheezing.

After 84 skips, still quite free ; a minute's rest.

„ 184 „ slight wheezing ; one or two minutes' rest.

„ 294 „ no wheezing : a little short of breath : two minutes' rest.

„ 360 „ chest quite clear thenceforward up to 450 skips, when she ceased for the evening.

She slept soundly throughout the succeeding night, waking, however, at 5 A.M. with slight wheeziness, which passed off while she was dressing. Two evenings later, 600 skips failed to cause the least sign of wheeziness.

§ 396. It might be anticipated that conditions which tend to increase vaso-constriction of the cutaneous area, or of areas other than the bronchial, would tend to intensify asthmatic

dyspnoea and to precipitate an impending attack. This anticipation is fulfilled. The invasion stage of most specific fevers, associated as it is with cutaneous vaso-constriction, is liable to precipitate the asthmatic paroxysm in those who are predisposed thereto. I have seen many examples; and Dr. Robertson of Brisbane tells me of a case in which an unusually violent attack of asthma in an habitual sufferer was concurrent with the initial rise of temperature in dengue.

Salter says: ¹—'I am acquainted with the case of an asthmatic lady whom a walk of two minutes in her garden will render asthmatic, if her chest is bare. This is evidently not from the respiration of cold air; for under identical circumstances, the mere fact of her chest being covered will entirely prevent the occurrence of asthmatic breathing: the same result as immediately follows if her feet get damp and cold.' This case and others shook Salter's belief that, in such cases, asthma is a 'mere reflex nervous phenomenon': ² he saw cases in which 'cold to the surface and extremities' deranged *immediately* the vascular balance of the bronchial mucous membrane; ³ but his deeply rooted conviction that the asthmatic paroxysm depends upon muscular spasm of the bronchial tubes led him to suppose that 'the vascular condition of the bronchial mucous membrane may be the link between the external cold and the bronchial spasm.' ⁴ When the vascular condition of the bronchial mucous membrane and its influence upon the lumina of the tubes are fully realized, there is of course no necessity for importing the factor of bronchial spasm.

Many of the instinctive habits of the asthmatic seem to be governed by the facility with which the vascular balance of the bronchial mucosa is deranged: witness his excessive fear of cold draughts, which he seeks to avoid by casing himself in flannel, by keeping closed the windows and doors, and living in a warm and stuffy atmosphere. His sudden abandonment of these precautions, when a paroxysm is present, is not inconsistent, for then the sensation of air-hunger overrides all other considerations.

§ 397. The influence of emotion upon asthma is susceptible of a vaso-motor explanation. Different emotions are associated with different vaso-motor manifestations in the same individual;

¹ *On Asthma*, Hyde Salter, 1868, p. 312.

² *Ib.*

³ *I*

⁴ *Ib.*

and the same emotions are associated with different vaso-motor manifestations in different individuals. For example, anger is most commonly associated with flushing, fear with pallor; but anger may lead in some cases to pallor. Hence we find that the emotions produce effects upon the asthmatic which are seemingly contradictory. Salter says: ¹—‘Psychical stimuli—excitement, fear, or other violent emotion—are adequate to the immediate production of the asthmatic spasm’; but again: ²—‘The cure of asthma by violent emotion is more sudden and complete than by any other remedy whatever; indeed, I know few things more striking and curious in the whole range of therapeutics.’

Generally speaking, I think, emotions associated with cutaneous anaemia—fear,³ etc.—tend more to induce, emotions associated with cutaneous hyperaemia—excitement of other kinds—tend more to disperse, asthmatic paroxysms. But there are many things to be taken into consideration: there is the action of the heart, which will be considered presently; and there is the condition of the circulation in the splanchnic, and probably other large vascular areas. Shock, whether from emotion, pain, or other causes, is probably always associated with dilation of the blood-vessels in the splanchnic area (Crile); and shock is known to disperse the asthmatic, and, indeed, many other neurosal paroxysms.

Salter thinks emotion acts by causing a ‘diversion of nervous energy’; but I submit, a *diversion of vascular pressure* offers a more tangible explanation of the facts.

§ 398. 4. Any modification in the action of the heart, whereby the work accomplished by this organ is reduced, would relieve the vascular distension of the bronchial area; and such

¹ *On Asthma*, Hyde Salter, 1868, p. 147.

² *Ib.* p. 210.

³ The vaso-constriction associated with the emotion of fear may, in ordinary circumstances, materially raise the blood-pressure. Clifford Allbutt, speaking of some blood-pressure observations, says:—‘On one occasion I observed a high blood-pressure in a patient in whom a high rate was not anticipated. No fault was found in the parts or arrangements of the instrument, and a second inflation revealed a still exorbitant though a lower rate; a third but a few minutes later registered an ordinary rate of about 120 mm. Hg, and remained steady about this figure. The previous excess I should still have attributed to some experimental fallacy, had not the patient, as I put the instrument aside, said to me that he had feared from it a violent electric shock, such as one which many years ago at a fair had put him in an agony which he had never forgotten. As the shock did not occur he was reassured, and the pressure fell. In patients who enter upon a consultation with acute anxiety of mind, the pressure at first is often excessive.’—*Lancet*, March 7, 1903, p. 646.

modifications can, I think, be clearly shown to relieve the asthmatic paroxysm. Many remedies, given in sufficient doses, cause weakening of the cardiac action, as is shown by a tendency to syncope or collapse. Of the class of drugs which he terms depressants or contra-stimulants, namely, ipecacuan, tartar-emetic, and tobacco, Salter says :¹—‘As soon as their characteristic effect is established, the dyspnoea ceases—completely ceases from that moment: no matter how intense the spasm may have been, the moment the sensations characteristic of collapse are felt, it yields, the respiration is free, and the patient passes from agony to ease. It is one of the most striking things to witness in the way of an effect of a remedy, that can be imagined.’ He further points out that in habitual smokers and in those who are unfortunate enough to establish a tolerance of tobacco, the beneficial influence of this drug is lost: ‘just in proportion to the sickness and faintness and other miserable sensations, is the relief of the difficult breathing.’²

The same is true of lobelia: Salter was disappointed with this remedy until he began to give it ‘in doses producing the characteristic depressant action of the drug.’³ Although he firmly believed that asthma in some cases at least is started reflexly through irritation of the gastric terminations of the vagus, Salter is careful to point out⁴ that ‘the relief by an emetic is clearly not mechanical, as it comes on the moment the nausea is felt, before any vomiting has taken place; moreover, an emetic affords relief even when the stomach has been previously empty, and contains nothing to be vomited.’ The sudden systolic weakness associated with nausea is well recognized.

§ 399. On the other hand, drugs and conditions which increase cardiac action may increase asthmatic dyspnoea or precipitate an impending attack. Ammonia may have this effect: so also may alcohol, doubtless in those cases in which systolic force is increased disproportionately to cutaneous and other vasodilation. The initial effect of exercise is, as we have seen, to increase arterial pressure: probably this is attained through obstruction of the venous circulation due to muscular contraction. Hence sudden exertion increases asthmatic dyspnoea and may even precipitate impending attacks, just as it may do in the case of migraine and other neurosal paroxysms.

¹ *On Asthma*, Hyde Salter, 1868, p. 184.

² *Ib.* p. 187.

³ *Ib.* p. 240.

⁴ *Ib.* p. 267.

§ 400. 5. Variations in the mass of the blood in circulation will have an important influence upon asthmatic paroxysms. The immediately beneficial effect of haemorrhage upon the asthmatic paroxysm has been mentioned (§ 330); its rationale is doubtless the same as in the case of migraine, namely, by reduction of blood-pressure in the first place and by acar-bonization in the second. The deleterious influence of repeated haemorrhage is, as already mentioned, to be ascribed in all probability to anaemia, decreased combustion, and consequent increased hyperpyraemia.

Some examples of the relationship of asthmatic attacks to haemorrhage may here be mentioned. Trousseau¹ refers to the case of a boy who for three years 'had been subject to frequent paroxysms of nervous asthma, which were so violent as to place him at death's door . . . he was only relieved by bleeding.' Dr. Berry of Southport, Queensland, has frequently performed venesection during severe asthmatic paroxysms, and he has never known this operation fail to give intense and immediate relief.

Greville MacDonald² relates a remarkable case of a boy with post-nasal growths and asthma. 'The examination of the naso-pharynx with the finger . . . provoked free haemorrhage, and the asthma never recurred, though nothing further was done to the adenoids.' Such a case is, perhaps, analogous to the permanent cure of headache by a single venesection (§ 330).

In the following case related to me by Dr. Thomas, late resident medical officer of the Sick Children's Hospital, Brisbane, the influence of haemorrhage upon the asthmatic paroxysm is well shown.

A child aged $2\frac{1}{4}$ years was attacked by his first asthmatic paroxysm at 4 A.M. His mother, who was herself an asthmatic and slept in an adjoining room, heard him wheezing, and realizing at once what had happened, hastened to his assistance. On reaching his bedside, however, she found him bleeding from a severe scalp-wound and the asthma gone. At 11 A.M. he was brought to the hospital with his head bound up: at this time, the asthma had returned. When the bandages were removed, the left superficial

¹ *Clinical Medicine*, New Syd. Soc., vol. i. p. 643.

² *British Medical Journal*, October 18, 1902, p. 1248.

temporal artery (which had been severed) recommenced to bleed, and the asthma once more quickly subsided.

Asthma may commence, or recommence, upon the cessation of an habitual hæmorrhage.

A medical man had suffered for some years from attacks of hay-fever with post-nasal catarrh and chronic vascular engorgement of the pharynx. His symptoms were relieved by irregular hæmorrhages from the nares and pharynx: he also suffered from asthma and then from hæmorrhoids, which bled freely and dispersed the asthma. Local treatment checked the tendency to nasal and pharyngeal hæmorrhage: and his piles were excised. Thereafter, he began once more to suffer from typical asthmatic paroxysms. (Case LXXXII.)

§ 401. It may here be mentioned that 'hæmoptysis not by any means a common event in asthma' may occur 'as an accompaniment of the asthmatic paroxysms, and in quantity proportionate to the intensity of the dyspnoea' (Salter).¹ The following is a case in point:—

A gentleman of 41 had suffered from asthma, purely nocturnal, since the age of 22: the disease followed acute pneumonia. At the age of 25, he began to cough up a little blood as the paroxysm was passing off. A week later, hæmoptysis to the extent of about a pint occurred during a severe asthmatic paroxysm, the latter ceasing instantaneously. The following night, he had another severe asthmatic paroxysm cut short by an extremely violent hæmoptysis—he is said to have brought up a bucketful of blood. A few weeks later, he had another slight hæmoptysis. Since then until the end of 1903, he has continued to suffer from nocturnal asthma but has had no further bleeding. His case was diagnosed as pulmonary phthisis with asthmatic complications. Under dietetic treatment he now remains quite free from all tendency to asthma. (Case XXXI.)

To realize the occurrence of hæmoptysis in asthma, in amount proportionate to the intensity of dyspnoea, is easy on the theory of vaso-dilation—as easy as it is to realize epistaxis, cerebral and other cranial hæmorrhages in migraine (§§ 330, 373) and hæmatemesis in gastralgia (§ 469), all of which are recorded on good evidence; but the theory of bronchial spasm would hardly assist us.

§ 402. SUMMARY OF THE PATHOLOGY OF ASTHMATIC DYS-PNOEA.—The following propositions and admissions regarding

¹ *On Asthma*, Hyde Salter, 1868, p. 371.

the pathology of asthmatic dyspnoea will serve to parry a charge of undue exclusiveness :—

1. The dyspnoea may be due to the swelling of the mucosa of the bronchioles from vascular distension.

2. Such vascular distension may be due to vaso-dilation of the supplying arteries.

3. Such vaso-dilation may be secondary to, and more or less compensatory of, some widespread vaso-constriction.

4. Such vaso-constriction may be due to hyperpyraemia. Each of these propositions involves certain admissions which, taken in inverse order, are as follows :—

4. The vaso-constriction may be due to humoral factors other than hyperpyraemia, for example, to the invasion stage of specific fevers, such as dengue; and to factors other than humoral, for example, exposure to cold and psychical causes such as fear.

3. The vaso-dilation may be primary, the vaso-constriction secondary and compensatory, as, for example, in hay-asthma.

2. The vascular distension may be due to causes other than vaso-dilation of the supplying arteries, for example, to venous obstruction from sudden exertion.

1. The dyspnoea may be due to causes other than swelling of the mucosa of the bronchioles; for we are not called upon to assume that bronchial constriction never plays a part in the asthmatic dyspnoea.

In my opinion hyperpyraemia, actual or relative (compare Chapter XIII), is the commonest cause of asthma. In asthma, more frequently than in migraine, I am inclined to regard the vaso-dilation as primary, the vaso-constriction as secondary; but this would by no means exclude hyperpyraemia, or relative hyperpyraemia, as the humoral factor.

ANGINA PECTORIS

§ 403. It has been argued that the affection, termed functional or vaso-motory angina pectoris, is in some cases an efficient a carbonizing process (§ 265); and that it may depend upon hyperpyraemia (Chapter IX). We have now to show that it is, at least in some cases, essentially vaso-motor in its mechanism.

VASO-MOTOR THEORY.—Nothnagel recorded a series of cases which go to prove 'that a sudden increase of tension in the

peripheral arteries, due to a cause acting upon the body from without, is capable in some persons of giving rise to phenomena approaching those of a paroxysm of angina pectoris.'¹ Lauder Brunton² demonstrated definitely, through the influence of amyl nitrite, that peripheral vaso-constriction is, in some cases, an essential factor in the affection.

But I believe I am correct in saying that none of those who accept the vaso-motor theory of functional angina pectoris lay any stress upon vaso-dilation. Some, on the grounds that the increased resistance introduced into the circulation by the peripheral vaso-constriction implies an increase of work on the part of the central pump, regard the pain as an expression of cardiac strain, or of a state of muscular cramp. Others, impressed with the frequent association between anginal seizures and obliterative disease of the coronary arteries, regard vaso-constriction, or 'intermittent spasmodic closure of the coronary vessels, having in its train an ischaemia of the cardiac muscle' (quoted³ by Morison), as the essential factor of the anginal pain. And yet it seems to me that a pathological degree of vaso-dilation of the coronary arteries, more or less compensatory of some extensive peripheral vaso-constriction, will enable us to correlate and explain a greater number of the observations which are recorded concerning this affection than any other supposition. It is, of course, unnecessary to assume that the vaso-dilation, compensatory of the peripheral vaso-constriction, is limited to the coronary area. Indeed, many cases strongly suggest that other areas frequently undergo vaso-dilation concurrently. Later I shall argue that, in some cases, there is an associated dilation of the bronchial area giving rise to asthmatic phenomena; and, in one of Dr. Hawkes's cases, the initial symptom of each attack was marked throbbing of both common carotids, visible as well as sensible, with great congestion of the face and head: this symptom occurred simultaneously with extreme coldness and pallor of the hands, arms, feet, and legs.

§ 404. As before suggested, the idea of compensation for vaso-constriction by an area of vaso-dilation, though fully recognized by physiologists, has not largely entered into

¹ *Text-book of Medicine*, Fagge, vol. ii. p. 22.

² *Pharmacology, Therapeutics, and Materia Medica*, 1865, p. 710 *et seq.*

³ Alexander Morison, *Lancet*, November 8, 1902, p. 1249.

pathological speculations. The oversight is, I think, well illustrated in the following paragraph :¹—‘ One point in which the paroxysm of angina seems to differ from what might be expected, on the view that it depends upon increased tension in the peripheral arteries, is its not being invariably, or even generally, attended with a reduction in the frequency of the pulse; among Nothnagel’s vaso-motorial cases there is only one in which a fall from 80 to 64 or 60 beats in the minute is noted’ (Fagge).

The circulatory phenomena of functional angina are thus stated by Liveing :²—‘ Although slowing is rare, the rhythm of the heart is often deranged, and the contraction of the arteries and the smallness of the radial pulse are often remarkable.’ It may be argued that, since vaso-constriction of the peripheral arteries is the rule and slowing of the heart-beat (cardiac compensation) the exception, there is probably some compensatory internal area of vaso-dilation; and this will lead us directly to consider whether a dilation of the coronary arteries is not at once the compensation (in part at least) for the peripheral vaso-constriction and the essential cause of the cardiac pain. The arguments which can be adduced in support of this hypothesis seem to me strong.

It has been argued that, in migraine and asthma, affections which may depend upon hyperpyraemia, extensive peripheral vaso-constriction tends to be compensated by internal vaso-dilation. There is, therefore, an *à priori* probability that the peripheral vaso-constriction of angina, an affection which may own the same humoral factor, is similarly compensated.

It has not been shown that vaso-constriction, whatever its localization, is capable of giving rise to pain in the area rendered ischaemic. On the other hand, the instances are innumerable in which vaso-dilation and pain in the distended area are associated; and it is certain that, in some of these, the association is that of cause and effect.

§ 405. Vaso-dilation of the coronary arteries and arterioles will lead to vascular distension in the area which they supply: such vascular distension will be greatly intensified by peripheral vaso-constriction or other conditions tending to raise the aortic blood-pressure; and we have seen that the local effect of

¹ *Text-book of Medicine*, Fagge, vol. ii. p. 23, 1901.

² *Megrim and Sick-headache*, 1873, p. 332.

vascular distension will vary with the nature and anatomical features of the tissue affected (§ 357). Now by far the greater part of the bulk of the heart consists of muscle: ¹ beneath the epicardium and endocardium there is a certain amount of elastic and connective tissue, the latter of which is prolonged with the blood-vessels into the muscular tissue; but this connective tissue is small in amount. Furthermore, the coronary arteries are relatively large: the heart muscle, for a muscle, is of a peculiarly close texture; and the capillaries are 'very numerous and closely arranged.'² On these and on other grounds, it seems to me, then, that we can hardly expect vascular distension to be followed by swelling of the heart tissue in degree adequate to preclude nerve-pressure, as in the case of asthma. And if not, then pain as a result is to be anticipated. I am aware that the heart, in a physiological condition, is regarded as to a large extent insensitive; but that does not necessarily apply to a heart when its tissues are affected with vascular distension to a pathological degree. For Gowers points out that there are many examples of acute pain being produced by morbid action, or by a morbid modification of physiological action, 'in structures which seem insensitive in health. We meet with it in the pleura, the peritoneum, and the intestinal wall. Indeed, the last is a pertinent example, because we are quite unconscious of intestinal contraction under normal conditions, and yet its increase as by a simple purgative may give rise to intense pain. These facts illustrate the constancy of afferent nerve impulses from all parts, whether we feel them or not, for pain can only be ascribed to the intensification of nerve impulses which are constant in less degree.'³

§ 406. Fagge says of the cases of functional angina described by Nothnagel: ⁴—'The earliest and most conspicuous symptoms of the paroxysms . . . were coldness and pallor with numbness and stiffness of the limbs: the palpitation, the feeling of oppression at the chest, the giddiness, the sense of impending death, being all secondary and attributable to the increased efforts which the heart is called upon to make to overcome the peripheral resistance.' Now there is no apparent reason why

¹ Quain's *Anatomy*, vol. ii. Part II. p. 367, 1899.

² *Ib.* p. 371.

³ 'A Lecture on Lumbago,' by Sir William Gowers, *Brit. Med. Journal*, January 16, 1904, p. 117.

⁴ *Text-book of Medicine*, 1891, vol. ii. p. 22.

the cardiac muscle should be an exception to the general rule that increased work implies increased blood-supply and consequent increased dilation of nutrient arteries; and such vasodilation would tend to reduce the increased work of the heart, for which the peripheral vaso-constriction is responsible. Hence we should have, on both grounds, a strong *à priori* argument in favour of vaso-dilation of the coronary arteries during the anginal seizure. The hypothesis of a general vaso-constriction in which the coronary arteries themselves partake, would imply a large increase of work on the part of the heart, with a concurrent large diminution of the supply of blood thereto. Such would be a combination of conditions, which, we shall see, may obtain ultimately as the final result of many complex disease processes (§ 875), but which seems inconsistent with what we know of the early conservative adaptations of the organism.

Quite recently, 'Professor Schäfer, by perfusing Locke's fluid through the coronary system of cat or rabbit and automatically registering the outflow—while leaving the vagi and accelerantes nerves in connection with the heart—and simultaneously recording the fluctuations of intraventricular pressure, finds that the result of excitation of either the vagus or accelerans was entirely negative, and no evidence was obtained that these nerves contain either vaso-constrictor or vaso-dilator fibres. Even the injection of supra-renal extract produces no effect whatever upon the rate of flow through the coronary vessels. It would appear that the coronary vessels do not receive vaso-constrictor fibres and that they are independent of the vaso-motor nervous system.'¹ This, if confirmed, would have an important bearing upon vaso-motor theories of angina. Obviously, it would be fatal to the view that angina depends upon 'intermittent spasmodic closure of the coronary vessels' (§ 403). But it would not induce us to alter materially the view that dilation of the coronaries is the proximate factor of the anginal pain. The absence of vaso-dilator fibres would of course preclude an *active* dilation of the arteries; and the absence of vaso-constrictor fibres would preclude dilation through *inhibition of vaso-constrictive impulses*; but the absence of both would not preclude an intense *passive* dilation (§ 353). Indeed, it may well be questioned whether an absence of all

¹ *Brit. Med. Journal*, September 17, 1904, p. 681.

vaso-constrictive impulses would not render the coronary arterial system peculiarly susceptible to any increase of general vascular tone.

§ 407. CONFIRMATORY CLINICAL EVIDENCE.—On the view that vascular distension in the dilated coronary area is the proximate factor of the pain, we can explain many of the clinical observations which have been made, or may be made, concerning angina pectoris. Anything which could induce, or increase, the vascular distension would tend to induce paroxysms or increase the pain of already existing paroxysms; and anything which could prevent or reduce vascular distension would tend to prevent paroxysms or relieve the pain of already existing paroxysms.

The vascular distension might be induced or increased (1) by increasing the peripheral vascular resistance, as by vaso-constriction in areas other than the coronary or by venous obstruction; or (2) by increasing the action of the heart. On the other hand, the vascular distension might be prevented or reduced (1) by reducing the peripheral vascular resistance, as by vaso-dilation in areas other than the coronary; or (2) by reducing the action of the heart.

Conformably :—

In Nothnagel's cases, already referred to, 'the attacks were . . . definitely traceable to external cold, and were relieved by hot foot-baths and frictions.'¹ In many of my cases, some of them advanced in life and suffering from organic heart affections, the application of hot fomentos to the chest, back and front, has given instantaneous and complete relief: in some, such relief has been more rapid, more complete, and sometimes more enduring, than the relief which followed the administration of amyl nitrite. The hasty swallowing of cold water will, according to Fagge,² induce a paroxysm of angina in some cases; while, in several of my own, sipping very hot water has afforded almost instantaneous relief. The influence of emotions, such as fear, liable to be associated with cutaneous vaso-constriction, is as marked in the case of angina as in the case of asthma, if not more so. The immediate relief afforded by the nitrites (amyl nitrite, nitro-glycerine), alcohol, ether, etc., is fully accounted for by peripheral vaso-dilation and consequent

¹ *Text-book of Medicine*, Fagge, 1891, vol. ii. p. 22.

² *Ib.* p. 19.

decreased work and decreased vascular distension of the heart muscle.

§ 408. Anstie refers to an extraordinary circumstance, reported by Guélineau,¹ in the 'Gazette des Hôpitaux' for 1861, namely, 'an epidemic outbreak of angina, in which numbers of men, belonging to a ship's crew, were simultaneously affected. The men had been badly fed, and their quarters were very unhealthy; but the powerful exciting cause seemed to be the rapid change from a *very hot to a very cold climate*.' The conditions to which these men were exposed were all highly favourable for the development of hyperpyraemia. They probably slept in a hot ill-ventilated fore-castle: they had been subject to the heat of the tropics: physical exercise was most likely then inadequate; and bad feeding at sea almost necessarily implies a deficiency of proteid in the form of fresh meat, with a corresponding excess of carbohydrates in the form of biscuit (for hyperpyraemia, depending on deficiency of proteid, see § 202). Such a crew is apt to be inadequately clothed as well as improperly fed, so that a sudden exposure to cold would quite probably occasion extreme cutaneous vaso-constriction. Why, however, the compensatory internal vaso-dilation should have affected the coronary arterial system in so many cases, does not appear to be clear: it did not do so in all, for Anstie states that 'other forms of neuralgia and severe colics were observed in others of the crew.' I have not seen Guélineau's original paper, but I should be surprised, rather than the reverse, if there was not on the sick roll a case or so of asthma.

§ 409. The initial effect of physical exercise is, as we have seen, to raise the blood-pressure, probably by increasing resistance in the venous circulation (§ 363). Hence sudden exertion of any kind, such as running, quick walking up hill or against a strong wind, coughing, defaecation (Heberden), etc., may all induce attacks of angina. *A fortiori*, a combination of conditions which increase peripheral resistance by vaso-constriction and venous obstruction, with conditions which increase cardiac action will be especially powerful: suddenly commenced quick walking up hill in the teeth of a strong cold wind, while insufficiently clad, is one of the most certain means of inducing an anginal seizure in one so predis-

¹ *Neuralgia and its Counterfeits*, 1871, p. 74.

posed. Finally, the influence of such a combination of conditions is still further increased, if a heavy meal has shortly preceded (Heberden). For food may act prejudicially in two ways: it may act, as will be argued presently, by distending the stomach, so that the heart has to act at a mechanical disadvantage; but it may also act, as we have seen in the case of headache and asthma, by increasing the carbon contents of the blood and so increasing peripheral vaso-constriction.

But physical exercise, persisted in, reduces blood-pressure by promoting widespread vaso-dilation (§ 363): hence regular physical exercise is a most—if not the most—valuable therapeutic measure in ‘functional’ angina. Consistently, Fagge remarks: ‘It is . . . a curious fact that some persons, after having been pulled up by the pain three or four times at the beginning of a walk, will afterwards go on with ease for several miles.’

A patient of mine, a young lady of 25, can keep herself free from angina by regular physical exercise; but, on some occasions without my sanction, she has hurriedly started to walk, when an attack, which in her case begins somewhat insidiously, has already commenced. The effect is to increase the pain for the first three-quarters of a mile: after that distance has been accomplished, the pain rather quickly abates, then ceases entirely, and does not recur, no matter how severe the succeeding exercise.

In fact this patient on such occasions simply walks off her impending anginal paroxysm, just as other persons are able to walk off an impending migraine, or an impending asthmatic paroxysm. An exactly similar sequence of events may take place with any form of exercise.

The patient just referred to is accustomed in wet weather to substitute skipping for walking. On the first occasion on which she practised this exercise, twenty skips brought on a slight anginal pain, whereupon she desisted for two or three minutes. On resuming, a further forty odd skips were required to cause the pain to reappear. After a short rest, she again recommenced, and this time she completed six hundred skips without further interruption. The pains, referred to as slight anginal, were likened by the patient to ‘stitches’; but since they occupied the same site as, and were similar in character

¹ *Text-book of Medicine*, 1891, vol. ii. p. 19.

to, the pain of her severe attacks, there cannot be much doubt that they were really minor anginal pains. Nevertheless, had this patient not been a sufferer from angina, the pains would certainly have been regarded merely as 'stitches,' whatever that may mean.

It is, I think, clear that, while we may ascribe the influence of exercise on angina to general vaso-dilation and the reduction of blood-pressure so brought about, we must, as in migraine, asthma, epilepsy, etc., admit that the fundamental factor is acarbonization of the blood.

§ 410. A full appreciation of the influence, immediate and remote, of exercise upon angina pectoris is, I am convinced, of the last importance in the practical therapeutics of this affection. Too frequently, we are apt to assume that anginal seizures *depend upon* some undiscoverable lesion or structural weakness of the heart: whereas I have reasons, which will be stated later (§ 875), for believing that the usual order of cause and effect is the exact opposite of this—that anginal seizures, quite unconnected with organic cardiac lesion, tend sooner or later, according to circumstances, to establish an organic weakness of the organ. The inevitable result of the prevalent view, even when it amounts to no more than a mere suspicion, is some curtailment of much-needed physical exercise; and the further result may be unfortunate.

A medical man at the age of 32 developed typical angina pectoris, each seizure being associated with palpable tightening of the radial. He consulted several leading physicians. No organic lesion was found. He was given general instructions as to his mode of life: these differed a little in detail with the physician consulted; but all were agreed that he must be especially careful to avoid anything in the shape of severe physical exercise. On the plan prescribed, he continued to suffer at irregular times, moderating attacks by the use of amyl nitrite. But he now enjoys complete freedom; and this result was attained in the first instance by a slight restriction of the more highly carbonaceous food-stuffs, combined with the substitution of a bicycle for a buggy and horse upon his daily rounds. (Case XLIII.)

This is no isolated case, but one of a series, some of which are detailed in the Appendix (Cases XLI and XLV inclusive).

Before leaving the subject of exercise and angina, a few points must be emphasized. Although I have good reasons to believe

that functional angina graduates, in many cases, into organic angina, the remarks I have made as to treatment by exercise must be taken as applicable only to the former. Further, exercise should be regarded as a means of preventing paroxysms: it should be practised in the clear intervals of paroxysms, not when such are impending; and, on each individual occasion, exercise should be commenced extremely gently and gradually increased in severity. When this is done, the danger of inducing a paroxysm subsides shortly after the commencement of the exercise and *does not recur thereafter*, that is, during the continuance of the exercise. We have seen that the same is true of asthma; and presently we shall see that it is true of epilepsy also.

§ 411. The influence of *pyrexia* upon angina runs a fairly exact parallel with the influence of exercise in the same affection. The commencement of exercise tends, as we have seen, to initiate or to intensify angina: the commencement of pyrexia may have the same effect; for both are apt to be associated with rise of blood-pressure. Many pyrexias in their initial stages are associated with some degree of cutaneous vaso-constriction, indicated, subjectively and objectively, by chilliness: in some, this amounts to rigor. In either case, it is reasonable to anticipate that the increased peripheral resistance, so introduced into the circulation, might precipitate an anginal seizure in a predisposed subject; and I know of one case (influenza) in which this occurred. But in most pyrexias all tendency to vaso-constriction ceases shortly after the initial stage: thenceforward, there is distinct general vaso-dilation, just as occurs in prolonged exercise. Hence angina, in common with migraine and asthma, will probably remain in abeyance throughout the later stages of pyrexia. I cannot quote from published medical records any observation to this effect; nor have my own observations on this point been numerous or usually definite. In one instance, however, the prolonged interruption by pyrexia of anginal seizures, which for some time had recurred almost every day, was very conspicuous: the intercurrent pyrexia was lobar pneumonia, succeeded by empyema.

§ 412. The influence upon angina of variations in the action of the heart may be observed in many circumstances. The initial precipitating influence of physical exercise is probably

due to increased cardiac action as well as to venous obstruction; and conditions associated with weak cardiac action often afford relief from the pain of a paroxysm. Many observations are recorded showing the abortive or relieving influence of nausea, vomiting, syncope, etc., upon affections such as migraine, asthma, epilepsy, and even paroxysmal mania (Floyer, Robert Whytt, Richter, Fothergill, Marshall Hall). Liveing says¹ 'the use of nauseants and emetics for such a purpose is a very ancient practice.' But I am unable to find in medical literature any instance in which such a result followed in angina pectoris. The following case, however, occurred in my own practice. The patient suffered for years from anginal seizures, which usually came on between 3 and 4 A.M., and one of which proved fatal. But for some years his own experience had led him to take emetics during an attack; and these rarely failed, when they acted, to give immediate relief. It may have been, of course, that in this case the angina was due mainly to flatulent distension of the stomach; but the time of occurrence (4 A.M.) was against such a mechanism, and pointed to peripheral vaso-constriction.

A lady patient of mine (the one referred to in § 409) suffers from slight syncopal, as well as anginal, seizures. The former as well as the latter are associated with peripheral vaso-constriction, as shown by the condition of the radial; but in the former there is no trace of pain. The two varieties of seizures alternate; and it seems to me that the essential difference between them consists in the mode of compensation for the peripheral vaso-constriction. In the anginal seizures, peripheral vaso-constriction is, to some extent, compensated by coronary vaso-dilation: in the syncopal attacks, peripheral vaso-constriction is compensated by reduction in the force of cardiac action. Conformably both varieties of attacks immediately give way to amyl nitrite inhalation. On some few occasions in this case, an unusually severe anginal seizure has passed finally into a partial syncope which always brought relief from pain. Here it is reasonable to suppose that compensatory coronary vaso-dilation became replaced by compensatory reduction in the force of cardiac action.

Similar cases, open to similar explanation, are to be found

¹ *Megrim and Sick-headache*, 1873, pp. 368, 371.

in medical literature. Thus Gairdner¹ describes the case of a man, supposed to be the subject of suppressed gout, who suffered for several years 'from occasional attacks of faintness, without manifold cause'; during the attacks 'the pulse was suppressed and the countenance sunk and pallid.' He died suddenly with the symptoms of angina pectoris. It seems probable that both varieties of attacks were due to peripheral vaso-constriction. This was Fothergill's opinion:² he gives other cases in illustration.

§ 413. ANGINA AND MALARIA.—We have noted the occurrence of a malarial migraine (§ 374); and we have explained it by a community of mechanism between migraine simple and rigor. We have now to note the occurrence of a malarial angina. Broadbent says:³—'A perfectly characteristic attack of angina has been described to me as having occurred in intermittent fever, and serious weakness of the heart was left behind for some time.'

Anstie also says:⁴—'Another occasional excitant of angina is an interesting link in the chain of proof that angina is *au fond* a neuralgia, namely, the malarial poison, which has, in a good many well-observed cases, distinctly induced the disease.' Anstie refers to several original and quoted cases in Dr. Handfield Jones's 'Functional Nervous Diseases,' second edition, 1870.

Such cases are susceptible of the same explanation as the cases of malarial migraine above referred to, namely, by a community of mechanism with rigor: the vaso-dilation, compensatory of the cutaneous vaso-constriction, would in malarial angina affect the coronary area in place of, or perhaps in addition to, the general muscular area, which must always undergo vaso-dilation in malarial rigor.

§ 414. ANGINA CAUSED BY FLATULENT DISTENSION OF THE STOMACH.—It has long been recognised that cases, indistinguishable (or nearly so) symptomatically from functional and organic angina, may arise through flatulent distension of the stomach. In a case of my own, the attack came on shortly after meals: the pain was intense, its character and distribution typical; and there was alarming collapse. There was no constriction of the radial artery; none of the usual vaso-dilators (nitrites) afforded

¹ Quoted by J. M. Fothergill, *Gout in its Protean Aspects*, 1883, pp. 96, 97.

² *Ib.* p. 104. ³ 'Lumleian Lectures,' 1891, *British Medical Journal*, p. 748.

⁴ *Neuralgia and its Counterfeits*, 1871, p. 74.

any relief ; but instant and complete relief followed eructation of gas, however induced. Such cases we are accustomed to speak of as 'pseudo-angina' ; but, I submit, without sufficient justification. For, if we believe the anatomical condition, proximately responsible for the pain of angina, to be one of exaggerated coronary vaso-dilation, then it is easy to see how gastric distension might determine a paroxysm. The heart is crowded upwards or, as Lauder Brunton expresses¹ it, is 'actually tilted upwards upon itself' : either through an increase in the curvature of the aortic arch, or otherwise, the organ works at a disadvantage : hence, greater systolic force is demanded, and, consequently, an added degree of coronary vaso-dilation, in order to provide for the increased blood-supply. In so far as the coronary circulation is concerned, a faulty position of the heart, causing increased resistance to the aortic outflow, will have an effect similar to that of an increase in the peripheral resistance, due to extensive vaso-constriction ; and we can understand the failure of the nitrites, or of other remedies, which act only upon the periphery.

It is quite feasible that, in persons subject to angina, some paroxysms may be incited by gastric distension, others by peripheral vaso-constriction. In the case above referred to, it was found that, in some paroxysms, amyl nitrite gave relief : these, however, were very few in comparison with the number in which the drug quite failed. The patient was a chronic dyspeptic as well as a sufferer from angina.

§ 415. SUMMARY OF PATHOLOGY OF ANGINA PECTORIS.—The following propositions and admissions, regarding the pathology of angina pectoris, may serve to parry a charge of undue exclusiveness :—

1. Angina may be due to pressure on the peripheral nerves of the heart.

2. Such pressure may be due to vascular distension of the heart walls from vaso-dilation of the coronary arteries.

3. Such vaso-dilation may be secondary to, and compensatory of, a tendency to rise of general blood-pressure.

4. Such tendency to rise of general blood-pressure may be due to vaso-constriction in other areas.

5. Such vaso-constriction may be due to hyperpyraemia.

¹ *Lancet*, November 23, 1903, p. 1503.

Each of these propositions involves certain admissions which, taken in inverse order, are as follows:—

5. The vaso-constriction may be due to humoral factors other than hyperpyraemia, for example, to malaria; and to factors other than humoral, for example, to cold, fear, anxiety.

4. The tendency to rise of general blood-pressure may be due to causes other than vaso-constriction, for example, to venous obstruction in sudden muscular exertion.

3. The coronary vaso-dilation may arise otherwise than as a compensation for a tendency to rise of general blood-pressure; for example, it may arise through flatulent distension of the stomach, displacement of the heart, and the consequent necessity for increased cardiac action.

2. The nerve-pressure may be due to causes other than mere vascular distension from vaso-dilation, for example, to an intra-vascular aneurism (§ 876).

1. Angina may be due to causes other than pressure on the peripheral nerves of the heart-wall, for example, to pressure on some adjacent nervous structures.

Nevertheless, I am inclined to regard hyperpyraemia, peripheral vaso-constriction, and secondary coronary vaso-dilation as the commonest pathological sequence in angina pectoris.

CHAPTER XI

§§ 416—465

Mechanism of the paroxysmal neuroses (*continued*)—Epilepsy: theory of idiopathic epilepsy: evidence of initial rise of blood-pressure, vaso-motor and other: evidence of modification of the heart-beat: brain anaemia the proximate factor of some convulsions: convulsions due to causes other than cerebral anaemia: relation of convulsions to rigor, malarial and other: summary of pathology of epileptic convulsions—The connexion between vaso-motor action and glycogenic distension of the liver—Physiological model of the paroxysmal neuroses: mechanism of menstruation: confirmatory clinical observations: the full meaning of menstruation.

EPILEPSY

§ 416. Vaso-motor theories of epilepsy were at one time predominant: they are still largely held: Thomas D. Savill thinks¹ that ‘attacks of idiopathic epilepsy are due to vascular alteration in the brain.’ Most authors, however, prefer to relegate the vaso-motor phenomena of the affection to a subordinate position. An eminent neurologist says:²—‘The vaso-motor theory of epilepsy is alike unneeded, unproved, and inadequate. The phenomena indicate that there is a discharge of grey matter, and there is nothing to warrant us in going beyond the grey matter concerned, in our search for the origin of the discharge.’ Such an exclusive pronouncement may be justified from a closely circumscribed neurological standpoint; but even so, there is much to be said on the other side. The primary neurosal theory is unsupported by any direct evidence: it does not enable us to understand the relations of epilepsy with other diseases, such as gout and fever; and, most unfortunate of all, it tends to concentrate attention exclusively upon the cerebral cortex and its intimate microscopic structure, and thus to discourage investigation in other directions.

Now, if we take a wide view of the natural history of

¹ *Lancet*, June 1, 1901, p. 1518.

² *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 755.

epilepsy and include therein the relationships of this affection with other diseases, such as gout and fever, which are usually regarded as of toxic, or at any rate, humoral, origin, we find, in spite of all that can be said to the contrary, much to encourage us in going behind the grey matter in our search for the origin of the discharge of grey matter. It has been already argued that, in at least some cases of epilepsy, the primary factor is hyperpyraemia (Chapter IX) ; and this humoral view almost inevitably constrains us to conceive of some theory of mechanism, which places vaso-motor action in a position of dominance.

Such a theory, we shall find, is easy of construction—indeed, it almost exists ready made: it will rest upon a moderately broad foundation of fact ; and it will enable us to correlate and explain many of the hitherto disconnected and unexplained observations, which have been made concerning epilepsy : to this extent, it will be coherent and symmetrical.

It will be convenient to set forth this theory in the first place, and, thereafter, to collocate and arrange in suitable order some of the many recorded observations upon which it is based and which it may be taken to explain.

§ 417. THEORY OF IDIOPATHIC EPILEPSY.—Moxon observed that, in some cases of epilepsy, the heart stopped beating just antecedent to the onset of convulsion ; and this led him to conclude that the unconsciousness and the convulsions were the direct result of the cerebral anaemia so induced. He ascribed the heart stoppage to inhibition by the pneumogastric, but he was careful to point out¹ that the ‘entirely unknown source of the pneumogastric impulse’ stood behind his explanation, ‘throwing on it the doubt whether the same unknown impulse which discharges the pneumogastric, may not play among the centres where consciousness is seated and itself involve a loss of consciousness.’ The theory I am about to frame will, if accepted, set this doubt at rest ; for it will go a step behind the pneumogastric impulse and offer for this a simple explanation, consistent with known physiological law.

I shall assume provisionally that, in epilepsy, as in most of the paroxysmal neuroses already considered, there is an initial widespread area of vaso-constriction tending to cause a rise in the general blood-pressure : that this vaso-constriction, whether because it is sudden or because it is very extensive, leaves no

¹ Croonian Lectures, *Lancet*, April 23, 1881, p. 650.

time or room for adequate compensation by an area of vasodilation; and that, consequently, cardiac inhibition through the vagus is demanded to check the continuous rise in the general blood-pressure so induced. So is occasioned a grave modification of the heart-beat of the nature of slowing and weakening, amounting perhaps quite often to actual cessation. In this way are produced a more or less sudden fall in the blood-pressure and a more or less sudden anaemia of the brain, and this is the proximate factor of the unconsciousness and of the convulsions. Synchronous with the initial rise of blood-pressure are the various premonitory symptoms or auras of the fit: synchronous with the sudden fall of blood-pressure is the commencement of the unconsciousness and of the tonic muscular spasm: synchronous with the recommencing or accelerating heart-beats, and the consequent progressive recovery of blood-pressure, is the relaxation of the tonic spasm and its substitution by intermittent or clonic convulsions, presenting progressively widening intervals. As the blood-pressure continues to rise, the clonic convulsions become less and less frequent, and finally cease.

§ 418. Moxon believed that the violent muscular contractions of the fit are adapted to complete the venous circulation to the right auricle and so assist in building up once more the blood-pressure, which the inhibition of the heart had allowed to fall. Conformably Leonard Hill says: '—The blood flow from the deep femoral vein of the dog during an epileptic fit (excited by essential oil of absinthe) is three to five times as great as during rest. The clonic contractions alternately suck the blood into the vessels of the muscles, and then compress the blood on into the veins.'

If we accept the above view of the mechanism of an epileptic fit, then each individual step in the complex process becomes conservative as regards its immediately antecedent step: the very convulsions stand between the patient and sudden death.² And further, on the theory of hyperpyraemia,

¹ *Text-book of Physiology*, E. A. Schäfer, 1900, vol. ii. p. 155.

² The following incident occurred in my own practice. I was preparing to operate; anaesthesia was nearly complete and I chanced to have my fingers upon the radial pulse. To my dismay the pulse flickered, then ceased absolutely. I called to the anaesthetist to commence artificial respiration; but, before he could do so, the patient went into a violent epileptic convulsion. I cannot help thinking that this patient owed his life to this convulsion. It was his first and so far as I know, his last.

the whole complex process becomes conservative as regards the condition of the blood.

§ 419. We may epitomize the steps in such an epileptic fit as follows :—

1. Hyperpyraemia attains its climax.
2. Vaso-constriction causing rapid rise in blood-pressure.
3. Cardiac inhibition, causing sudden fall in blood-pressure.
4. Sudden cerebral anaemia, causing unconsciousness and tonic spasm.
5. Recommencement of the heart-beat, causing rise of blood-pressure, and returning cerebral circulation.
6. Relaxation of tonic spasm : clonic spasm.
7. Re-establishment of blood-pressure and cerebral circulation : cessation of all convulsion.
8. Sleep recuperative of exhaustion and damage.

Result : decarbonization of the blood.

§ 420. Most of the clinical descriptions of major epilepsy harmonize fully with the theory above set forth. Trousseau says :¹—‘As he falls down the epileptic is not red, as has been wrongly stated, but deadly pale . . . after these tonic contractions have lasted a few seconds and the thorax remained perfectly motionless, the face begins to redden, and it is then and then only, and not when the individual falls, that the veins of the neck get distended and the face turns livid, remaining so for a pretty long time.’ Goodhart says :²—‘Sometimes even in infants the character of the adult fit is maintained ; there is the initial pallor, followed by lividity and convulsions—the fit commencing with a cry and then succeeded by somnolence.’ Gowers is an uncompromising opponent of vasomotor theories of epilepsy ; yet there is nothing in his description of an attack of *haut mal* which is inconsistent with the theory we are adopting. He says :³—‘The colour of the face, unchanged at first, rapidly becomes pale, then flushed and ultimately livid as the fixation of the chest by the spasm stops the movements of respiration.’

§ 421. EVIDENCE OF INITIAL RISE OF BLOOD-PRESSURE, VASO-MOTOR AND OTHER.—I do not know that I can quote

¹ *Clinical Medicine*, New Syd. Soc., vol. i. pp. 43, 45.

² *Diseases of Children*, sixth edition, p. 523.

³ *Diseases of the Nervous System*, 1893, vol. ii. p. 735.

from medical literature any direct evidence of widespread peripheral vascular spasm, antecedent to cardiac inhibition. But I have distinctly observed such occurrence in one case. The patient was an old-standing epileptic, and it was determined to try the effect of a seton. Knowing that, with this patient, fits were liable to be precipitated by slight causes, I was carefully observing the radial pulse during the insertion of the bistoury, which was done without general anaesthesia. The immediate result of the puncture was a tightening of the radial followed by a few almost imperceptible beats, pallor, and a slight general convulsion.

But the initial vaso-constriction, especially when it affects, as seems most usual, the cutaneous area, may be inferred, with but small chance of error, from the observations of many writers. Horatio C. Wood says :¹—‘ Not rarely, *directly before the paroxysm*, the patient complains bitterly of intense coldness.’ Several of Haig’s epileptic patients told him they often shivered with cold *just before an attack came on.*² And Trousseau³ mentions a case in which the fit commenced by the patient ‘looking haggard with his teeth chattering.’ (The italics in the above quotations are mine.)

§ 422. Nevertheless it would doubtless be fallacious to infer that the vaso-constriction, responsible for the initial rise of blood-pressure, affects always the cutaneous area. Vaso-constriction of the splanchnic area, for instance, is well worthy of consideration. This is known to occur in asphyxia, wherein ‘the cutaneous vessels are widely dilated and engorged, the face is livid, but the abdominal organs are pale and bloodless (Heidenhain).’⁴ As a net consequence of these vascular changes, the general blood-pressure rises rapidly (E. H. Starling);⁵ and Gowers has placed it on record that accidental asphyxia may lead directly to recurrent epilepsy. He says,⁶ the influence of asphyxia ‘was well shown in a child, aet. 3½, who tried to swallow a large piece of potato, which stuck in his throat and stopped his breath. He became livid, unconscious, and convulsed before the obstruction was dislodged

¹ *American Text-book of Medicine*, Pepper, 1893, vol. i. p. 618.

² *Uric Acid in Disease*, 1897, p. 183.

³ *Clinical Medicine*, New Syd. Soc., vol. i. p. 41.

⁴ *Manual of Physiology*, Stewart, 1899, p. 163.

⁵ *Text-book of Physiology*, E. A. Schäfer, vol. ii. p. 307.

⁶ *Epilepsy*, 1901, p. 32.

with a spoon. The convulsive twitchings continued for some minutes, and twenty minutes passed before he regained consciousness. Three days afterwards, he had another fit, and they continued until he came under treatment several months later.'

§ 423. It would certainly be fallacious to infer that all the arteries undergo constriction simultaneously: some, as we have seen in asphyxia, undergo dilation concurrently with vaso-constriction elsewhere. Hence it is quite conceivable that during the widespread vaso-constriction which is leading up to the cardiac inhibition preceding the fit, the brain may be hyperaemic, generally or in part, and the face may preserve its colour or even be more flushed than usual. All we are called upon to assume is that the net result of the vascular changes is a rise of blood-pressure sufficiently rapid to demand vagus inhibition of the heart-beat.

On this understanding, the vascular changes, occurring as they do synchronously with the rise of blood-pressure, offer a reasonable explanation of the epileptic, as they do of the migrainous, asthmatic, anginal, and other, *aurae*. Some of these vascular changes may be peripheral and constrictive. Fagge says:¹—'The patient perhaps experiences a sensation of coldness or weight in a limb; and the part is found on examination to be pale and cold to the touch, and to have its sensibility distinctly blunted.' Others of the vascular changes may be peripheral and dilative. Trousseau says:²—'A local determination of blood may occur in the finger, for instance, causing it to swell, reddening the skin and rendering it successively within a very short time red, and of a more or less deep violet colour. . . . The swelling is real, not apparent; for rings previously easy suddenly become too tight for the fingers.' Or again, vascular dilation and vascular constriction may alternate. Trousseau says:³—'The skin may become excessively pale after having been injected for some time.'

§ 424. But many *aurae* are unassociated with appreciable objective changes in the part whence they seem to arise. Then it is not unnatural to believe that invisible vascular changes, similar in character to the visible peripheral vascular changes just described, are taking place in the cerebral centres and are

¹ *Text-book of Medicine*, 1891, vol. i. p. 751.

² *Clinical Medicine*, New Syd. Soc., vol. i. p. 61.

³ *Ib.*

the immediately responsible factors. On this view, we can understand many of the auræ of the special senses, observable also in migraine; and we can appreciate the time differences between the auræ of epilepsy and of migraine. In epilepsy, the vascular changes are, as we have argued, precipitate; in migraine, they are deliberate; and Gowers, in contrasting the visual auræ of the two affections, says: ¹—‘The epileptic sensation is extremely brief and precedes loss of consciousness: the migrainous sensation is deliberate, slow in evolution, occupying more minutes than the seconds during which the epileptic sensation exists.’

§ 425. That a partial cerebral anaemia is capable of giving rise to the phenomena of an epileptic aura, has been demonstrated experimentally by Leonard Hill, who says: ²—‘I myself have twice produced clonic spasms in myself by compression of one carotid. The first effect on applying the compression was a sensation in the eye on the same side: then there followed a sensory march of formication down the opposite side of the body. This began in the fingers, spread up the arm, then down the leg. Finally clonic spasms of the hand occurred, accompanied by an intense feeling of vertigo and alarm. Consciousness of the clonus was aroused only by the sensation of the hand striking the arm of the chair as it went into clonic spasm. The central motor discharge in the brain seemed to be accompanied by no consciousness. These effects of compression of one carotid vary in different men, no doubt in relation to the freedom of anastomosis in the circle of Willis.’ Schiff had a similar experience.

§ 426. I am arguing that extensive vaso-constriction is, in some cases at least, the immediate antecedent of the cardiac inhibition, which is responsible for the unconsciousness and the convulsions; and that the various auræ are synchronous phenomena. If this is true, it ought to be possible, by means which quickly promote general vaso-dilation, to anticipate the cardiac inhibition and thereby avert an impending fit. This expectation is amply fulfilled. Amyl nitrite causes rapid widespread vaso-dilation; and ‘Dr. Crichton Browne found that,³ when administered immediately after the appearance of the

¹ *British Medical Journal*, 1895, vol. i. p. 1625.

² *The Physiology of the Cerebral Circulation*, p. 142.

³ *Pharmacology, Therapeutics, and Materia Medica*, Lauder Brunton, pp. 71 1 712.

aura, it prevented the fit which would otherwise have come on.'¹ 'This fact made it seem probable that some more stable remedy of the same class would prove efficacious as a preventive'² (Wharton Sinkler); but the expectation has not been realized. The nitrites do no more than defer the attack, and 'some of the patients complain that, when a fit does occur under such circumstances, it is more than usually severe'³ (Putzel). That, of course, is exactly what we should have anticipated: the exaggerated severity of the deferred fit is explicable by the postponement of the decarbonization and the consequent increase of hyperpyraemia. Again, heat to the surface of the body causes cutaneous vaso-dilation; and hot baths, perhaps reinforced by mustard, are a well-tried remedy in the convulsions of young children.

§ 427. Sometimes, it would seem, there occurs, through the intervention of unknown factors, a spontaneous vaso-dilation capable of checking the rapid rise of blood-pressure. In this event, cardiac inhibition is anticipated, and the impending convulsion turns out to be abortive. Gowers says:⁴—'The phenomena which attend the sudden termination of threatened attacks are sometimes peculiar and instructive. In one case, a cold and shaky feeling in the legs passed up the back to the head, which felt as if it would burst: when this sensation became intense, there was a sudden flow of saliva and a watery discharge from the nostrils: then there was a copious flow of tears for a few seconds, and the sense of fulness in the head suddenly ceased, and also the secretion from the mouth and nose.' Such abortive fits may be regarded as stepping-stones, bridging the gap between epilepsy and other paroxysmal neurosal affections. The distinctive symptoms will depend largely upon the nature of the compensation for the vaso-constriction common to all. If this is by vaso-dilation, everything

¹ Fagge argues that the abortive influence of amyl nitrite does not necessarily prove that vaso-motor action is an essential factor in an epileptic fit. He says:—'Venesection is sometimes useful, apparently under the same circumstances as those in which the nitrite does good. Yet they must produce contrary effects.'*Text-book of Medicine*, 1891, vol. i. p. 758. Surely venesection and amyl nitrite produce at least one effect in common, namely, a sudden fall of blood-pressure; and this effect is the only important one from the standpoint of the vaso-motor theory of epilepsy, which I am endeavouring to substantiate.

² Wharton Sinkler in Pepper's *American Text-book of Medicine*, 1893, p. 1092.

³ *Treatise on the Common Forms of Functional Nervous Disease*. L. Putzel, 1883, p. 89.

⁴ *Epilepsy*, second edition, p. 116.

will depend upon its localization. We can have little doubt that, if in the above case vaso-dilation had affected the mucosa of the bronchioles, asthmatic, instead of salivary, nasal, and lachrymal, phenomena, would have usurped the place of the convulsive phenomena, just as happened in a case detailed by Salter and referred to in § 500. Many other affections, not usually included in the class of paroxysmal neuroses, might be explained on similar grounds; for example, the serous diarrhoea sometimes observed to follow fright, might be accounted for by a sudden vaso-dilation of the intestinal mucosa, compensatory of the emotional vaso-constriction of the cutaneous area.

§ 428. The rising blood-pressure, due to vaso-constriction, may be checked by therapeutic measures other than those which operate through vaso-dilation. A weakening of the cardiac systole would be efficient, and such may result from vomiting or even nausea. Richter says: ¹—‘I know of no medicine which will so certainly prevent an epileptic fit as a vomit given an hour before the attack. This, indeed, can only be had recourse to when we can foresee the fit, that is, when the disease is periodical or preceded by a forewarning’; and Liveing ² points out ‘that it is not always necessary for this curative influence that actual vomiting should occur’—that the induction of nausea alone may be sufficient. The modification of cardiac action so involved might be regarded as anticipatory, averting the necessity for vagus inhibition, if, indeed, it be not itself due to a modified form of vagus inhibition.

§ 429. The action of haemorrhage upon epilepsy has been already mentioned (§ 331): it is similar in all respects to its action upon headache, asthma, etc.; and it is to be explained on similar grounds, namely, by reduction of blood-pressure and by acarbonization of the blood. Practically, the use of venesection is restricted to special emergencies. Da Costa, speaking of the status epilepticus, says: ³—‘In some cases, bleeding has been practised with benefit.’ And Broadbent ⁴ has found that in cases in which there is a continuous high blood-pressure between the fits, venesection, especially when combined with calomel, has a marked influence in

¹ *Megrim and Sick-headache*, Liveing, 1873, p. 368.

² *Ib.* p. 370.

³ *System of Therapeutics*, H. A. Hare, vol. iii. p. 251.

⁴ *The Pulse*, p. 297 *et seq.*

reducing the number of attacks and even, in some cases, of abolishing them altogether.

§ 430. The beneficial influence of pyrexia (including acute gout) upon recurrent epilepsy has been considered, and we have ascribed it to acarbonization of the blood; but there can be little doubt that the result is proximately due to the vascular dilation which follows pyrexial acarbonization. Gowers, after referring to the fact that, during an acute febrile disease, patients are usually free from attacks, points out that 'an¹ exception is scarlet fever, during which they sometimes continue with increased severity.' For a long time I was unable to offer any explanation for this exception, and said so in an article in the 'Australian Medical Gazette' for September 1903. On reading this admission of ignorance, Dr. J. Fergusson of Toronto, Canada, was kind enough to write me as follows:—

'On this point, may I mention to you that, during the last day or two of the invasion stage of scarlet fever and the first two or three days of the eruptive stage, there is high arterial tension. I do not know of any other febrile disease with this characteristic. The cases of scarlet fever with a low arterial tension during the above days are usually of the malignant type with deep sepsis and great depression. This explanation makes scarlet fever fit in with your theory. . . . I have long taught that the changes in circulation account for most cases of convulsions.'

These peculiar vascular features of scarlet fever probably account for the 'remarkable influence of scarlet fever in the causation of epilepsy' (Gowers), already referred to (§ 329). Gowers² points out that, in most of the cases arising through scarlet fever, 'there was no evidence of renal disease: the fits commenced either during the acute disease or during uncomplicated convalescence. In many instances, the convulsions were succeeded by attacks of *petit mal*, which changed to severe fits only after some years. In a few, convulsions ushered in the disease, persisted throughout the illness, and continued afterwards as permanent epilepsy.'

§ 431. Valuable evidence as to the dominant influence of blood-pressure in epilepsy is obtained from observing the effect of conditions which tend to raise blood-pressure, whether through venous obstruction or peripheral vaso-constriction:

¹ *Epilepsy*, Gowers, 1901, p. 212.

² *Ib.* p. 28.

conditions operating in either way are capable of precipitating convulsive attacks. Trousseau¹ says of a case:—‘The attacks . . . were brought on by the slightest painful emotion, the least variation of temperature, a draught of cold air.’ I know an epileptic who frequently has a fit immediately he gets out of bed in the morning, but fits, in these circumstances, are practically limited in his case to the winter; and several mothers of epileptic children have assured me that fits are often brought on by cold or wet feet. Maisonneuve, Lauret, Reynolds, and Trousseau² all believed that fright is a not infrequent cause of epilepsy in the first instance. And Gowers says: ³—‘Mental emotion—fright, excitement, anxiety—is the most potent cause of epilepsy. The most frequent is fright.’ Fright, as a cause of epilepsy, was noticed by Hippocrates. All these emotional states, but especially fright, are liable to be associated with conspicuous vaso-constriction of the cutaneous area; and it is a commonplace, that intense fright may cause the heart to stand still. May not this stoppage of the heart, *which is no mere figure of speech*, be a compensation for a sudden rise of blood-pressure, brought about by a rapid and extensive vaso-constriction of the cutaneous area, a vascular condition testified to by the appearance and sensations of the subject? And if so, have we not a simple explanation of how a person may be frightened into a fit?

The initial effect of violent exercise is, as we have seen, to cause a rise in the blood-pressure amounting to about 20 mm. : hence sudden exertion may precipitate a fit. Esquirol says: ⁴—‘Violent exertion may provoke the seizures.’ Reynolds knew fits to be brought on by ‘a violent effort, such as straining to raise a heavy weight.’⁵ The general convulsions, which Fagge says ⁶ ‘are not of very infrequent occurrence’ at the end of a violent attack of coughing in pertussis, are explicable in the same way or by a tendency to asphyxia; and Steffen says⁷ that ‘a momentary stoppage of the heart’ has been observed in these circumstances.

On the other hand, exercise, persisted in, tends to lower the general blood-pressure, as already mentioned; and I have else-

¹ *Clinical Medicine*, New Syd. Soc., vol. i. p. 40.

² *Megrin and Sick-headache*, Liveing, 1873, p. 185.

³ *Diseases of the Nervous System*, 1895, vol. ii. p. 782.

⁴ *Megrin and Sick-headache*, Liveing, 1873, p. 171.

⁶ *Text-book of Medicine*, 1891, vol. i. p. 1138.

⁵ *Ib.*

Ib.

where quoted Broadbent to the effect that fits rarely come on during exertion (§ 308). Clearly, the exercise prescribed for epileptics, as for sufferers from migraine, asthma, angina, etc., must on each occasion be commenced gently and progressively increased in severity.

§ 432. The epileptic fits which occur in plumbism are susceptible of explanation by the high blood-pressure which rules in this condition. Conformably, Oliver says: ¹—‘For the attacks of acute lead encephalopathy, nothing gives such good results in my opinion as inhalation of nitrite of amyl; the slow pulse under its influence becomes quickened, the arterial tension is reduced, and convulsions are undoubtedly warded off.’

Gowers says: ²—‘Analogous convulsions are sometimes met with in chronic renal disease, apart from any acute symptoms of uraemia.’ Such also are explicable by the high blood-pressure common in this disease.

§ 433. EVIDENCE OF MODIFICATION OF THE HEART-BEAT.—I have already called attention to the ‘momentary stoppage of the heart’ noticed by Steffen in the convulsions associated with pertussis (§ 431). The same has been noticed by many observers in the more common convulsions included under the term ‘epilepsy.’

In two cases, Moxon ³ had his fingers on the pulse at the wrist during the development of an epileptic fit, and in both the pulse ceased entirely *before the convulsion began*; in another, he was auscultating the heart when the sounds ceased suddenly and the patient went into ‘severe epileptiform convulsions.’ Moxon’s house-surgeon, Mr. Lane, had noticed the failure of the pulse at the wrist in two cases. Hughlings Jackson informed Moxon that, on several occasions, he had known ‘the pulse to disappear during the paleness of the face in the onset of attacks of *petit mal*’; and Hilton Fagge ⁴ was listening to the heart sounds, when they suddenly ceased and the patient, a previous epileptic, went into a fainting fit with ‘a little twitching of the muscles of one or both hands.’ Moxon refers to another case in which frequent *petit mal* was associated invariably with heart stoppage. Broadbent ⁵ was

¹ *British Medical Journal*, vol. i. p. 691.

² *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 734.

³ Croonian Lectures, *Lancet*, 1881, vol. i. p. 649 *et seq.*

⁴ *Text-book of Medicine*, vol. i. p. 750.

⁵ *Lancet*, 1887, vol. i. p. 710.

auscultating a patient when a fit commenced: the patient became pale, unconscious, and exhibited slight quiverings of the muscles of the face and movements of the arms, 'but the most striking fact was a complete arrest of the heart for a sufficient time to cause serious anxiety.' 'In a case reported by Thornton it was proved by the stethoscope that, in the first stage of the attack, the heart ceased to beat for many seconds';¹ and quite recently Dr. R. G. Herb² was listening to the heart in a case of aortic regurgitation: the sounds ceased, the patient became unconscious, rigid, and went into violent general convulsions.

Some may contend that, if stoppage of the heart were other than a mere occasional incident in epileptic fits, it should have been observed more frequently. But, if we bear in mind the infrequency and shortness of duration of the whole epileptic attack, the fact that cessation of the heart-beat occupies only a short period within the attack, and the impossibility, in practically all cases, of predicting the exact time of occurrence of an attack,—then, on the doctrine of chances, it would seem somewhat remarkable that stoppage of the heart has been observed so often as is the case.

§ 434. But, even if heart stoppage can be disproved in many cases, that will not disprove the dominance of the vascular factor—brain anaemia—in convulsions: it may well be that a degree of retardation short of actual stoppage can give rise to sufficient cerebral anaemia; and it is evident that there may be every grade of vagus inhibition between that which leads to slight retardation of the heart-beat and that which leads to cessation.

Now extreme retardation, just before the fit, has often been observed. Dr. Burnett³ noted a pulse of 20, at times as low as 14, 'in the minute before the fit.' Horatio C. Wood says: ⁴—'In syncopal cardiac epilepsy, the habitual pulse-rate is much below the normal, and at the moment of the attack diminishes to twelve, ten, or even five, per minute.' Haig observed that just before a fit the pulse is often slow and of high tension. Broadbent⁵ looks upon 'convulsive attacks, when they occur

¹ *Epilepsy, etc.*, H. A. Hare, p. 83.

² *British Medical Journal*, April 6, 1901.

³ *Megrim and Sick-headache*, Liveing, 1873, p. 338.

⁴ *American Text-book of Medicine*, Pepper, 1893, vol. i. p. 618.

⁵ *The Pulse*, p. 122.

in connexion with an infrequent pulse, as a result of cerebral anaemia.' And Hobart Amory Hare says :¹—'The latest and most elaborate studies on the epileptic pulse with which the writer is acquainted are those of Mons. V. Magnon, who has shown that, during the clonic stage of the convulsion, the arterial pressure is increased to a very great extent as well as the pulse-rate, but that, during the first or tonic stage, the pulse-rate falls and the rhythm is so altered that a complete systole and diastole may occupy six times the normal period. Afterwards the pulse passes to the normal or into a condition of increased force and frequency.' It is, of course, highly probable that an epileptic convulsion, initiated by a sudden fall of blood-pressure, may *result*, like any other form of sudden violent exertion, in an abnormally high blood-pressure temporarily. Indeed, there is in epilepsy a factor conducing to high blood-pressure, which factor does not enter materially into sudden physiological exertion : in a fit of major epilepsy, the tonic spasm of the respiratory muscles induces an appreciable degree of asphyxia ; and Crile has shown that during asphyxia there is marked splanchnic vaso-constriction.

In the hypothesis that cardiac inhibition, in some degree, is an essential factor in many epileptic fits, we may have a sufficient explanation of the favourable influence of belladonna upon epilepsy—an influence taken much advantage of by Bretonneau, Trousseau,² and other physicians who practised in the pre-bromide days ; for, as Lauder Brunton³ observes, 'belladonna paralyses the power of the vagus over the heart' and thus diminishes the sensibility of that organ to changes of pressure.

§ 435. BRAIN ANAEMIA THE PROXIMATE FACTOR OF SOME CONVULSIONS.—That sudden brain anaemia is competent to give rise to all the phenomena of an epileptic fit, is well known. Kussmaul ligatured the cervical vessels in rabbits. He says :⁴—'General convulsions usually followed in from eight to eighteen seconds after complete withdrawal of arterial blood. . . . We found in every instance that the closing of all four arteries was necessary to produce rapid convulsions. If but

¹ *Epilepsy, etc.*, p. 26.

² *Clinical Medicine*, New Syd. Soc., Trousseau, vol. i. p. 94.

³ *Pharmacology, Therapeutics, and Materia Medica*, p. 40.

⁴ Quoted by Moxon, Croonian Lectures, *Lancet*, 1881, April 23, p. 649.

one carotid or one subclavian has remained pervious, we have never seen convulsions take place, even when the ligature has remained on the other three for several hours.'

Similar experiments, leading to even more pertinent results, have recently been performed by Leonard Hill. This physiologist¹ 'has found that artificial cerebral anaemia in cats or monkeys, produced by ligation of the four cerebral arteries, produces tonic spasm . . . that if the clamp or ligature be loosened on a carotid so that the blood flows back to the hemisphere, clonic spasms almost immediately occur. This will again give place to tonic spasm on closing the artery; and again on removing the clamp, allowing the blood to flow to the hemisphere, the clonic spasms supervene.' Clamping and releasing the supplying blood-vessels must lead to vascular conditions of the brain, precisely the same as those which result from stoppage of the heart followed by recommencement of its pulsations; and the objective clinical manifestations are identical in both cases.

It seems clear that the intensity of the convulsion is, to some extent, proportionate to the degree of cerebral anaemia; for tonic spasm implies a far higher number of muscular contractions than clonic spasm. The gradation of the former into the latter, as the circulation recovers and the brain anaemia becomes less, may be watched in the human subject: it was especially conspicuous in a case mentioned by Voisin and Petit,² 'in which a wound that was being dressed stopped bleeding with the onset of the fit, and no pulse could be felt at the wrist; but, *at the end of the spasmodic stage*, the pulse reappeared beating 142, the blood-pressure rose and the wound began to bleed freely once more.' (Italics mine.)

§ 436. Although cerebral anaemia may be the common proximate factor of most convulsions, it is not necessary for us to assume that, in all such cases, the cerebral anaemia results from vagus inhibition, compensatory of rapidly rising blood-pressure: for example, cerebral anaemia responsible for convulsions and death may arise directly through severe haemorrhage. Nevertheless, I am inclined to think that vaso-constriction, or other conditions tending to raise suddenly arterial

¹ Quoted by F. W. Mott, Croonian Lectures, *Lancet*, 1900, vol. i. p. 1849.

² *Uric Acid in Disease*, Haig, 1897, p. 228.

pressure, antecede cerebral anaemia more often than might at first sight be supposed. Goodhart regards swooning as 'largely a matter of peripheral spasm':¹ by peripheral spasm, we could explain the syncope which sometimes attends cold bathing; and the swooning, which the author last mentioned says may, in some cases, attend each violent paroxysm of coughing,² might be explained by vagus inhibition, compensatory of sudden rise of blood-pressure.

Such considerations tend to the conclusion, often held by others, that many syncopal attacks differ from epileptic attacks, in degree, rather than in kind. Foster says:³—'In ordinary fainting, which is loss of consciousness due to an insufficient supply of blood to the brain, the diminution of blood-supply is not great enough to produce . . . convulsions.' During micturition, many persons experience a more or less involuntary shiver: this, I imagine, is the expression of a momentary vasoconstriction of the cutaneous area, reflex through stimulation of the urethra; and Gowers says:⁴—'I have known micturition to be attended with a moment's loss of consciousness.' Such could be explained by compensatory vagus inhibition of the heart; and the momentary lapse of consciousness would constitute a minor epileptic attack. This view would enable us to understand the major epileptic attacks which, in some persons, mostly epileptic, but sometimes free from 'idiopathic' epilepsy, follow the grosser urethral stimulation due to the passage of a catheter. Violent paroxysmal cough, which Goodhart says may lead to swooning, leads in other cases, as we have seen (§ 431), to convulsions. Gowers, speaking of recurring causeless faints, says:⁵—'Many of these cases are probably on the border line of epilepsy, into which some would pass unless relieved. There is indeed some reason to think that cardiac faints, often recurring, may establish in the brain a tendency to pass into a state of similar functional abeyance—essentially *petit mal*.' To my mind, it is only the belief that epilepsy may depend upon brain anaemia which makes it possible to conceive of a border line between epilepsy and syncope: on any other view, the two conditions seem

¹ *Lancet*, 1901, December 21, p. 1715.

² *Text-book of Physiology*, 1895, p. 639.

³ *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 799.

⁴ *Ib.* p. 1714.

⁵ *Ib.* p. 751.

widely separated. The gradation between syncope and convulsions is conspicuous in haemorrhage: profuse haemorrhage will account for a high grade of cerebral anaemia: syncope is the commonest result, but general convulsions are 'the final phenomena of death under these circumstances' (Broadbent).¹ The conclusions we have now arrived at, that convulsions may be due, on the one hand, to the cerebral anaemia of cardiac inhibition compensatory of the widespread vaso-constriction of hyperpyraemia and, on the other hand, to cerebral anaemia which is a part of the general anaemia of haemorrhage, would seem to elucidate the aphorism of Hippocrates, that 'convulsions take place either from repletion or depletion.'²

§ 437. Fagge says: ³—'One great distinction between the attacks which are epileptic and those which may properly be referred to fainting, is that the former generally, if not always, occur without any definite exciting cause.' But the exceptions to this rule are numerous: we have seen fits precipitated by exposure to cold, sudden exertion, emotion of various kinds; and the following case might, I think, be classified either as epilepsy or as syncope.

A hospital wardsman, attending his first operation case, became, at the sight of blood, blanched, and fell to the ground, not suddenly, but gradually, as in an ordinary faint. The other attendants were directed to loosen his collar and leave him to recover; but almost immediately he went into slight, but quite distinct, general convulsions, lasting perhaps three-quarters of a minute: never before had he suffered a similar attack, nor has he done so since.

I have seen other cases presenting equal difficulty of classification; and so apparently have many others. Dr. James Adam says: ⁴—'The idea of sudden cerebral anaemia in epilepsy is one that dies hard, and will take a good deal of dislodging from the mind of anyone who has observed, as I have several times, the initial groan and epileptiform movements which sometimes accompany simple syncope. For example, these symptoms occurred in an attack of syncope brought on in an asthmatic man aged 54 by slight intra-nasal interference; and again in a cabdriver, while having an abscess opened. In neither case was there any question of epilepsy before or since.'

¹ *The Pulse*, W. H. Broadbent, 1890, p. 282.

² *Genuine Works of Hippocrates*, Adams, vi. Aphorism 39.

³ *Text-book of Medicine*, 1891, vol. ii. p. 15.

⁴ *British Medical Journal*, May 9, 1903, p. 1081.

§ 438. I am not sure that we are as yet fully entitled to deny the possibility of convulsions arising through a sudden constriction of the cerebral arteries—a constriction inadequately extensive to raise the general blood-pressure to the point at which cardiac inhibition is demanded, but adequately intense to cause marked anaemia in the area of distribution of the constricted artery or arteries. It may be that such cerebral arterial constriction is never sufficiently extensive to cause loss of consciousness and general convulsions—*haut mal* in short; but it may well be that such constriction is sufficient to cause localized anaemia of the cerebral centre concerned—a localized anaemia capable of causing an aura and localized convulsions. For it is admitted that minor epileptic attacks may occur without the slightest, even momentary, loss of consciousness. Gowers says:¹—‘In the cases in which the minor attacks consist of sudden starts or of a visual sensation, consciousness may be apparently unaffected.’ H. C. Wood describes² a case in which ‘the patient had a distinct aura in the hand, rising up the arm in the usual manner, but suffering arrest in the neck, at which time, without any loss of consciousness, there were violent convulsive movements of the muscles below the position to which the aura had reached.’ This attack may be compared with the personal experience of Leonard Hill when compressing one carotid (§ 425).

It is true Kussmaul found, as already stated, that perviousness of any one of the four cerebral arteries is sufficient to prevent convulsions. But anastomosis between these arteries within the cranium is extremely free. It is otherwise with arteries which arise beyond the circle of Willis; and there seems no reason why, with them, vaso-constriction should not lead to cerebral anaemia of the centre, sufficient to cause convulsion in the muscles of the corresponding limb. Broadbent says:³—‘It will be remembered that Hughlings Jackson attributed convulsions to spasm of the cortical arterioles; and I may perhaps add that for many years I have held the view that uraemic convulsions are due to stoppage of the circulation in the cortical capillaries and not to the direct action of any poison.’ We know now that the cortical arterioles are well supplied with nerves; and extreme unilateral variations in the

¹ *Diseases of the Nervous System*, 1893, vol. ii. p. 746.

² *American Text-book of Medicine*, Pepper, 1893, pp. 615, 616.

³ *British Medical Journal*, January 4, 1902.

calibre of the intra-ocular arteries—the visible arteries nearest to the cerebral arteries—have frequently been observed.

C. E. Beevor and Marcus Gunn¹ describe the case of a man of 34, who, from the age of 7, had been liable to attacks in which he had suddenly become blind for a few minutes, the loss of sight especially affecting the right eye. Finally, he had ‘complete loss of vision in the field of the right eye above the horizontal line with paleness of the optic disc in its lower half and evident shrinking of the lower half of the arteria centralis retinae.’ The authors add that other symptoms clearly showed this case to be a periodic neurosis of probably a minor epileptic type.

Finally, I would ask the following question:—Do any of the current theories, which exclude cerebral anaemia as a factor in major epilepsy, *explain* the occurrence of unconsciousness?

§ 439. CONVULSIONS DUE TO CAUSES OTHER THAN CEREBRAL ANAEMIA.—So far, I have argued as if cerebral anaemia were the proximate factor of all convulsions—the irritant or stimulus which calls forth the sudden discharge; but there is nothing to be gained by taking so exclusive a view. If it is admitted that in some cases this pathological conception holds good, that is sufficient for the present purpose.

It may be that many conditions, other than anaemia, are efficacious. It is known that electrical stimulation of the cortex can give rise to convulsive movements in the limb corresponding to the convolutions stimulated. Further, Gowers states that, in some cases, no alterations in the cardiac or vascular states precede a fit; and he refers to a tracing by Voisin which ‘shows that the heart’s action may be perfectly normal *during the stage of aura*.’² (Italics mine.) Nevertheless, though they all may render such less probable, no one of these observations can be accepted as finally excluding cerebral anaemia as the proximate factor of the convulsions in these cases.

There seems nothing to show that electrical stimulation of the cortex does not cause convulsions through localized vaso-constriction of the cortical arterioles and consequent localized cerebral anaemia. The arteries of the grey matter are, as already stated (§ 372), well supplied with vaso-motor nerves; and, as Leonard Hill points out, ‘by . . . the appli-

¹ *Trans. Ophth. Soc.*, 1898, 1899.

² *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 741.

cation of the galvanic current, the peripheral arteries of the frog can be thrown into contraction.'¹

It is never possible to be sure that no vascular changes precede a fit: at most we can only say that no perceptible changes occur: some vascular changes, for example constriction of some cerebral artery or arteries, would presumably manifest themselves only by the occurrence of convulsion.

As regards the tracing which shows that the heart's action may be perfectly normal *during the stage of aura*, this again is not inconsistent with cerebral anaemia as the proximate factor of the fit. The stage of aura is marked by vaso-motor variations: these may be both constrictive and dilative (§ 423); and the constriction and dilation may be in accurate counterpoise. In this case, there would be no alteration of blood-pressure and, consequently, no cardiac variation; and, should this condition of things continue, the attack would *consist* of the aura. Cardiac inhibition, however, may occur, but only when constriction has overbalanced dilation: such probably occurs quite suddenly in many cases; and *then it marks the termination of the stage of aura*.

Gowers says:²—'Hemiplegia, occurring at any period of life, may be followed by recurring convulsions; but this sequel is far more frequent in the cases in which the onset of the paralysis is during childhood.' This fact might be adduced as evidence against vaso-motor theories of epilepsy; yet it is by no means necessarily inconsistent therewith. The cerebrum exerts an inhibitory influence over the lower centres,³ amongst which must be placed the vaso-motor centre; and lesions responsible for hemiplegia would undoubtedly damage all the cerebral functions, amongst them the inhibitory functions. Consequently, it might be held that hemiplegia leads to recurrent epilepsy through permanent diminution of the normal cerebral inhibition. This view receives support from the frequent occurrence of epileptic fits amongst congenital idiots.

Manifestly, it would be a difficult task to exclude cerebral anaemia, brought about directly, or indirectly through cardiac inhibition, as the proximate factor of epileptic fits in any case. But did success attend the task in some cases, that would have no necessary bearing upon many others.

¹ *Text-book of Physiology*, Schäfer, vol. ii. p. 130.

² *Epilepsy*, Gowers, 1901, p. 154.

³ *Text-book of Physiology*, Schäfer, vol. ii. p. 711.

§ 440. THE RELATION OF CONVULSIONS TO RIGOR, MALARIAL AND OTHER.—It is admitted that convulsions and rigor are, at times, interchangeable—that, with many children, convulsions usher in an acute disease, the commencement of which would, in adults, be marked by rigor. Of children having a tendency to nervous affections, Trousseau says:¹—‘Such subjects are liable to be seized with convulsions when fever is setting in, whether that fever be dependent upon measles, small-pox, scarlatina, an intestinal affection, or a simple pulmonary catarrh, *just at the moment of the first rigor announcing the febrile condition.*’ (Italics mine.) Trousseau, indeed, regards rigor as convulsions, less the cerebral phenomena.

Now it seems to me that, as in the nearly parallel case of the relationship between migraine and rigor, the relationship between convulsions and rigor is one of community (up to a certain point) of mechanism. In rigor, a rapid rise of general blood-pressure is anticipated by extensive vaso-dilation of the functionally active muscular layer. If, for any reason, this compensation fails or is inadequate, cardiac inhibition may be demanded and may lead to general convulsions. Thus it would be correct to say that rigor, at the commencement of a fever, prevents convulsions; and conversely. We may further imagine that, in children, in whom nervous action of all kinds is notoriously precipitate, the vaso-constriction of rising temperature at the onset of pyrexia develops too suddenly or too widely to permit of adequate compensation, other than by vagus inhibition of the heart-beat: hence the frequency of convulsion in these circumstances in childhood.

We have noted the occurrence of a malarial migraine (§ 374), and of a malarial angina (§ 413). These facts, together with the above considerations, will prepare us for the discovery of a malarial epilepsy. Hobart Amory Hare² refers to cases mentioned by Jacobi, Payne, and Hamilton, and avers that such occur occasionally in the Southern States and in Brazil. ‘In Hamilton’s case a young man, who had lived for many years in an exceedingly malarious region, had more or less periodic epileptic attacks, attended with great preliminary rise of temperature and intense congestion of the face and head. . . . Change of the place of habitation and the use of quinine

¹ *Clinical Medicine*, New Syd. Soc., vol. ii. p. 218.

² *Epilepsy: its Pathology and Treatment*, 1890, p. 92.

removed the disease entirely.' Clearly such epileptic fits are substitutive of malarial rigors.

Recently 'Maraudon de Montyel¹ has investigated the bearing of malaria in epileptics. In fourteen epileptic cases observed, malarial infection was followed by grave results. In some persons epilepsy which had been in abeyance for a long time revived, and in other instances epileptic attacks appeared only after malarial infection. Generally the epileptic attacks appeared in the intervals of the malaria.'

The cardiac results of the intense peripheral vaso-constriction, associated with malaria, is fully recognized by Broadbent, who says :²—' The prominent phenomenon of rigor is general arterial spasm ; and, in the cold stage of malarial fevers, this may be carried to such a degree as to bring the heart to a standstill by the resistance produced. It is from this cause that the cold stage of malignant or remittent fevers is attended with danger of fatal syncope or serious nervous complications.'
(? General convulsions.)

§ 441. SUMMARY OF PATHOLOGY OF EPILEPTIC FITS.—Accepting the pronouncement of Gowers that an epileptic fit implies a sudden discharge of grey matter, I would submit the following propositions :—

1. Such discharge may be due to cerebral anaemia.
2. Such cerebral anaemia may be due to cardiac insufficiency.
3. Such cardiac insufficiency may be compensatory of rapid rise of blood-pressure.
4. Such rapid rise of blood-pressure may be due to extensive vaso-constriction, inadequately compensated by vasodilation.
5. Such extensive vaso-constriction may be a response to hyperpyraemia.

Each of these propositions involves certain important admissions. Taken in inverse order, these admissions are as follows :—

5. The extensive vaso-constriction may be due to humoral factors other than hyperpyraemia, for example to malarial and other toxæmias, asphyxia, etc. ; and to factors other than humoral, for example emotion, such as fright, sudden exposure to cold, etc.

¹ *Rev. de Méd.*, December 10, 1899, referred to in *Medical Annual*, 1901, p. 373.

² *The Pulse*, W. H. Broadbent, 1890, p. 153.

4. The rapid rise of blood-pressure may be due to factors other than vaso-constriction, for example venous obstruction in sudden exertion.
3. The cardiac insufficiency may arise otherwise than as a compensation for rapid rise of blood-pressure, for example, through haemorrhage.
2. Cerebral anaemia may arise otherwise than through cardiac insufficiency, for example through vaso-constriction of some cerebral artery or arteries, as in some cases of minor epilepsy.
1. The sudden discharge of grey matter may be incited by causes other than cerebral anaemia.

My own opinion is that the commonest pathological sequence is hyperpyraemia, but much more frequently relative hyperpyraemia (compare Chapter XIII), peripheral vaso-constriction, and secondary cardiac inhibition: this, at any rate, in the case of major epilepsy and in minor epilepsy associated with loss of consciousness.

THE CONNEXION BETWEEN VASO-MOTOR ACTION AND GLYCOGENIC DISTENSION OF THE LIVER

§ 442. Of the pathological acarbonizing processes already considered, some, like migraine, operate mainly, if not solely, through restriction of income. Anorexia, total cessation of digestion and absorption, vomiting, diarrhoea,—any, or all, of these are liable to be present; and they depend, as has been argued, largely upon the block in the portal circulation which is caused by the glycogenic distension of the liver (§ 257). Now, in migraine at least, the commencement of the digestive revolt is commonly concurrent with the commencement of the cerebral and sensory symptoms, which we have ascribed to exaggerated vaso-motor action. It remains for us, therefore, to connect together the two series of phenomena.

We have seen that, under the ordinary conditions of modern civilized life, absorption from the alimentary canal, though varying in degree at different periods of the day, is continuous throughout (§ 300). This will involve a continuous delivery of glycogen-forming material by the portal vein to the liver and a continuous formation of glycogen by the liver. Under normal conditions, the glycogenic distension

of the liver will be prevented from attaining to pathological dimensions by the continuous escape of hydrated glycogen or sugar from the organ through the hepatic veins. Hence a cessation of the escape of sugar might be sufficient to cause the glycogenic distension of the liver to attain its maximum.

Now such a cessation would imply an increased activity of the sugar-dehydrating or glycogenic function of the liver; and the liver is probably no exception to the general rule that increased functional activity involves an increased supply of arterial blood. Hence, in all probability, the proximate factor of glycogenic distension of the liver will be an increase in the supply of blood through the hepatic artery.

§ 443. Many considerations lend support to this view. If the functional capacity for glycogen-formation is directly dependent on the supply of arterial blood, then anything which diminished the supply would tend to cause glycaemia, perhaps glycosuria; while anything which increased the supply would tend to cause glycogenic distension of the liver.

The supply of blood through the hepatic artery might be diminished by direct interference in laboratory experiments on animals; and Schäfer¹ says that a very appreciable transformation of liver glycogen into sugar occurs as a result of interference with the hepatic circulation.

Apart from direct mechanical interference, the supply of blood might be diminished by vaso-constriction of the hepatic artery itself, or by some widespread or general vaso-dilation of the systemic arterioles (compare § 357). Puncture of the spinal bulb of a well-fed rabbit in the immediate neighbourhood of the vaso-motor centre causes temporary glycosuria; and it seems not improbable that the proximate factor of the increased hydration of liver glycogen implied in this case is a temporary vaso-constriction of the hepatic artery. It is true, as Foster points out, that there is no evidence that the puncture operates by means of vaso-motor action: there is, however, so far as I know, no evidence against such a supposition. And Schäfer² argues that 'in all probability the vaso-motor centre is stimulated by the puncture, for other forms of stimulation of the vaso-motor centre also tend to produce a temporary diabetes, such as prolonged stimulation of most sensory or afferent nerves'; and he thinks it possible, therefore, 'that the

¹ *Text-book of Physiology*, vol. i. p. 925.

² *Ib.* p. 927.

glycaemia is due to the *diminution of the amount of oxygenated blood* passing to the liver through the hepatic artery.' (Italics mine.)

In some cases, stimulation of sensory nerves, such as the sciatic, which usually causes rise of blood-pressure, is associated with glycosuria.¹ In these cases, until we have a demonstration to the contrary, it is open for us to assume that the vaso-constriction, responsible for the rise of blood-pressure, *includes* the hepatic artery, and so with the temporary glycosuria which is known to follow, in some cases, the injection of suprarenal extract or adrenalin.² This drug causes widespread vaso-constriction, and it is open for us to hold provisionally the view that the hepatic is one of the constricted arteries.

§ 444. Widespread vaso-dilation, leading to a fall of general blood-pressure, as already stated, will lead, other things equal, to a diminution of the arterial supply to the liver; and many things, which produce these effects, have been observed to cause temporary glycosuria. Thus, section of the splanchnic nerves causes vaso-dilation of the splanchnic area with consequent great fall of blood-pressure (Leonard Hill);³ and this procedure has, in the hands of Hensen, given rise to glycosuria.⁴ Section of the spinal cord at various levels causes vaso-dilation and flushing of the parts cut off from the vaso-motor centre, with corresponding fall of general blood-pressure (Foster);⁵ and 'section of the spinal cord at various levels' has, in the hands of Schiff, caused glycosuria.⁶ Chloroform anaesthesia causes a fall of blood-pressure of 20 to 40 mm. Hg (Leonard Hill);⁷ and the inhalation of chloroform has been followed by glycosuria (Saundby).⁸ Amyl nitrite causes widespread vaso-dilation and heavy fall of blood-pressure; and 'when nitrite of amyl is given to animals, either by inhalation or hypodermically, sugar appears in the urine' (Lauder Brunton).⁹ Haemorrhage causes rapid fall of blood-pressure; and, after haemorrhage, the amount of sugar in the blood is somewhat increased,

¹ *Text-book of Physiology*, Schäfer, vol. i. p. 925.

² *Progressive Medicine*, June 1903, pp. 320, 321.

³ *Text-book of Physiology*, Schäfer, vol. ii. p. 93.

⁴ *Renal and Urinary Diseases*, Saundby, 1896, p. 226.

⁵ *Text-book of Physiology*, Foster, 1895, p. 322.

⁶ *Renal and Urinary Diseases*, Saundby, 1896, p. 226.

⁷ *Text-book of Physiology*, Schäfer, vol. ii. p. 80.

⁸ *Renal and Urinary Diseases*, Saundby, 1896, p. 229.

⁹ *Pharmacology, Materia Medica, and Therapeutics*, Lauder Brunton, 1885, p. 710.

though the increase is insufficient to give rise to glycosuria. The increased glycaemia after haemorrhage is ascribed by Schäfer¹ 'either to accession of lymph (which contains a larger proportion of sugar than does blood), or to the operation, through the agency of the nervous system, causing an increased production of sugar from the liver glycogen.' From our standpoint it seems improbable that the fall of general blood-pressure and consequent diminution of arterial blood-supply by the hepatic artery are without influence in causing increased hydration of liver glycogen.

§ 445. But there are other conditions, such as physical exercise (§ 731), epileptic fits (§ 744), and pyrexia (§ 738), which are all associated with a fall of blood-pressure, but in which glycosuria is rarely, if ever, observed: indeed, it is well known, as already pointed out, that the first and last of these conditions are capable, in some cases, of dispersing an existing glycosuria (§§ 64 and 271). The reason seems obvious. Doubtless in all these cases there is an increased conversion of liver glycogen into sugar through diminished supply of arterial blood through the hepatic artery; for, as we have seen (§ 68), physical exercise (physiological and pathological) and pyrexia tend to empty the liver of glycogen; 'and Pavy found in his experiments that whenever an animal struggled . . . the quantity of sugar in the blood of the vena cava and carotids was at once increased' (Lauder Brunton).² But both physical exercise and pyrexia are associated with a marked increase in the rate of combustion. Hence the extra sugar so liberated is no doubt rapidly burnt off, and thus glycosuria is avoided. Probably, however, such increase of combustion is at times inadequate; for slight glycosuria has been noticed after epileptic fits in a few cases.

The view that glycosuria may depend upon diminution of the arterial blood-supply through the hepatic artery, secondary to widespread vaso-dilation and low general blood-pressure, receives important support from the well-accredited observation that at least one well-known cause of exaggerated blood-pressure, namely renal cirrhosis, is capable of dispersing glycosuria. Von Noorden says:—'It is interesting and noteworthy that glycosuria very often disappears in patients in

¹ *Text-book of Physiology*, E. A. Schäfer, 1898, vol. i. p. 159.

² *Disorders of Assimilation, Digestion, etc.*, T. Lauder Brunton, 1901, p. 21.

whom granular atrophy of the kidney has developed (Frerichs, Stockvis, Fürbringer). The diabetes is cured, but we do not know the connexion.' This statement of Von Noorden's is quoted and endorsed by Pavy.¹

§ 446. I am well aware that many experiments can be quoted which seem to show that the vascular condition responsible for an increased conversion of hepatic glycogen into sugar is an *increase* of the arterial supply through the hepatic artery.² When direct evidence from the physiological laboratory is conflicting, the clinician can only fall back upon probabilities; and, for many reasons, the latter view seems improbable. The high probability seems to be that the dehydration of sugar into glycogen constitutes the *glycogenic function* of the liver, and that this function demands, as do all functions, an ample supply of arterial blood; further, that the reconversion of glycogen into sugar occurs as a result of a partial *abeyance* of this function, most likely through a restriction of the supply of arterial blood. Otherwise we could hardly account for the rapid reconversion of all the liver glycogen into sugar after death, when function of all kinds ceases. Finally, there is one experiment which demonstrates that dilation of the hepatic artery *alone* has no influence to cause glycosuria. Pavy 'isolated the hepatic artery, portal vein and hepatic duct, and then carefully divided all the remaining structures in the lesser omentum, including therefore the nerves passing to the liver. Notwithstanding that the hepatic nerves had been thus divided . . . no sugar appeared in the urine' (Lauder Brunton).³ Manifestly, division of the hepatic vaso-motor nerves *alone* would cause marked increase in the supply of arterial blood to the liver, since the operation, if carefully performed, would have little influence in reducing the general blood-pressure. It is only when vaso-dilation of the hepatic arteries is associated with some widespread vaso-dilation, such as that which occurs in the splanchnic area, that the consequent fall of general blood-pressure reduces the supply of arterial blood to the liver; and then, as we have seen, glycosuria is apt to arise.

§ 447. The view that an increase in the supply of blood

¹ *Lancet*, November 28, 1903, p. 1496.

² *Diabetes Mellitus*, Williamson, 1898, pp. 66, 67.

³ *On Disorders of Assimilation, Digestion, etc.*, T. Lauder Brunton, 1901 p. 24.

through the hepatic artery is the proximate factor of the glycogenic distension of the liver in migraine, cannot, of course, be supported by direct evidence. It is, however, probable on many grounds, and it is entirely consistent with the vaso-motor phenomena of this affection. We have seen that, with widespread vaso-dilation produced in various ways, there is an exaggerated tendency on the part of the liver to dispose of its store of glycogen, and we have ascribed this to a diminished supply of blood through the hepatic artery. In migraine, on the contrary, there is commonly widespread vaso-constriction and, according to our views, an exaggerated tendency on the part of the liver to the formation and retention of glycogen, this resulting in distension; and we have seen that the vaso-constriction is compensated more or less by internal areas of vaso-dilation. Now in such vaso-dilation the hepatic artery might easily be supposed to share. But, even without active vaso-dilation, the widespread vaso-constriction, unless fully compensated, would materially accelerate the flow of blood through unconstricted arteries, and amongst them through the hepatic artery.

§ 448. What would be true of the glycogenic distension occurring in migraine would be true of that which occurs in the less complex bilious attacks, in some cases of asthma and epilepsy (those associated at each paroxysm with dyspeptic symptoms), and probably of most recurrent affections which achieve a carbonization of the blood by restricting the nutritious income from the alimentary canal. Thus bilious attacks and biliousness generally, recurrent anorexias and dyspepsias, would have a claim to rank as vaso-motor affections. Conformably, William Russell says: ¹—'Take a simple and commonly recognized type of case—the person with good appetite, the hearty and large feeder, who partakes freely of proteid food two or three times a day, and drinks wine, spirit, or malt liquor regularly. When a person of this type gets a "bilious attack," it is well known that his arterial tension is raised; but this arterial tension is usually, probably always, associated with hypertonus.'

It would be true also that the physiological distension of the liver owns a vaso-motor mechanism. While normal digestion and absorption are in full progress, the portal veins contain a bountiful supply of glycogen-forming material, and the circu-

¹ *Brit. Med. Journal*, June 4, 1904, p. 1298.

lation therein is rapid. It is at this time, above most others, that the glycogenic function is essential in order to arrest the sudden intrusion of sugar in quantity into the systemic circulation. Probably, then, there is at this time dilation of the hepatic artery; and the increased supply of arterial blood, so assured, contributes to the condition of physiological congestion of the liver, which is always assumed to be present during digestion. Thus increased *supply* of glycogen-forming material demands increased power of the glycogenic *function*: the former is assured by the *portal veins*, the latter by the *hepatic artery*. It has often been said that a sensation of chilliness after meals is a mark of good digestion. Such chilliness probably depends upon cutaneous vaso-constriction, compensatory of the large splanchnic vaso-dilation inseparable from the process of digestion; and, by maintaining the general blood-pressure, such vaso-constriction would serve to keep up the flow of arterial blood through the hepatic artery, and thus avert hyperglycaemia and glycosuria.

§ 449. If it is true that, when digestion and absorption, and therefore income and accumulation, are in full progress, the glycogenic function of the liver is most essential, then it follows that, during physical exercise, when expenditure is rapid, the glycogenic function of the liver is least essential. Under the former condition, I have argued that the supply of arterial blood is increased: conformably, there are grounds for believing that, under the latter, the supply of arterial blood is diminished. For the effect of physical exercise, as so often pointed out, is to produce general vaso-dilation and fall of blood-pressure, lasting during the exercise, and for some considerable time thereafter. This seems a good example of these marvellous adaptations of variations of blood-pressure, which are constantly occurring in response to variations of functional activity. Functional activity of the muscular system involves rapid expenditure: hence activity of the glycogenic function, which presides over storage or physiological accumulation and over regulation of income, is comparatively in little demand; and the arterial blood-supply is diverted accordingly.

§ 450. The above view of the vascular mechanism of glycogenic distension of the liver would explain an experience of many persons who suffer from recurrent bilious attacks, migraine, etc., namely, that, towards the end of the inter-

paroxysmal period, exposure to cold—which, through causing cutaneous vaso-constriction, tends, other things equal, to increase the flow through internal arteries, and, amongst these, through the hepatic artery—is peculiarly apt to precipitate a paroxysm. It might explain also a highly interesting observation made by Fothergill¹ to the effect that the persistent north-east wind, which prevailed throughout May 1880, ‘found out every person who “had a liver” without respect to persons. Patient after patient at the hospital had to have the plan of treatment arrested for the time, in favour of one adapted to the intercurrent state of liver disturbance. Private patients required the same “change of front.” The east wind finds out the liver, albeit it lies snugly ensconced under the diaphragm and protected by the abdominal walls; and the expression “a bilious chill,” extends from an acute condition, resembling a cold in duration, to a more persisting state.’ All the symptoms, which Fothergill says accompanied these cases, are explicable by glycogenic distension, incited by vaso-dilation of the hepatic artery, correlative of cutaneous vaso-constriction from cold. And it may be mentioned that in India there exists a widespread prejudice against bathing in really cold water on account of the tendency of this practice to cause hepatic congestion.

§ 451. Acute glycogenic distension would manifest itself by some temporary enlargement of the liver; and temporary enlargement of this organ is to be observed at times in connexion with the paroxysms of many of the vaso-motor affections referred to in this and the preceding chapters.

Some hepatic swelling during the ordinary bilious attack will, I think, be generally admitted without special evidence. Duckworth² finds that the liver is commonly somewhat tumid and painful in certain headaches and some forms of migraine. Haig³ has observed ‘marked enlargement of the liver’ during ‘uric acid storms,’ which he regards as identical practically with migraine attacks.

More than one lady has informed me that, during an attack of sick headache, there is distinct increase in the circumference at the waist line, sufficient at times to demand removal of the corset. In some of these, I had an opportunity to make a physical examination, and,

¹ *Indigestion and Biliousness*, 1881, p. 201.

² *Treatise on Gout*, 1890, p. 35.

³ *Uric Acid in Disease*, 1897, pp. 440, 441, 483.

although I was unable to determine hepatic enlargement in one case, yet I assured myself that the increase of girth was real and did not, in this case, depend upon gaseous distension of any of the hollow viscera: I do not think that minor grades of hepatic enlargement are always demonstrable by percussion and palpation. In some other cases, however, the hepatic enlargement was objectively clear: this was so in two cases of typical migraine, in one of gastralgia, and in one of recurrent anorexia.

‘Rendu¹ . . . gives the case of a lady (the subject of asthma) who was liable to severe hepatic crises, apparently congestive, without any vomiting. The attacks were excited by indigestion, by the onset of the catamenia and particularly by moral influences, and were liable to alternate with attacks of diarrhoea, which brought relief rather than distress and a diminution of the hepatic swelling.’ Dr. A. Jefferis Turner has given me the notes of an almost identical case.

A woman, aged 67, otherwise healthy and giving a previous history of good appetite and digestion, suffered from the following irregularly recurrent attacks, which always came on between midnight and early morning. The first symptom was a curious sensation in the chest: soon after severe dyspnoea, apparently asthmatic, with wheezing and retro-sternal pain: a few minutes later, vomiting and purging. Each attack lasted a half to two hours, and was accompanied by cold feet and cold perspiration. Dr. Turner examined her *shortly after* an attack. He found the liver projecting two fingers’ breadth below the costal margin and slightly tender to pressure: a pulse of 80, rather high tension: various dyspeptic manifestations and obstinate constipation. She was ordered a small aperient dose of calomel twice weekly, and her carbonaceous intake was considerably restricted. Five weeks later the attacks, which had occurred three times in the ten days before commencing treatment, had not recurred.

Such cases are explicable on the view that they depend upon hyperpyraemia and are hybrid conservative acarbonizing processes. The pathological mechanism would include extensive vaso-constriction, vaso-dilation of the bronchial and perhaps adjoining areas, dilation of the hepatic artery, glycogenic distension of the liver, and mechanical congestion of the portal venous system: the cutaneous anaemia, asthma, retrosternal pain, vomiting and purging would be the clinical manifestations; and acarbonization of the blood would be attained partly by increased katabolic expenditure, partly by diminished income.

¹ *Gout and Goutiness*, Ewart, 1896, p. 225.

A similar combination of acarbonizing measures, similarly explicable, is to be observed in some cases of epilepsy. Voisin and Petit¹ 'lay great stress on the occurrence of gastric troubles before, and during, the fits or series of fits, but if the series is coming to an end, then the tongue clears, and the gastric symptoms subside: if the gastric symptoms do not subside, the epileptic phenomena will continue.' We may, I think, read these valuable observations as follows:—When the acarbonizing convulsions have succeeded in dispersing the hyperpyraemia, then, and not until then, will the glycogenic distension of the liver subside, and the secondary dyspeptic manifestations, dependent thereon, disappear.

§ 452. It has been argued that pathological distension of the liver by glycogen implies deficiency, if not absence, of bile, gastric, pancreatic and intestinal juices from the alimentary canal (§ 73). Such a condition is probably amongst the chief proximate factors of retarded digestion; and retarded digestion, under the thermal, microbic and other conditions obtaining in the intestine, will lead naturally to the development of putrefactive processes. These, indeed, have been observed and investigated by Herter and Smith; and the horribly foetid dejecta which, Haig² points out, are 'often met with after an attack of dyspepsia, bilious attack,' etc., thus receive a simple explanation.

§ 453. The above view of the mechanism of the anorexia and dyspepsia of migraine and other vaso-motor acarbonizing processes, which operate solely or mainly by restriction of income, leads us to some further deductions. Believing as we do that the digestive revolt is the salutary or conservative portion of the paroxysm, we must regard the other vaso-motor manifestations which are without acarbonizing influence, for example the headache of migraine and the abdominal pain of gastralgia, as unnecessary complexities of vaso-motor action, except, of course, in so far as they imply compensation for vaso-constriction. We are encouraged in this by observing that paroxysms of recurrent anorexia and dyspepsia, affections probably identical with migraine minus the head complications, are as salutary in their effects as the more complex paroxysms; and

¹ Haig, in *Uric Acid in Disease*, 1897, p. 227, referring to *Archives de Neurologie*, 1895, Nos. 98, 99, 100 et seq.

² *Uric Acid in Disease*, 1897, p. 217.

it has been argued that 'expensiveness,' or want of accurate adaptation, is a feature characteristic of most pathological conservative actions.

Again, if it is true that physiological glycogenic distension of the liver is adapted to regulate the carbon contents of the blood, then, in the pathology of all affections which operate by means of a pathological degree of glycogenic distension, we must include a certain inefficiency of physiological distension: we must regard the intermittent and conspicuous, as substitutive of the remittent and inconspicuous, hepatic regulation of the nutritious income.

A PHYSIOLOGICAL MODEL OF THE PAROXYSMAL NEUROSES: MECHANISM OF MENSTRUATION

§ 454. The physiological—or, as it has been termed, semi-physiological—process of menstruation, is truly analogous to the paroxysmal neuroses. Just as they do in most cases, it depends upon a progressively increasing accumulation of carbonaceous material in the blood; and, like most of them, it is a recurrent acarbonizing process. In its mechanism, it is closely related. The affinity of mechanism between migraine and menstruation was clearly perceived by Möllendorff. Having argued that the explanation of the phenomena of migraine must be sought in a morbid condition of the ganglionic system of nerves, he suggests that 'the¹ phenomena of menstruation must themselves be regarded . . . as the result of a similar disposition of the sympathetic and the consequent dilation and repletion of the uterine vessels.' It will not, I think, be difficult to prove the truth of this suggestion; but the affinity of migraine to menstruation will be no closer than that of asthma, and but one step more close than that of epilepsy.

As already argued, the mechanism of the paroxysmal neuroses consists essentially of a widespread vaso-constriction, more or less compensated by localized areas of vaso-dilation, or by cardiac modification. The same is true of menstruation.

§ 455. Of this process, Hermann says:²—'There is increased vascular tension everywhere. . . . According to Giles,

¹ *Megrim and Sick-headache*, Liveing, 1878, p. 308.

² *Diseases of Women*, p. 517.

the increased vascular tension is greatest on the day preceding, and the first two days of, menstruation.' James Mackenzie¹ says that increased arterial pressure 'may take place normally with the recurrence of the menstrual period. The evidence is most obvious immediately before the discharge begins, and relief usually follows once the discharge is freely established.' 'Broadbent² has remarked that the pulse is often slow and of high tension in menstruation.' 'Barnes's³ well-known case of hernia of the left ovary, in which the sphygmograph, applied to the left ovary, showed a high blood-pressure preceding menstruation, has been frequently referred to.' And Oliver⁴ finds that, during the menstrual period, the calibre of arteries, as exemplified by the radial, ceases to respond to changes of position: he regards this phenomenon as due to transitory vaso-constriction, and compares it to the condition often found in the gouty and in migraine.

That the extensive vaso-constriction, responsible for the rise of blood-pressure, affects the cutaneous, amongst other, areas, seems evident by the subjective and objective cutaneous symptoms. There is distinct chilliness, and the skin tends to be cold to the touch, anaemic, dry, and a little shrivelled, presenting accentuations of lines and wrinkles.

The compensatory vaso-dilation of menstruation is not far to seek: it affects the uterus at any rate, probably the other internal and the external organs of generation, and possibly the pelvic organs generally to some extent. The vascular distension so caused is the proximate factor of the sense of weight in the pelvis and inguinal regions, of the dull sacral pain, and of the characteristic sanguineous discharge.

§ 456. On the view that menstruation is a periodic haemorrhagic decarbonizing process, depending on an intermenstrual accumulation of carbonaceous material in the blood, it is impossible to imagine any device better adapted to the purpose than are the vascular changes which, I am arguing, constitute the mechanism of menstruation. The combination of widespread vaso-constriction with pelvic vaso-dilation results inevitably in vascular distension of the dilated area; and since a portion of this area consists of a free mucous surface, the

¹ *The Study of the Pulse*, 1902, p. 71.

² *Uric Acid in Disease*, Haig, 1897, p. 260.

³ Dr. Helen MacMurchy, *Lancet*, October 5, 1901.

⁴ *Brit. Med. Journal*, 1896, vol. i. p. 1375.

tissues of which are newly formed, soft and highly vascularized, haemorrhage is the natural result. Further, such haemorrhage will reduce, proximately through diminution of the amount of blood in circulation, and more remotely through decarbonization, the exalted blood-pressure upon which the haemorrhage immediately depends. So the loss will bring itself to a natural termination and restore the vascular system and the blood to the normal intermenstrual condition.

§ 457. Clearly, the menstrual process is essentially similar in its mechanism to paroxysmal neuroses such as migraine, asthma, and gastralgia. Superficially, it differs therefrom in its invariable termination in haemorrhage. But this difference obviously depends upon the anatomical features of the tissue affected by the vaso-dilation; for most, if not all, paroxysmal neuroses are liable to terminate in haemorrhage, whenever the vaso-dilation encroaches upon a mucous membrane. For example, in migraine associated with vaso-dilation of the nasal mucosa, epistaxis¹ is not infrequent: in asthma, in which affection a comparatively non-vascular and non-erectile mucosa is the part always affected, haemoptysis² is rare, but it may occur and in amount proportionate to the severity of the dyspnoea, that is, to the intensity of the vascular distension; and in paroxysmal gastralgia, in which, as we shall see, the vaso-dilation, at least in some cases, encroaches upon the gastric mucosa, profuse haematemesis³ is by no means infrequent.

More commonly, of course, the vascular distension resulting from the vaso-dilation of the paroxysmal neuroses is not relieved by haemorrhage, but terminates with the production of the symptoms peculiar to each neurosis. The menstrual parallel to such non-haemorrhagic paroxysmal neuroses is found in certain cases of dysmenorrhoea. In these, the pain may be inversely proportionate to the haemorrhage. It must be ascribed to an anatomical condition of the distended area, similar to that of the migrainous distended area, with this difference, unimportant from our present standpoint, that the anatomical condition, in such cases of dysmenorrhoea, must be regarded as pathological. Thus either anything which, at the onset of the menstrual vaso-dilation, prevents the natural swelling

¹ *Megrin and Sick-headache*, Liveing, 1873, pp. 325, 326.

² *On Asthma*, Hyde Salter, 1868, p. 371.

³ Bertrand Dawson, *Brit. Med. Journal*, November 29, 1902, p. 1709.

of the internal generative organs, such for example as old adhesions binding down the ovaries and tubes, or anything which interferes with the escape of exuded blood from the uterus, such as flexions or stricture, will intensify nerve-pressure and cause exaggeration of the menstrual pain, which, in some slight degree, may perhaps be regarded as physiological. This is without prejudice to the dysmenorrhoea which is due to painful contractions of the uterus.

The fundamental similarity of menstruation to the paroxysmal neuroses is further exemplified in the tendency to the restriction of income through glycogenic distension of the liver which so frequently announces the process (§§ 93 and 168) : it will be still further exemplified when we come to consider the relation of blood-pressure to the urinary excretion of water, uric acid, and urea (§§ 757 to 768).

§ 458. CONFIRMATORY CLINICAL OBSERVATIONS.—The vasomotor theory of menstruation just propounded is entirely consistent with, and fully explanatory of, a long series of recorded clinical observations. Further, it leads up to what seem to me some entirely new observations, some of which are highly important from the standpoint of practical therapeutics.

The most prominent *symptoms* of menstruation readily fall into line. Widespread vaso-constriction, conspicuous in, but not necessarily limited to, the cutaneous area, fully accounts, as we have seen, for the condition of the skin. Compensatory vaso-dilation, most marked in, but not restricted to, the pelvic area, accounts for the symptoms referable to the ovaries, uterus, and other pelvic organs. Inadequate compensation for the former by the latter vascular condition explains the high blood-pressure; and this, in turn, explains a long series of phenomena.

The retardation of the pulse during menstruation may be regarded, under Marey's law, as a cardiac compensation for the rise of blood-pressure. Increased diuresis, pointed out by Dr. Helen McMurchy¹ as common at the menstrual period, may also be explained by the rise of blood-pressure (compare § 757).

Amongst the symptoms of pathological high blood-pressure Broadbent² lays special stress upon headache, insomnia, mental depression, irritability, vertigo, loss of energy, and neuralgia. This list is practically identical with the list which

¹ *Lancet*, October 5, 1901.

² *The Pulse*, 1890, pp. 176, 177.

Dr. Helen McMurchy,¹ from the study of 100 cases, gives of the commonest symptoms attending menstruation. The coincidence is far too complete to be fortuitous; and the obvious inference is that the symptoms, in both cases, depend upon the vascular condition, or upon the humoral condition responsible for the vascular condition (compare § 168 and § 730).

§ 459. In some of the paroxysmal neuroses (migraine, gastralgia, now and then asthma and epilepsy), I have argued that the widespread vaso-motor action, which is the essential feature of the attack, extends its influence to the hepatic artery, causing this to dilate and so operating on the liver as to lead to glycogenic distension (§§ 442 *et seq.*). The vaso-motor action associated with menstruation would seem to have a similar tendency; for many of the presumed symptoms of glycogenic distension, such as anorexia, dyspepsia, biliousness, diarrhoea, haemorrhoidal distension, or haemorrhage, are, as we have seen (§ 163), recurrent, in different cases, at each menstrual period.

We have admitted that the compensatory vaso-dilation of menstruation is not necessarily limited to the pelvic area; and amongst the numerous symptoms associated frequently, or occasionally, with this process, are many which point to a more than usual degree of vascular distension in various localities. Some of these are probably best explained by an active vaso-dilation of the arteries supplying the distended part. Amongst these, are the commonly noticed mammary and thyroid swellings, and the rarely occurring laryngeal congestion and oedema. Concerning the latter, Niel² says that, in some cases at the outset of the menstrual flow as well as in adult life and at the menopause, there is liable to arise spasm of the glottis due to a violent congestion of the vocal cords and the whole larynx, and usually associated with intense congestion of the post-nasal pharynx. This, however, is transient—it usually lasts but a few minutes, disappearing as rapidly as it comes. In adult life, these vocal disturbances usually come on *at the time for the flow to make its appearance*, even when menstruation is regular and in the absence of any pathological condition of the uro-genital tract.

§ 460. The menstrual incidence of the paroxysmal neuroses

¹ *Lancet*, October 5, 1901.

² *American Year-book of Medicine and Surgery: Surgery*, 1903, p. 457, quoted from *Gaz. de Gyn.*, February 15, 1902.

has been referred to (§§ 315 to 319) and explained by the tendency to hyperpyraemia, which is normally recurrent at the commencement of the menstrual epoch. But it is equally explicable upon a vascular, as upon a humoral, view. The paroxysmal neuroses depend upon extensive peripheral vaso-constriction, and their menstrual incidence is explained by the periodic peripheral vaso-constriction, which is responsible for the exalted blood-pressure of menstruation: hence the attacks occur chiefly upon the day on which menstruation is impending or commencing, at the time when, according to Mackenzie (§ 455), the blood-pressure attains its highest point. Later in the period, when, as Mackenzie points out, the flow has succeeded in reducing the blood-pressure, neurosal attacks of all kinds are much less frequent; and the fact that the blood-pressure falls, when the flow has become well established, is consistent with the well-authenticated fact that checked menstruation (or failure of the flow to appear from causes other than absence of the carbonaceous surplus) has a greatly exaggerated tendency to precipitate paroxysms.¹ We may regard the areas of vaso-dilation, peculiar to paroxysmal neuroses, such as migraine, asthma, angina, gastralgia, etc., when these occur at the menstrual period, as supplementary to the pelvic vaso-dilation of menstruation. The apparent superfluity of explanation herein involved is due to the fact that, in all the cases referred to, the vascular is secondary to, that is depends upon, the humoral condition.

For the explanation of some other instances of vascular distension during menstruation, it would probably be sufficient to assume an absence of the protective vaso-constriction locally in the presence of general high blood-pressure. Amongst phenomena so explicable are recurrent monthly nasal hyperaemia graduating into overt coryza,² congestion of

¹ The following extraordinary case may be regarded as illustrating, more clearly perhaps than a less common case, the dependence of convulsions upon hyperpyraemic vaso-motor action, pending the establishment of decarbonization through uterine haemorrhage (precocious incidental menstruation). Dr. William Frew found a female infant, one day after birth, suffering from slight general convulsions. 'The temperature in the rectum was normal, but the surface of the body and especially of the face, hands, and feet, was cold.' Convulsive twitching continued in modified degree until the afternoon of the third day after birth. Then a haemorrhagic vaginal discharge appeared and lasted three days. Concurrently, the nervous phenomena gradually subsided and ceased altogether with the cessation of the flow. The infant remained healthy; nor did the haemorrhage recur. *British Medical Journal*, June 21, 1902.

² Dr. H. McMurchy, *Lancet*, October 5, 1901.

the dental pulp,¹ and haemorrhages from the external ear, throat, and upper part of oesophagus,² not to mention innumerable varieties of 'supplementary' haemorrhage,³ determined by organic lesion in various parts of the body: in no case, however, can we exclude localized active vaso-dilation.

§ 461. The influence of exercise and pyrexia in diminishing the menstrual flow has been explained on the ground that all three are acarbonizing agents (§§ 181 and 275). But their influence could be explained also by the fact that all three tend to cause vaso-dilation and fall of blood-pressure. Here again the apparent superfluity of explanation is due to the fact that the vascular is secondary to, that is depends upon, the humoral condition. The fact that the onset of pyrexia is apt to precipitate menstruation has been referred to and explained (§ 275).

We have seen that emotion operates upon the asthmatic in ways which are seemingly contradictory; and we have explained this by the different vaso-motor effects of emotion—effects which vary with the nature of the emotion and with the individual (§ 397). Emotion is liable to produce similarly divergent effects upon the menstrual process, checking the flow in some cases, precipitating it in others; and the explanation, in both cases, is doubtless to be found in the divergent vaso-motor manifestations of emotion.

§ 462. Heat and cold may operate upon the menstrual process in a manner exactly parallel to their action upon migraine, asthma, angina, and other vaso-motor affections. General hot bathing causes vaso-dilation of the whole cutaneous area, and from enquiries which I have made I find that during immersion the menstrual flow is distinctly reduced, the reduction persisting for some few hours thereafter. I confess that until lately I was under the impression that a general hot bath had the opposite influence.

Arguing from the vaso-motor theory of menstruation and from the influence of general hot bathing, general cold bathing should exaggerate the flow. Is this deduction consistent with fact? Women, as a rule, avoid cold bathing during menstruation, a practice which is dictated by fear of checking the flow. Of course, cold locally applied, as in a cold vaginal douche, would

¹ *Rev. Méd.-chir. des Mal. de Femmes*, December, 1891.

² Dr. H. McMurehy, *Lancet*, October 5, 1901.

³ *Menstruation and its Disorders*, Giles, 1901, p. 76.

tend to induce pelvic vaso-constriction, and thus to check the flow. The result here would be analogous to the relief of the asthmatic dyspnoea by the inhalation of cold air, or to the relief of headache by an ice-cap. Further, it might be that cold applied to the neighbourhood of the perinaeum and pubes would be sufficient, and it is well known that getting the feet wet and cold may terminate a period. But no such partial application of cold is fairly comparable with general cold bathing, which must cause general cutaneous vaso-constriction and thereby, *other conditions remaining unchanged*, increase the vascular distension of the uterine mucosa. On arriving at this deduction, I instituted a series of enquiries amongst healthy adult women as to the effects of general cold bathing during menstruation; and I obtained the following results:—

The majority, believing that cold bathing during menstruation is dangerous, had systematically avoided it and substituted warm or tepid water at their menstrual periods. Some had discovered, accidentally in the first instance, that no bad result followed cold bathing during menstruation, and had continued the practice. Three of these had noticed that general cold bathing tended to increase the flow. And one, a very stout girl of 25, whose periods—as so often happens with stout women—were habitually scanty and infrequent, took general cold baths *only during the menstrual periods*. This she did with the avowed intention of increasing the flow. Although in her case I could find no evidence that she suffered in any way from deficient menstruation, yet she imagined that she was the better for menstruating more freely; and her experience was that cold bathing both increased and prolonged the flow. She informed me that, whenever she omitted the bathing, the loss was a mere trace and lasted but one day. I came across no instance in this series in which general cold bathing had arrested the flow.

Nevertheless, I should be loth to deny that, in some cases, general cold bathing is capable of checking menstruation. In making this admission, it must be pointed out that the influence of a general cold bath is complex. The procedure can hardly be dissociated from shock, and shock, however induced, is capable of checking menstruation. And there is also the power of suggestion to be considered. These conflicting influences are probably sufficient to account for divergent effects of hot and cold bathing upon the menstrual process in different women. Tilt says: ¹—‘A hot bath will stop the menstrual

¹ *Uterine Therapeutics*, 1878, Tilt, pp. 252, 253.

flow in some women in whom it is made more abundant by putting the feet in cold water';—I am inclined to think that this is more the rule than the exception—and he points out that Dr. Chapman regarded ice-bags to the lumbar spine as the best emmenagogue.

A priori, an efficient means of reinducing the menstrual flow, which had been checked by shock, emotion, chill, or other pathological influence, would be the administration of a hot vaginal douche while the patient is fully immersed in a cold bath. Thus artificially we should intensify the power of the normal machinery of the process. Such a measure would be the reverse of the combinations of general heat and local cold, which, we have seen, are successful in relieving the paroxysms of migraine and asthma.

§ 463. Perhaps the clearest evidence of the indispensability to the menstrual process of peripheral vaso-constriction is to be found in the swift and definite influence of amyl nitrite. The inhalation of a single capsule during menstruation results in a sudden diminution in the amount of the flow, a diminution which may persist for some time. Indeed, there is no small danger of stopping the flow altogether.

In the case of a young lady, who suffered from anginal seizures limited for the most part to the first two days of the menstrual period, amyl nitrite never failed to give instant relief from the cardiac pain; but the use of the drug had to be abandoned because it invariably terminated abruptly the menstrual flow, with the further unfortunate result that the number of succeeding anginal paroxysms was greatly increased.

Amyl nitrite is stated to give great relief in the dysmenorrhoea which depends upon uterine spasm.¹ The inference seems to be that the drug operates by causing relaxation of the uterine muscular fibre. But, as already stated (§ 393), there is no evidence to show that the nitrites, in medicinal doses, act upon muscular fibre other than that which constitutes the middle coat of arteries. In any case, however, the above inference is unnecessary. For there can be little doubt that there are at least two varieties of dysmenorrhoea, namely (1) that which depends upon vascular distension of the sensitive structures of the internal generative organs, inadequately relieved by the flow of blood *into* the uterus, and (2) that

¹ *Practical Therapeutics*, H. A. Hare, 1900, p. 72.

which depends upon uterine contractions, incited to secure discharge of blood *out* of the uterus. Now amyl nitrite admittedly relaxes the peripheral vaso-constriction, and thereby reduces the pelvic vascular distension, of menstruation: it tends, so to speak, to reverse the whole vaso-motor machinery of the process. The reduction of the pelvic vascular distension will relieve directly the pain of the first variety of dysmenorrhoea, and indirectly, through diminution of the blood-flow into the uterine cavity, the pain of the second variety. Conformably, it will be found in many cases of dysmenorrhoea—those which palpably do not, as well as those which presumably do, depend upon uterine spasm—that amyl nitrite affords marked temporary relief. Theilhaber¹ has recently pointed out that, in some cases, dysmenorrhoeal pain is most severe from twelve to twenty-four hours before the flow appears and abates somewhat thereafter. In such cases, at least, it is reasonable to refer the pain directly to the vascular distension; and in one such, which came under my notice, amyl nitrite never failed to give instant relief.

Not alone the nitrites, but anything which is capable of promoting vascular relaxation elsewhere, will reduce the pelvic vascular distension, and thereby relieve dysmenorrhoeal pain dependent thereon. Dry cupping over the loins, hot hip and general baths, and hot alcoholic drinks, have all been used more or less effectively: hot gin and water is a well-known—probably a too well-known—household remedy. But, as elsewhere pointed out, alcohol has a twofold action, increasing the force of the heart-beat as well as dilating the arterial channels. Hence we should expect to find in some cases, that alcohol would exaggerate dysmenorrhoeal pain. This is certainly rare but I know of one case in which this result was invariable.

§ 464. It is obvious that the nitrites, and measures which operate similarly in dysmenorrhoea, deal with an effect only,—with the vaso-motor effect of the inter-menstrual carbonaceous accumulation in the blood. This, in some cases, may be regarded as excessive relatively to the discharging capacity of the menstrual mechanism. At any rate, it is certain that some cases of dysmenorrhoea may be successfully treated by restricting the amount of the carbonaceous accumulation

¹ *Centralbl. f. Gynäk.*, 1902, No. 3, referred to in *American Year-book of Medicine and Surgery*, 1903: *Surgery*, p. 459.

between the periods, and so modifying the violence of the vasomotor action to which this accumulation gives rise. The accumulation may be restricted by decreasing the carbonaceous income to the blood, by increasing the carbonaceous expenditure by the blood, or by a combination of these means. The carbonaceous income may be restricted by diminishing the carbonizing functions, as by reducing the proteid of a mixed diet, or by diminishing the carbonaceous intake, as by largely cutting down the starches, sugars, and fats of a mixed diet. I have frequently seen the latter plan reduce in a material degree the amount of the menstrual flow, and at the same time relieve dysmenorrhoea in some cases. The carbonaceous expenditure of the blood may be increased by pyrexia and physical exercise. During pyrexia of any duration, as we have seen (§ 275), the menstrual flow is diminished, often abolished, and dysmenorrhoea is relieved or ceases: both these results have followed in several cases which were under treatment by seton for other affections (Case LVI). The salutary influence upon some cases of dysmenorrhoea, menorrhagia, and the *symptoms of menstruation* generally, of systematic physical exercise between the periods can hardly be over-estimated.

§ 465. THE FULL MEANING OF MENSTRUATION.—We are now, I think, in a position to formulate a complete view of the meaning and mechanism of the menstrual process. During the inter-menstrual period, there is, as we have seen (§ 159), a reconstruction of the uterine mucosa. These local anabolic changes are now generally admitted to be a preparation on the part of the uterus for the special function of utero-gestation. They may be regarded from two distinct, though correlated, points of view: (1) as an erection of the scaffolding necessary for the building of the foetus; and (2) as an early manifestation of that variation of metabolism whereby katabolic is in part replaced by anabolic decarbonization.

Concurrently with the provision of the necessary scaffolding, there is also the provision of a part of the necessary supplies. This consists, as already argued (§ 159), in a gradual accumulation of carbonaceous material in the blood. We have explained the absence of any nitrogenous accumulation on the grounds that storage of nitrogenous material is inconsistent with the policy of the organism (§§ 5 and 11).

But the supplies so provided will have to be conducted to

the site of the function, the uterus. This is readily effected through an alteration of vascular balance. There occurs an increase of peripheral vaso-constriction in wide areas, associated with, and to some extent compensated by, a localized pelvic vaso-dilation. By this means, the blood, containing the supply of raw material, is to some extent shut off from areas where it is less needed, and delivered more rapidly and in greater quantity at the site of the superadded function—on the building site, so to speak. Similar variations of vascular balance doubtless occur, whenever function of any kind, katabolic or anabolic, is in exaggerated operation.

All is now in readiness for the anabolic function of utero-gestation; and the further course of events will depend altogether upon whether conception has or has not taken place—upon the more or less incidental factor of impregnation.

Assuming conception to have occurred, the increased carbonaceous supply delivered at the uterus through the increased blood-supply is utilized in the anabolism of the growing foetus. The peripheral vaso-constriction, which is an essential part of the mechanism of the increased blood-supply, involves some degree of high blood-pressure; and this continues, probably increases progressively through increased cardiac action, and passes into the well-recognized physiological high blood-pressure of pregnancy (compare § 736).

On the other hand, conception may not have occurred. In this event, the preparations for utero-gestation, both of function and supply—of scaffolding and part of the building material—will require demolition and clearance. Now instruments for such demolition and clearance (destruction and excretion) are ready to hand: they seem identical with those which are utilized in the construction and accretion of utero-gestation, and consist in the alterations of vascular balance whereby the increase of blood-supply to the uterus is secured.

Towards the end of the inter-menstrual period, there is an increase of blood-pressure, due no doubt to an increase of peripheral vaso-constriction: this, according to Mackenzie, attains its maximum immediately before the flow commences. As a result, there will be a marked increase of the vascular distension or congestion of the uterine mucosa. This will not be relieved by consumption of the increased blood-supply by anabolism, as happens when conception has occurred.

Consequently, the vascular distension will increase until it leads to rupture of the newly formed vessels of the uterine mucosa.

This immediately pre-menstrual congestion is referred to by Giles, who says :¹—‘The mucosa is first highly congested. . . . Then dark-red spots appear, due to the formation of lacunæ in the superficial parts of the stroma under the epithelium ; soon the epithelium gives way, and free blood is found in the uterine cavity, derived from the ruptured lacunæ. The surface epithelium is cast off, with portions of the stroma and of the glandular epithelium, and the *débris* is carried away with the blood or forms clots, which are found at first on the inner surface of the uterus, and become gradually disintegrated or are discharged whole. The destructive process is now finished, and the uterus enters on the period of recuperation in the post-menstrual week.’

Thus the normal menstrual flow involves the demolition, in part at least, of the scaffolding erected in anticipation of the building of the foetus. It is also a hæmorrhagic decarbonizing process, whereby the inter-menstrual carbonaceous accumulation is finally dispersed ; and the peripheral vaso-constriction, with consequent rise of blood-pressure, so far from being a mere symptom of menstruation, is an essential factor in the process. The mechanism of menstruation is largely identical with the mechanism of utero-gestation ; and the process must be regarded as a result of the failure of conception.

But the vascular changes, though essential to the menstrual flow, can hardly be regarded as absolutely essential to the demolition and clearance of the uterine scaffolding : they can only, I think, be regarded as normally concurrent therewith and perhaps as, in great part, advantageous thereto. This seems to be shown by the occurrence of cases such as the following² :—

A girl of 15, after once menstruating in the ordinary way, began to suffer at regular intervals of a month from bleeding at the nose : this occurred two or three times a day, for three successive days, and it was attended with malaise and other symptoms like those which had attended the natural flux. She became pregnant and the hæmorrhage then ceased, to return six weeks after delivery. (Obermeier, vol. iv., Virchow’s ‘Archiv.’)

The above case suggests very strongly that the uterine

¹ *Menstruation and its Disorders*, A. E. Giles, 1901, pp. 13, 14.

² Referred to in Fagge’s *Text-book of Medicine*, 1891, vol. i. pp. 1132, 1133.

scaffolding may be demolished and cleared in the complete absence of haemorrhage from the uterine mucosa. If this suggestion is correct, then we may have to conclude that the vascular variations resulting in vascular distension of the uterine mucosa are not essential to the destruction and clearance of the uterine scaffolding, but only to the discharge of the accumulated carbonaceous supply. The case also demonstrates that normal menstruation is more than a mere 'expression of rhythmic preparations of the uterus for pregnancy' (compare § 671).

On the view here adopted, the menstrual flow has but an indirect connexion with ovulation: the flow depends primarily upon the metabolic variation introduced by the evolution of ovarian activity at puberty (§ 159), secondarily upon the resulting carbonaceous accumulation, and proximately upon the eventuating alteration of vascular balance.

CHAPTER XII

§§ 466–509

Some less common paroxysmal neuroses—Periodic or recurrent gastralgia : its dependence on hyperpyraemia : mechanism—Some neuralgias : priority of vaso-motor action : evidence of hyperpyraemia : malarial neuralgia—Raynaud's disease : a vaso-motor neurosis : its dependence in some cases on hyperpyraemia—Recurrent oculo-motor and other paralyses—Recurrent temporary amblyopia : malarial cases—Hydrops articulorum intermittens—Paroxysmal vertigo—Atypical affections—Mechanism of the paroxysmal neuroses collocated and correlated.

§ 466. If we admit the priority of vaso-motor action in the neuroses, migraine, asthma, angina, and epilepsy, we must be prepared to extend this conception over a much wider territory. For many recurrent affections, usually regarded as largely nervous, some of which have been incidentally referred to and others as yet unmentioned, are as intimately allied to the above-named four affections as these four affections are to each other. The former, equally with the latter, are capable of mutual replacement, and they may be mitigated and aggravated by the same measures which would mitigate and aggravate the vaso-motor disorder, upon which their manifestations presumably depend. Many of them, moreover, can be shown to depend upon hyperpyraemia, which, we have seen, is so common a cause of ultra-physiological vaso-motor action ; but they can only be regarded, for the most part, as attempts at acarbonization.

This extended relationship has been perceived more or less clearly by many authors. Quite recently, Goodhart compares together paroxysmal sneezing, asthma, and Raynaud's disease. He says :¹—‘ All three are probably due to allied causes ; and although in all three the results are of different order . . . yet the clinical history in all of these is not unlike.’

¹ *System of Medicine*, by T. Clifford Allbutt, vol. v. p. 291.

PERIODIC OR RECURRENT GASTRALGIA

§ 467. This affection, as already pointed out, is, in its typical forms, an efficient acarbonizing process (§ 261).

ITS DEPENDENCE ON HYPERPYRAEMIA.—That it is, in some cases at least, a manifestation of hyperpyraemia, is probable on many grounds. It is mainly a nocturnal complaint: Graves says of a case: ¹—‘Most usually the attacks commence several hours after he has been asleep, and awake him at one, two, or three o’clock in the morning’: this is the period when combustion stands at its lowest, and when, consequently, hyperpyraemia is highly probable. The attacks in women are very frequently menstrual, and they are especially liable to occur in cases of checked or delayed menstruation. Mr. John R. Pollocks² describes an extremely severe attack of menstrual gastralgia.

Gastralgia has frequently been observed to replace, and be replaced by, most of the other neurosal affections already considered. Clifford Allbutt says: ³—‘Of associated affections, migraine is by far the commonest; and if we associate migraine and neuralgia of the head and face together, the number of cases in which these are found with gastralgia is very great, seeming to be fully 80 per cent. . . . Another disorder, commonly associated with gastralgia, is asthma, an observation which scarcely needs either explanation or much asseveration. . . . With both the vagus neuroses run the cardiac neuroses, including true angina.’

In a case of mine, the patient, aged 36, had suffered for many years from migraine, recurring as often as once a week: four years before I saw him, there had been an interval of three or four months, during which his head ceased to trouble him: during this interval, however, he had three or four extremely violent attacks of gastralgia: at the end of this period, the headaches returned, and thenceforward he remained free from all gastralgic symptoms (Case XLVIII).

In another case, long-standing periodic gastralgia ended by becoming almost continuous, the patient, a girl of 19, becoming extremely emaciated and falling into a state of anorexia nervosa. A three months’ course of Weir-Mitchell treatment, *minus over-feeding for some weeks*, was finally successful in removing all morbid mani-

¹ *Clinical Medicine*, vol. ii. p. 240.

² *Brit. Med. Journal*, August 15, 1903, p. 361.

³ *Neuroses of the Viscera*, Clifford Allbutt, *Lancet*, vol. i. 1884, p. 507.

festations; but, during early convalescence, the gastralgic attacks were replaced by regularly recurrent painless bilious attacks for a period of eight weeks (Case XLVII).

§ 468. MECHANISM.—Everything goes to show that this affection is a vaso-motor affection—that, in its essential mechanism, it is similar to migraine, asthma, angina, etc., and depends upon an extensive area of vaso-constriction, associated with, and compensated wholly or in part by, a more or less localized area of vaso-dilation. Conformably with this view and with the proved existence of malarial migraine, malarial angina, and malarial epilepsy, Roberts says of gastralgia: ¹—‘Occasionally it results from the action of malaria.’

Clinical evidence of cutaneous vaso-constriction seems ample. As with the other paroxysmal neuroses, the attacks are often precipitated by conditions which are capable of promoting vaso-constriction of the skin, such as external cold, ‘anxiety, alarm, anger, etc.’ ² (Graves). Clifford Allbutt says: ³—‘The intensity . . . of most severe cases of gastro-enteralgia may be seen in the ashen cold face and blue nails.’ The implication in this sentence is that the condition of the skin results from the pain; but, on the vaso-motor theory we are adopting, we must invert this order and ascribe the pain indirectly to the cutaneous vaso-constriction, directly to the compensation for the vaso-constriction. In the case of a medical man, described by Liveing, ⁴ the attacks were always accompanied by chilliness and cold extremities, and most relief was obtained from remedies which combat cutaneous vaso-constriction, such as turpentine fomentations and a full dose of hot brandy and water. In three of my own cases, the chilliness of the surface was marked: in two of these, it amounted to a rigor; and, in one of these latter, to a very severe rigor with chattering of the teeth. All these patients resorted to heat externally in the shape of hot blankets, hot bottles, etc.: in each case, some relief from the pain was experienced; but in none did the pain entirely cease until the chilliness of the surface had been entirely overcome. We have seen parallel occurrences in migraine and asthma (§§ 361 and 393). I have found amyl nitrite an extremely useful emergency

¹ *Theory and Practice of Medicine*, Fred. Roberts, 1883, p. 578.

² *Clinical Medicine*, Graves, vol. ii. p. 239.

³ ‘Neuroses of the Viscera,’ *Lancet*, vol. i. 1884, p. 512.

⁴ *Megrim and Sick-headache*, 1873, pp. 213, 214.

drug in gastralgia : in the first case in which Dr. Hawkes tried it, the gastric pain had been nearly constant for about a week, and instant relief, lasting two hours, followed the inhalation of one capsule.

It is of course not always possible to locate the site of the internal vaso-dilation, nor to assert that it is constant in all cases. The character of the pain, described as 'peculiarly visceral . . . of the quality produced by a blow on the epigastrium or testicle,'¹ suggests the neighbourhood of the solar plexus. But, in at least one of my cases (the one last mentioned in whom rigor was severe), it seems certain that the gastric mucosa participated in, if it did not monopolize, the vaso-dilation.

The patient, a man of 38, had suffered for years from recurrent gastralgia. At one period in his history, the attacks were remarkably uniform in their recurrence and in their characteristic features : they came on at almost exactly 2 A.M., every third Monday. They were not due to food in the stomach, since the last meal was always a small one and was taken at 5.30 P.M. on Sunday : the patient, an habitually active man, himself ascribed them to the absence of exercise on Sunday. The attacks were always associated with violent retching, and on one occasion he vomited, according to his wife's statement, about two pints of pure blood. This gave instant relief from pain : after this particular attack, the patient seemed to convalesce more rapidly and more completely than on other occasions ; and the ensuing interval of freedom lasted five, instead of the usual three, weeks.

§ 469. The vaso-motor theory we are adopting in this, as in the other paroxysmal neuroses already discussed, prepares us for the occurrence of haematemesis in gastralgia—an event truly analogous to the occurrence of ecchymoses, epistaxis, and cerebral haemorrhage in migraine and of haemoptysis in asthma. This form of haemorrhage is recognized clinically. Dr. Bertrand Dawson,² in opening a discussion on the Pathology, Prognosis, and Treatment of Haematemesis, refers to cases simulating gastric ulcer, as 'haemorrhagic gastralgia' presumably due to nervous disturbance. 'It was impossible to diagnose these cases from gastric ulcer, although certain indications, including a hyperacidity in ulcer, were useful . . . Dr. Hale White considered that at the bedside gastric ulcer

¹ *Megrin and Sick-headache*, Liveing, 1873, p. 213.

² *British Medical Journal*, November 29, 1902, p. 1709.

was diagnosed far more often in women than in men, in the proportion of 5 to 1; and in women 50 per cent. of the cases occurred in early life, probably from including cases of another disease. The mortality of gastric ulcer was greater in men than in women. The explanation was that, in the cases in women, the haematemesis was not due to gastric ulcer alone. The stomach had been opened on account of haematemesis without any ulcer being found, but merely oozing; similarly, at necropsies no source for the haematemesis had in some cases been found; in six of such cases specified, all the patients were women. Differentiating this disease from gastric ulcer, were the age, sex, long duration, little wasting, and the occurrence of cases of good health. Periodicity, whether menstrual or other, would not exclude ulcer, since hyperpyraemia, whether menstrual or other, may be periodic, may manifest itself by high blood-pressure, and thus lead to bleeding from an ulcer.

‘Dr. Essex Wynter¹ . . . had been struck with the fact that 80 per cent. of cases of haematemesis occurred in young women with scarcely a death, and that the fatal cases occurred equally in men and women, and at a later age. Evidence of healed lesions in the stomach was very rarely met with at necropsies on general cases. This was an argument against many of the cases of haematemesis being due to gastric ulcer.’

It seems highly probable that some of the cases here referred to were cases of vaso-motory gastralgia in which the area of vaso-dilation largely affected the gastric mucosa. This view receives strong support from actual observations of the bleeding surface made during gastrotomy. Mayo Robson describes two cases in which he operated, both in young women. Concerning the first, he says:²—‘I counted no less than seven bleeding points. As two of them were bleeding freely, I took them up by artery forceps and ligatured the mucous membrane *en masse*: the other points stopped on exposure to air.’ Concerning the second, he says:—‘I opened the stomach and carefully explored the interior, when, though I could find no evidence of any large ulcer, I found a considerable number of bleeding points, three of which I ligatured *en masse*, afterwards swabbing the whole of the interior of the stomach with a sponge saturated with tincture of hamamelis.’

¹ *Brit. Med. Journal*, November 29, 1902, p. 1710.

² *Lancet*, December 13, 1902, p. 1627.

It is significant that no ulceration was found in either case, nor does the author state that he observed any signs of even superficial erosion. It is true some of those who took part in the subsequent discussion seemed to assume that a commencing erosion, indistinguishable by the naked eye, is the anatomical cause of the bleeding in such cases. But this seems highly improbable on many grounds. The history of the cases is that of *sudden profuse* haematemesis, and exploration showed, as just stated, *numerous* bleeding-points. If we believe that a process of microscopic ulceration or erosion is the essential cause of the bleeding, we must believe also that in each individual lesion the erosive process attained the haemorrhagic stage, by perforating the walls of some small blood-vessel, simultaneously; which is hardly conceivable. Therefore it seems to me that the erosion hypothesis falls to the ground. On the other hand, a sudden intense vaso-dilation of the gastric mucosa, compensatory of, and intensified by, an extensive area of vaso-constriction, such as occurs in gastralgic paroxysms, and assisted perhaps by some nutritional weakness of the vascular tissues, would fully explain all the phenomena in such cases: the pain would of course be obviated or cut short by the haemorrhage, as in the case of migrainous epistaxis.

§ 470. If this view proves to be correct, then the indication for treatment in the emergency of this variety of haematemesis will be clear, namely, the relief of vascular distension in the dilated gastric area. This may be accomplished in two ways: (1) by promoting vaso-dilation generally, especially in the extensive constricted areas of the skin; and (2) by promoting vaso-constriction locally in the dilated gastric area. We should probably attain our object most effectually by proceeding in both ways. The cutaneous area is readily accessible to treatment: it may be dilated by heat to the surface generally, as in hot-air or vapour baths, or by amyl nitrite. Vaso-constriction of the gastric mucosa may be attained simultaneously by cold directly applied, as by the administration of ice pills. Theoretically, adrenalin would be contra-indicated, since it has a general as well as a local influence and promotes general vaso-constriction. It is, however, readily conceivable that the local action of this drug might preponderate over its general action, in which case it would prove a useful haemostatic in such cases.

§ 471. If the mechanism of gastralgia is such as we are assuming it to be, it follows that the emergency treatment suggested for gastralgic haemorrhage will be applicable for the relief of pain in non-haemorrhagic cases; and the rationale of such relief will be identical with that of the relief of the headache of migraine and of the dyspnoea of asthma by the same combination of heat, applied to the general surface, with cold applied locally to the distended vascular areas (§§ 360 and 394). Furthermore, the principle involved in all such hydrotherapeutic procedures brings up for reconsideration the whole question of the non-operative treatment of internal haemorrhage. The idea that internal haemorrhage may depend upon peripheral vaso-constriction as well as upon localized vaso-dilation is not, I imagine, widely entertained. Hence very often we are apt to be content with the application of ice *to the surface of the body* in the neighbourhood of the bleeding point, in cases in which its direct application is impossible. But, on the vaso-motor theory, the promotion of cutaneous vaso-dilation, whether by heat, the nitrites, or other agents, will be a therapeutic indication scarcely, if at all, less important than the promotion of vaso-constriction in the bleeding area (compare §§ 676 *et seq.*).

§ 472. It would appear that, in gastralgia, as in migraine, asthma, and angina pectoris, the vaso-dilation may be inadequate to compensate for the widespread vaso-constriction which occurs. Hence cardiac inhibition is demanded; and slowing of the pulse has been observed in many cases¹ (Liveing).

SOME NEURALGIAS

§ 473. PRIORITY OF VASO-MOTOR ACTION.—From long observation of two typical cases of trigeminal neuralgia, in one of which he removed the greater part of the Gasserian ganglion with complete symptomatic cure, and from a review of the numerous and divergent therapeutic measures, operative and other, which have proved successful in the hands of others, Dr. Hawkes argues² that the manifestations of this complaint do not depend on an ascending neuritis of the fifth nerve or on an interstitial inflammation of the ganglion, but upon disordered

¹ *Megrin and Sick-headache*, Liveing, 1873, pp. 214, 217, 238, 330.

² *The Mechanism of Trigeminal Neuralgia*, C. S. Hawkes, *Australasian Medical Gazette*, November 20, 1903, pp. 498, 499.

vaso-motor action. He points out that, while they might be held to explain the microscopic changes usually found in the ganglion and the cessation of pain after removal thereof, neuritic theories cannot explain the paroxysmal nature of the pain, the increase of radial constriction, which in both of his cases preceded or accompanied each paroxysm of pain, the flushing at the site of pain, the lachrymation, salivation, and nasal discharge, or the fact 'that the usual pain areas do not coincide with the areas of distribution of the fifth nerve,' but correspond accurately with the area of distribution of the accompanying arteries—an area which is relatively small. He further points out that on no theory of this affection other than the vaso-motor theory can we explain the curative influence of excision of the superior cervical ganglion of the sympathetic of the corresponding side—an operation which he proposes to adopt in future cases.

§ 474. An extremely lean woman, aged 50, under my care, affected with very chronic fibroid phthisis, suffers from a great variety of neuralgic affections. Her radial pulse shows habitual high blood-pressure. At different times, she suffers from unilateral facial neuralgia, brachio-cephalic neuralgia, neuralgia of the pubes and urethra, and from typical, though mild, anginal paroxysms. These diverse neuralgias alternate: they never concur. The facial variety is often associated with involuntary muscular twitchings of the painful area, commencing in the orbicularis palpebrarum, but extending to the rest of the corresponding half of the face: the urethral variety is associated with intense dysuria. All the varieties, except the angina, are associated with visible cutaneous vaso-dilation at the seat of pain; and all of them, without any exception, are associated with distinct tightening of the radial and with considerable cutaneous anaemia of most non-painful cutaneous areas. Finally, anything which is capable of promoting widespread vaso-dilation gives instant relief in all the affections named. All of them are relieved by amyl nitrite, though this is apt to leave a continuous dull headache for some hours: all of them are benefited by nitro-glycerine in frequent small doses, though this has also some corresponding disadvantages; and all of them are promptly, though temporarily, dispersed by the application to the surface of the body of hot fomentations, provided that these are sufficiently hot, cover a sufficient area,

and are *not applied directly to the hyperaemic and painful part*. Thus, at various times, the application to the chest, back, and front of hot, moist, or dry flannels has given immediate relief from the hemifacial pain, and the hemifacial convulsions: angina has ceased instantaneously in the same circumstances; and so have the pubic and urethral neuralgia and the dysuria. Synchronously with the cessation of the pain in each case, the flushing of the painful area becomes less sharply defined, and the radial artery resumes its habitual volume or becomes larger and softer than before the attack.

The case above described is unique in my experience, but unique only through the extreme diversity of the neuralgic manifestations. On the other hand, I have notes of numerous cases in which neuralgia is associated both with vaso-dilation and flushing of the skin over the site of pain and with synchronous constriction of the radial and more or less extensive cutaneous anaemia: in all the cases, immediate relief, though not always complete, has been attained by some or all of the above-mentioned therapeutic measures. In such, it seems impossible to avoid the conclusion that the mechanism of the pain is essentially vaso-motor.

§ 475. While I would not be understood as claiming a vaso-motor mechanism for the pain of all seemingly idiopathic neuralgias, yet I am driven to confess that, the more I consider this possibility, the larger becomes the number of cases in which this explanation seems the only satisfactory one.

Thus Anstie says¹ that a 'characteristic of neuralgic patients in general is . . . a certain mobility of the vaso-motor nervous system and of the cardiac motor nerves. . . . Within my own experience it has always seemed to be the case that persons who are liable to neuralgia are specially prone to sudden changes of vascular tension under emotional and other influences which operate strongly on the nervous system. . . . The commencement of pain is generally preceded by paleness of skin and sensations of chilliness. At the commencement of the painful paroxysm, sphygmographic observation shows that the arterial tension is much increased, owing in all probability to spasm of the small vessels.'

Conditions which are liable to be associated with cutaneous vaso-constriction are amongst the commonest exciting factors

¹ *Neuralgia and its Counterfeits*, 1871, pp. 10, 11.

of neuralgia. Fright is usually so associated, and through this association has been explained the undoubted influence of fright to initiate recurrent epilepsy and to precipitate asthmatic and anginal seizures. But fright may initiate recurrent neuralgia: Anstie¹ mentions a case in which a single fright was accompanied by a neuralgic paroxysm of the ilio-inguinal region, which thereafter continued to recur with regular daily periodicity; and Gowers² refers to a case in which violent facial neuralgia, recurrent for five years, was undoubtedly due to the fright induced by the unexpected discharge of a gun. Cold, it will be admitted, is the commonest of all causes of vaso-constriction of the skin; and Gowers says:³—‘No single actual excitant of neuralgia is so frequent as exposure to cold, sometimes general, sometimes local and affecting the part in which the neuralgia is felt. Valleix found a history of exposure to cold in one-third of his cases. Cold may not only produce neuralgia but may also excite paroxysms of pain when the neuralgia is due to some other cause. . . . In some cases there is a remarkable sensitiveness to atmospheric influences.’

§ 476. Anstie⁴ has called attention to the graduation, in the course of time, of typical migraine into facial neuralgia; and it is highly improbable that the latter affection differs fundamentally in its mechanism from the former. Again, as we have seen above and as may be seen throughout Anstie’s masterly monograph, neuralgias of widely differing distribution are apt to alternate with, or complicate, typical angina pectoris, gastralgia, and other essentially vaso-motor affections.

The actual site of the vascular distension responsible for the pain of neuralgia doubtless varies in different cases. It may be that, in some, the site is the central sensory centre or some ganglion subordinate thereto, though the first seems highly improbable to me: it may be that, in others, the site is extra-neural, the vascular distension operating by compressing the sensory nerves or nerve terminations; but I cannot doubt that, in many, the site is the trunk of the sensory, or mixed sensory and motor, nerve itself. Only on the last view can we explain the well-known phenomena of the painful and tender points pointed out by Valleix.

¹ *Neuralgia and its Counterfeits*, 1871, p. 45.

² *Dis. Nerv. System*, 1893, vol. ii. p. 797.

³ *Ib.* pp. 797, 799.

⁴ *Neuralgia and its Counterfeits*, 1871, p. 121.

These are extremely numerous, but they are, for the most part, unvarying in their exact localization. On the face and head, the most important are the supra-orbital and infra-orbital, the nasal, malar, temporal, inferior dental and parietal: on the trunk and limbs, the points are numerous and almost equally constant. But, wherever situated, they correspond as a rule 'to the place at which a nerve-trunk emerges from a bony canal, passes over a hard structure, or passes through a fascia to become superficial' ¹ (Gowers). The history of these points in a case of neuralgia is, according to Anstie,² that at first they are *the site of the most acute pain during the neuralgic paroxysm*; later, and in inveterate cases they become acutely sensitive to pressure *at all times*. On the vaso-motor theory, vascular distension from vaso-dilation will tend to cause swelling of the nerve-trunk: this will be resisted by the surrounding or adjoining inextensible tissues of the bony or fascial foramina or of the subjacent bony prominences; and so there will be, in these situations, a maximum of nerve pressure and pain. The mechanism of the pain will be as simple as, and identical with, the pain experienced on pressure of the ulnar nerve against the internal condyle of the humerus. In both instances, the pain felt locally will be due to pressure on the *nervi nervorum*: the pain felt in the peripheral distribution of the nerve will be due to pressure on the main fibres of the nerve in their continuity. On the same vaso-motor and mechanical view, the subsequent development of tenderness 'in those situations which have been the foci or severest points of the neuralgic pain' ³ is readily explicable; for frequently recurring pressure on nervous tissues will naturally lead to permanent irritative or inflammatory changes. I cannot see that it is possible to explain the full history of these painful and tender points on the view, so commonly held by neurologists, that the vaso-motor phenomena of neuralgia are secondary and incidental.

§ 477. The local so-called complications of neuralgia may, for the most part, be regarded as due, directly or remotely, to localized vaso-dilation affecting the nerve trunk or the nearly adjoining tissues. So may be explained the following, which are amongst those referred to by Anstie: ⁴—Diffused soreness of the

¹ *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 800.

² *Neuralgia and its Counterparts*, 1871, p. 10.

³ *Ib.* p. 10.

⁴ *Ib.* chap. ii.

scalp, due to temporary skin congestion : congestion of conjunctiva to a deep crimson : intensely red congestion of the nostril of the affected side : decided unilateral redness of the face, often attended with noticeable tumefaction : flushing and diffuse tenderness of the calf in sciatica : profuse lachrymation : copious thin nasal flux on the affected side, sometimes, however, semi-purulent or bloody : increased salivation : tonic or clonic convulsions of muscles of the affected area, as of the face in trigeminal neuralgia, of the leg in sciatica : iritis, glaucoma, corneal cloudiness or even ulceration, herpes unilateralis : localized hypertrophies of tissues, such as the hair, epithelium of the tongue, the periosteum surrounding bony foramina, and fascia similarly situated : increased pigmentation of skin near painful part, at first recurrent, later more or less permanent : acute erysipeloid inflammation of the skin, with fiery, brawny induration and *vesiculation*, following the distribution of the affected nerve, but extending beyond these confines, it may be, to the whole corresponding half of the face and head : and many more. It is not so easy, perhaps, to explain localized impairments of function, such as localized paralyses and patches of anaesthesia, or atrophic changes, such as patches of grey hair. It may be of course that, in some cases, the vascular distension is sufficiently intense to cause pressure paralyses, motor or sensory ; and that in others frequent over-stimulation by localized plethora tends to ultimate atrophy. But local atrophic changes (excluding grey hair and atrophies resulting from disuse) seem far less frequent than local hypertrophies.

It may be objected that many of the above ' complications ' are found only in cases in which there is distinct neuritis. This may be admitted ; but I shall argue presently that there is no sharp line of demarcation between the vascular distension or active hyperaemia, due to vaso-dilation, and inflammation, and that, consequently, neuralgic affections tend to graduate into neuritis.

§ 478. The view that the pain of ' idiopathic ' neuralgia depends proximately upon vascular distension of the nerve-trunk affected is consistent with the following clinical observations. 1. ' The pain is seldom referred to the skin : usually it is more deeply seated and often corresponds to the position of the nerve-trunk and its branches ' ¹ (Gowers). 2. Slight pressure

¹ *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 798.

over an affected nerve-trunk increases the pain : firm pressure thereon gives distinct relief¹ (Gowers). 3. 'Compression of the carotid occasionally cuts short an attack of pain, and the repetition of this treatment, continued for a long time, has even produced permanent alleviation'² (Gowers) : in my experience, compression of the carotid on the affected side in unilateral facial neuralgia, as in unilateral migraine, has always resulted in cessation of the pain during the continuance of the compression ; and the removal of the pressure has been followed by immediate recommencement of the pain. In obstinate neuralgias of the head, Trousseau practised division of the temporal and occipital arteries with considerable success. Of one case he says :³—'The neuralgia ceased as soon as the section (of the temporal) was made. . . . The neuralgia was cured for a rather long period, and, although it returned subsequently, I still regard the case as a very successful one. Division of the occipital artery is not less efficacious in the treatment of neuralgia seated in the posterior region of the head ; and it is often found necessary to divide both arteries.' Trousseau could not account for the suddenness of the relief which followed these operations. He says :—'I am well aware that these vessels, especially the occipital, are accompanied by nervous twigs of some importance ; but although I understand how the pain ceases in parts supplied by nerves included in the section, I cannot understand the complete cessation of pain in the greater number of nerve-twigs, which a moment before caused such acute pain, and which have no apparent connexion with the cut branches.' On the view of priority of vaso-motor action, such difficulties vanish ; and it is easy to see why the pain should reappear when the collateral circulation has become fully established. 4. 'In one patient intense fronto-occipital neuralgic pain was excited by every act of defaecation'⁴ (Gowers) ; like all other forms of sudden exertion, defaecation causes a sudden rise of blood-pressure and thus increases vascular distension. I should be surprised to learn that the passage of quite loose motions in the above case precipitated neuralgic attacks. 5. 'In some cases alcohol, even in small quantities, invariably intensifies or induces the

¹ *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 799.

² *Ib.* pp. 831, 832.

³ *Clinical Medicine*, New Syd. Soc., Trousseau, vol. i. p. 510.

⁴ *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 799, footnote.

pain: in other cases, it gives relief'¹ (Gowers); this accords with the varying twofold action of alcohol already referred to (§ 366), whereby migraine, dysmenorrhoea (§ 463), and other affections depending on vascular distension, are in some cases exacerbated, in others relieved.

'Two² classes of neuralgias have been distinguished,—“symptomatic,” in which the pain is a symptom of organic disease of the nerves; and “idiopathic,” in which the malady, in the first instance at least, consists only in functional disturbance. . . . But the distinction of the two forms of nerve-pain is often very difficult in practice' (Gowers). Now the view here adopted largely diminishes the necessity for, as well as the value of, such distinction. Frequently recurring, still more a condition of chronic, vascular distension, will lead eventually in the case of the nervous, as of other, tissues, to irritative or sub-inflammatory changes. This anticipation is entirely consistent with the clinical observation that in many cases neuralgic paroxysms, at first clearly intermittent and presenting intervals during which no trace of tenderness or enlargement can be detected, graduate ultimately into more or less continuous neuralgic conditions, associated with chronic tenderness and some enlargement of the nerve-trunk.

In the case of a gentleman of 55 suffering from sciatica of some years' standing, there can be no doubt that the condition of the nerve at present is one of neuritis. But the history of the case makes it inconceivable that this was so primarily. For, long before the neuralgia 'settled down' into the sciatic nerve, this patient had suffered from alternating neuralgias of widely different distributions, amongst which were several attacks of sciatica of sudden onset, short duration, and complete and rapid subsidence.

In such cases, the inference is that the neuritic condition of the nerve-trunk results from the frequent recurrence or persistence of the factors responsible for the neuralgic pain. Fothergill³ refers to the graduation of functional sciatica into neuritis of the sciatic nerve, quoting Fuller in support.

§ 479. A similar argument may be applied to the Gasserian ganglion in some cases of severe trigeminal neuralgia. 'Dr. Sidney Schwab⁴ gives an account of the systematic study of six Gasserian ganglia which had at various times been

¹ *Dis. Nerv. System*, Gowers, 1893, vol. ii. p. 799.

² *Ib.* p. 795.

³ *Gout in its Protean Aspects*, 1883, p. 86. ⁴ *Lancet*, April 4, 1903, p. 980.

excised in cases of severe and intractable facial neuralgia. . . . The complete disappearance of the symptoms of neuralgia, when the ganglion was removed, or when the root which connected it with the brain was divided, showed that the ganglion was the seat of the disease. . . . All the specimens were fixed and hardened while fresh, and sections were prepared according to the latest methods, including Nissl's and Held's, which are in use for revealing changes in the nerve-cells and nerve tissues generally. Complete serial sections were made of every ganglion parallel to the largest diameter. . . . The nerve-cells in the ganglia exhibited in all cases signs and changes indicative of prolonged irritation and over-stimulation, in some respects closely resembling the appearances produced (artificially) by electric stimulation for several hours. . . . The nerve-cells in the peripheral parts of the Gasserian ganglion showed changes varying from a slight degree of chromatolysis to profound changes of total cell disintegration and nuclear migration. In three of the six ganglia pigmentation was observed around the nuclei of the nerve-cells. This pigmentation was so different in character and distribution from that present in normal conditions, that it would be regarded. . . as a deviation from the normal. In one of the ganglia a sclerosis of the tissue with excess of fibrous formation was found.'

It seems to me that the above are just the morbid appearances which we should expect to find in a nervous structure which had been the seat of repeated or prolonged vascular distension; and if so, then the structural changes must be regarded, not as causative of, but as owing a common factor with, the recurring pain. At any rate, the structural changes are clearly not essential; for 'Head states that a ganglion he examined "showed nerve-cells so perfect that they could be used as a standard specimen of the normal staining of the ganglion."' ¹

Against the peripheral origin of the pain of idiopathic neuralgia implied in the vaso-motor theory, may be advanced the radiation of pain into adjoining areas. But in no form of neuralgic pain is radiation more common and more widespread than in the pain due to the obviously peripheral cause, a

¹ *The Mechanism of Trigeminal Neuralgia* C. S. Hawkes, *Australasian Medical Gazette*, November 20, 1903, p. 498.

carious tooth. Salter says¹ that 'pains in the shoulder and acromion, over the insertion of the deltoid, or at the bend of the elbow, not infrequently depend on this cause; and he cites the case of a lady who, whenever any of the teeth in the left side of the lower jaw became tender from caries, was immediately attacked with severe neuralgia at a circumscribed spot in the forearm.'

§ 480. EVIDENCE OF HYPERPYRAEMIA.—That the pathological vaso-motor action, which, in many cases, constitutes the mechanism of neuralgic paroxysms, is often incited by the humoral condition of hyperpyraemia, there seems ample evidence. This can, however, be only briefly stated here.

Pathological conditions commonly associated with hyperpyraemia are amongst the commonest causes of neuralgia. 'Over-work of mind or body, over-lactation, prolonged fatigue, and anaemia of every degree and causation, are frequently met with as its immediate antecedents.'² (Compare §§ 322, 309, and 233.) The post-pyrexial stage may induce it (compare § 104): Gowers says:³—'Neuralgia is an occasional sequel of various acute diseases which depress the nervous system, but it follows none so often as influenza.' Neuralgia is a frequent expression of those constitutional states known as lithaemia, the gouty diathesis, irregular or abarticular gout, conditions which, I shall argue, depend upon hyperpyraemia (§ 858). It is also common in plumbism⁴ (Gowers).

§ 481. Neuralgic paroxysms are peculiarly apt to arise or recur at such times or periods as, according to this argument, hyperpyraemia is most liable to be present. In many cases, the paroxysm commences some hours after the patient has been asleep and wakes him at one, two, or three in the morning: Graves⁵ adduced this peculiarity in the case of gastralgic paroxysms, as evidence of their neuralgic nature. Gowers says:—'The pain may be worse at the catamenial periods, and may even occur only at those times'; and there can be no doubt that checked menstruation, from any accidental cause, greatly intensifies this tendency to monthly exacerbation, and may even initiate attacks. Neuralgia⁶ 'is rare before puberty.'

¹ *Text-book of Medicine*, Fagge, 1891, vol. i. p. 389.

² *Dis. Nerv. System*, 1893, vol. ii. p. 796.

³ *Ib.* p. 797.

⁴ *Ib.* p. 817.

⁵ *Megrin and Sick-headache*, Liveing, 1873, p. 202.

⁶ *Dis. Nerv. System*, 1893, vol. ii. p. 795.

Puberty in the female, as already argued, is more likely to become associated with hyperpyraemia than in the male (§ 174): hence probably, though 'women are more prone to neuralgia than men . . . the excess of females among the sufferers disappears in the second half of life.'¹ At the menopause, we have inferred a special liability to hyperpyraemia; and Tilt says:²—During the change of life, 497 neuralgic affections were divided amongst 500 women, some taking more than their share, but this . . . gives no idea of the endless variety of neuralgic affections that may be met with in the upper classes of society.'

§ 482. Many neuralgias may be observed to disappear under increased acarbonization of the blood, physiological, pathological, or therapeutic. Increased formation and deposition of fat concurs with convalescence from neuralgic conditions frequently: pyrexias of all kinds commonly disperse neuralgias for the time being: of 'gouty' neuralgia, Gowers says:³—'The pain may disappear when an attack of acute gout is developed.' Dr. Samuel S. Wallian⁴ treated 13 cases of neuralgia by oxygen inhalation: 6 were cured or fully relieved: 3 sensibly relieved; and 4 little or not at all relieved. He also treated 6 cases of sciatica in the same way: 3 were cured or fully relieved: 1 sensibly relieved; and 2 little or not at all relieved.

The alternation of neuralgias of the most diverse distributions with the formal paroxysmal neuroses, migraine, angina pectoris, asthma, epilepsy, etc., and with numerous other manifestations of hyperpyraemia, is in itself strong evidence of the hyperpyraemic origin of neuralgia in many cases (for instances of such alternation, see Liveing's monograph on Megrin and Sick-headache). The frequent alternation with the first two named disorders led Anstie to classify both as neuralgias, a classification which now seems amply justified, whether we consider their humoral causation or their mechanism.

§ 483. Finally, by far the most generally successful non-operative treatment for most 'idiopathic' neuralgias consists, in my experience, of a hygienic and dietetic management adapted to preclude hyperpyraemia. This may be attained by

¹ *Dis. Nerv. System*, 1893, vol. ii. p. 795. ² *Change of Life*, 1882, p. 211.

³ *Dis. Nerv. System*, 1893, vol. ii. p. 816.

⁴ *Oxygen and other Gases in Medicine and Surgery*, pub. F. A. Davis, 1889, p. 240.

increasing the decarbonizing functions, katabolic and anabolic, of the tissues by a due supply of proteid, by the enforcement of physical exercise short of fatigue, by residence in a suitably cool or cold climate, and by carefully graduating the carbonaceous intake in accordance with the decarbonizing capacities of the tissues for the time being.

Gowers says : ¹— ‘ I have known severe neuralgia to occur first on the patient commencing a purely vegetable diet, to disappear when meat was taken, and recur with severity at each of four successive attempts to return to vegetarianism.’

A medical student, reading hard for examination and taking practically no exercise, commenced to suffer from severe occipital neuralgia, starting each day before dawn and persisting until the late afternoon. He used spectacles, for which his eyes had been carefully measured by an ophthalmologist (this was in the eighties, however) : his teeth were put in good order ; and he tried a great variety of drugs and combinations of drugs. Becoming disheartened at obtaining no relief, he determined to experiment upon himself. Having been obliged to pay great attention to economy, his diet had consisted in the main of carbohydrates, meat having formed a small part of only one of his three daily meals. He had heard that ‘ pain is the prayer of a nerve for healthy blood.’ Acting on this view, he took a fair-sized beefsteak thrice daily. Four days later, the neuralgia, which had recurred each day for five or six weeks, ceased absolutely and did not return. No other change in his habits or conditions of life had been made. He ceased to use his glasses.

§ 484. MALARIAL NEURALGIA.—The adoption of the vasomotor theory of neuralgia enables us to understand the relation of neuralgia to malaria, just as it has enabled us to understand the relation of migraine, angina, epilepsy, and gastralgia to malaria (§§ 374, 413, 440, and 468) : in all cases, the relations are of mechanism, and the various neurosal paroxysms are modifications of the malarial rigor, perhaps in some degree substitutive thereof.

In malarial rigor, there is, at the commencement and throughout the cold stage, extreme general cutaneous anaemia : this is necessarily associated with vaso-dilation of the muscular layer ; later, as the vaso-dilation extends to the skin, the rigor gradually moderates and finally ceases. Of

¹ *Diseases of the Nervous System*, 1893, vol. ii. p. 824.

two cases of malarial neuralgia, Anstie says :¹— ‘A semi-algide condition always ushered in the attacks’: coincidentally, ‘there was unilateral flushing of the face and congestion of the conjunctiva to a slight degree’:² later, the semi-algide condition ‘was gradually exchanged . . . for a condition in which the pulse was . . . compressible,’³ and ‘the pain became duller and more diffused contemporaneously with the lowering of the arterial pressure,’⁴ that is, of course, with the generalization of the vaso-dilation.

Of ‘a case of extremely severe intercostal neuralgia of a perfectly periodic type occurring in a patient whose constitution has been thoroughly saturated with tropical marsh-poison, and in whom the spleen was still much enlarged,’ Anstie says :⁵— ‘The neuralgia was so terrible, and accompanied by such severe algide phenomena at the beginning of the attacks, and such a sense of throbbing as the pain developed, as to lead to serious suspicions of hepatic abscess, for the moment; but the course of events soon corrected this idea.’

Dr. Labbé (‘Journal des Praticiens,’ February 9, 1901, p. 90)⁶ says that ‘malarial neuralgia has a particular evolution which distinguishes it from neuralgia due to other causes. . . . It does not appear as a simple complication added to the ordinary symptoms of malarial infection, but acts as a *substitute for these symptoms and replaces the attack of fever.*’ He relates an illustrative case in which ‘from the day the facial neuralgia appeared the febrile attacks disappeared completely.’ During the attacks, ‘the affected side of the face becomes red and hot and covered with sweat. The eye becomes closed, congested, and filled with tears, and the slightest touch on the face causes severe pain.’ (The italics in the above quotation are mine.)

RAYNAUD’S DISEASE

§ 485. A VASO-MOTOR NEUROSIS.—This affection is already classed by most authors as a vaso-motor neurosis. Vaso-constriction which, we have seen, is essential in the commoner affections of the class, is here generally admitted to be the proximate factor of the most conspicuous of the pathological

¹ *Neuralgia and its Counterfeits*, 1871, p. 19.

² *Ib.*

³ *Ib.*

⁴ *Ib.*

⁵ *Ib.*

⁶ Quoted in *Med. Review*, May 1901, p. 291.

manifestations peculiar to the disease. It is more or less general over the surface, as shown by Raynaud himself, but is intensified in certain parts of the extremities, the distribution of the intensified constriction varying with the individual case. It is not, however, limited to the surface and the extremities: Raynaud refers to cases in which 'narrowing of the arteries of the fundus oculi is clearly seen'¹ concurrently with the most intense degree of vascular spasm of the extremities.

Vaso-motor action will explain many of the affinities of Raynaud's disease. Thus 'in a few cases the subject of Raynaud's disease is liable to headaches, which may resemble attacks of *migraine*'² (Munro): 'epilepsy is not uncommon'³ (Munro): Cleman records the case of a man who, after suffering for years from local asphyxia with occasional attacks of gangrene, was seized with *angina pectoris*,⁴ which was apparently the cause of his death. We have noted the relations of migraine, angina pectoris, epilepsy, gastralgia, and neuralgia to malaria (§§ 374, 413, 440, 468, and 484). A similar relation may be traced in the case of Raynaud's disease: in one case 'it seemed to Calmette'⁵ that the attack of arterial spasm in the extremities, occurring, as it did, daily between 2 and 2.30 P.M., replaced the ordinary febrile attack': in another, recorded by the same observer,⁶ the attacks of fever coincided with attacks of local asphyxia, which did not occur except at that time. I have seen symmetrical gangrene of the toes caused apparently by the action of the cold bath in the later stages of typhoid fever; and minor grades of local syncope and local asphyxia are not uncommon in cases treated by this method.⁷

§ 486. ITS DEPENDENCE IN SOME CASES ON HYPERPYRAEMIA.—It would seem that anything which is capable of causing extreme vaso-constriction may, in certain circumstances, give rise to Raynaud's phenomena; and if so, then we shall have to include hyperpyraemia. There is a certain amount of evidence which renders it probable that this blood-state is responsible for some cases at least. The association of Raynaud's disease with the formal paroxysmal neuroses, themselves amongst the most common manifestations of hyperpyraemia, is in itself important evidence. Further than this,

¹ *Raynaud's New Researches*, New Syd. Soc., p. 165.

² *Raynaud's Disease*, T. Munro, 1899, p. 153.

³ *Ib.* p. 129.

⁴ *Ib.* p. 130.

⁵ *Ib.* p. 49.

⁶ *Ib.* p. 50.

⁷ *The Cold Bath Treatment of Typhoid Fever*, F. E. Hare, p. 89.

conditions liable to cause hyperpyraemia are liable to cause Raynaud's disease; and conditions which can disperse hyperpyraemia may relieve Raynaud's disease. Raynaud says: ¹—'The only well-marked exciting cause has in several instances in women appeared to be the suppression of the menses; and on the other hand, we have seen considerable improvement, or even complete cure, coincide with the re-establishment of that function.' Raynaud refers ² also to an extraordinary case, in which gangrene occurred 'each month in a young woman, aged 23 years, at the extremities of the fingers, ears, nose, etc.' The disease may apparently arise from plumbism ³ (Sainton), which, I have argued, leads to hyperpyraemia and to so many hyperpyraemic manifestations. 'It may follow specific fevers, such as measles, or measles and whooping-cough together, typhus, enteric, influenza, diphtheria, and perhaps pneumonia and even erysipelas' ⁴ (Munro). Hutchinson ⁵ says it may occur in gouty subjects (compare Chapter XIV), and Munro, ⁶ in Bright's disease (compare §§ 885 *et seq.*). It has been argued that post-pyrexial hyperpyraemia is common, and that gout is a manifestation of hyperpyraemia: later, I shall argue that some cases of Bright's disease depend primarily upon hyperpyraemia, and that this is liable to persist after the development of the renal affection.

Raynaud's disease has alternated with insanity (Ritti), ⁷ an occasional manifestation of hyperpyraemia (§ 799). It has been known to disappear during pregnancy: Raynaud ⁸ says of one of his original cases:—'It is a remarkable fact that the complete disappearance of attacks of local syncope has always been noted by this lady as the first index of a commencing pregnancy.' Dupuytren employed venesection in Rognetta's case with marvellous success (Munro). ⁹ In a case complicated by early phthisis and glycosuria, Raynaud enjoined a strictly nitrogenous diet amongst other hygienic measures, and cured the patient of all three disorders (Munro). ¹⁰ And 'Short has recorded great improvement under thyroid extract' (Munro). ¹¹ With the possible exception of insanity, all the

¹ Quoted by Munro, *Raynaud's Disease*, 1899, p. 53.

² *Raynaud's Original Thesis*, New Syd. Soc., p. 91.

³ *Raynaud's Disease*, Munro, p. 56, also *Med. Review*, November 1902, p. 649.

⁴ *Raynaud's Disease*, Munro, p. 56.

⁵ *Ib.* p. 124. ⁶ *Ib.* p. 141.

⁷ *Ib.* p. 204.

⁸ *Raynaud's Original Thesis*, New Syd. Soc., p. 33.

⁹ *Raynaud's Disease*, Munro, p. 225. ¹⁰ *Ib.* p. 138.

¹¹ *Ib.* p. 225.

above, as so often pointed out, concur in promoting a carbonization of the blood.

RECURRENT OCULO-MOTOR AND OTHER PARALYSES

§ 487. Recurrent oculo-motor paralysis is, probably in some cases, dependent on hyperpyraemia; and its symptoms are explicable by vaso-motor action. Gowers says¹ it is perhaps more closely allied to migraine than to any other disease; and Charcot termed it 'migraine ophtalmique.' It affects chiefly women, and the attacks have occurred at each menstrual period.² 'They are sometimes associated with pain in the head and sometimes with migraine'³ (Osler). Möbius⁴ says the attacks always begin with the symptoms of migraine. James W. Russell,⁵ in describing a 'case of migraine with ophthalmoplegia,' refers to six similar cases recorded in English medical literature. In some of these, the paralysis passed off completely during the interval: in others, it was persistent in some degree.

'G. J. Rossolino⁶ reports a very interesting case of recurring facial paralysis associated with migraine.'

I know of a case in which some degree of aphasia, preceded by formication and hemianaesthesia, and lasting some hours, followed a picnic in which there was heavy eating and drinking. The nervous symptoms were associated with foul tongue and complete anorexia: they subsided completely under calomel and temporary abstention from food. Hyperpyraemia, glycogenic distension of the liver, and pathological vaso-motor action, affecting some of the cerebral arterioles, would fully explain such a case.

RECURRENT TEMPORARY AMBLYOPIA

§ 488. This affection is explicable by localized vaso-constriction, whether in the cerebral centre or in the peripheral retina; and such vaso-constriction may depend upon hyperpyraemia. In the 'Transactions' of the Ophthalmoscopical Society for the

¹ *Diseases of the Nervous System*, 1893, vol. ii. p. 192.

² *Ib.*

³ *Text-book of Medicine*, 1894, Osler, p. 791.

⁴ *Progressive Medicine*, 1902, September, p. 288.

⁵ *British Medical Journal*, May 2, 1903, p. 1021.

⁶ *American Year-book of Medicine and Surgery: Medicine*, 1902, p. 435.

year 1898-9, Priestly Smith 'recalled the case of a policeman, who, in changing from day to night duty, took two large meals at a short interval, slept heavily thereupon and woke blind in both eyes. One eye never recovered and presented the signs of a blocked central artery. . . . In such cases, he thought the disturbance in the blood-vessels must be largely due to reflex vaso-motor action, associated probably with a depraved condition of the blood, such as lithaemia.' I have quoted this case, which cannot of course be regarded as purely functional, because it seems to me highly suggestive of the pathology and pathological mechanism of the temporary form of amblyopia. The proximate history of the attack—heavy meals followed by sleep, or, in other words, the sudden irruption into the blood of carbonaceous material in large amount, immediately succeeded by reduced combustion—is the proximate history of many vaso-motor disorders depending on hyperpyraemia, such as migraine, asthma, angina, and epilepsy; and the blocking of one of the arteries affected is an accident which has occurred in migraine, usually a purely functional disorder (§ 372). Later, it will be argued that 'lithaemia' and hyperpyraemia are identical (§ 858).

§ 489. MALARIAL CASES.—To the already long list of paroxysmal vaso-motor affections, namely, migraine, angina, epilepsy, gastralgia, neuralgia, and Raynaud's disease, which may be due to malaria and which, as already argued, are modifications of the malarial rigor, we must now add this functional amblyopia. T. K. Munro¹ points out, on the authority of Gowers, that 'Ramorius (1877) has recorded cases of malarial poisoning complicated with paroxysmal amblyopia and narrowing of the retinal vessels, the fundus in the intervals being normal.'

HYDROPS ARTICULORUM INTERMITTENS

§ 490. This affection, Strumpfell says,² is 'a rare but quite typical disease in which large swellings, usually of the knee-joints but sometimes of others, develop at perfectly regular intervals of from one to four weeks. . . . Their nervous character is attested by their rapid onset and disappearance,

¹ *Raynaud's Disease*, T. K. Munro, 1899; also *Medical Ophthalmoscopy*, Gowers, 1890, p. 287.

² *Text-book of Medicine*, p. 555.

and by their combination with other nervous symptoms, e.g. angina pectoris, vaso-motor disturbance, etc.' E. G. Brekett and F. J. Cotton describe two cases of this affection. They are of opinion that rheumatism, gout, or gonorrhoea may predispose to it. 'The view most generally accepted is that it is a vaso-motor neurosis. In favour of this are the concurrence of angio-neurotic oedema in some cases and of functional nervous disorders in others, and the influence of mental conditions on the attacks.'¹

Similar to, if not identical with, hydrops articulorum intermittens are probably the following:²—'Twenty cases of a passive, quiet effusion into the knee-joint occurring in women and young girls, which is always associated with menstrual irregularities or uterine trouble. In no case did recovery occur while the uterine or catamenial irregularities continued, but in every case their correction was followed by prompt improvement in the condition of the knee' (W. H. Bennett).

Since the catamenial irregularities were of the nature of insufficient flow, such cases are highly suggestive of hyperpyraemia, due to the deficient haemorrhagic decarbonization (§ 239).

PAROXYSMAL VERTIGO

§ 491. Many cases of this disorder, even such as are labyrinthine in origin (Menière's disease), are susceptible of explanation by perverted vaso-motor action, dependent on hyperpyraemia or other conditions. Of Menière's disease, Gowers says:³—'Vaso-motor disturbance sometimes precedes the onset, and connected with it are various cephalic sensations, from general pulsation, greatest in the head, or a "rushing to the head," to a sense of "something passing over the brain," and other allied sensations.' And again:—'Other neurotic affections sometimes coexist: true epilepsy may accompany independent aural vertigo, and this affection is sometimes met with in the subjects of migraine. . . . Disorders of the digestive system are common . . . while some patients present conspicuous evidence of gout.' Fothergill says:⁴—'The relations of

¹ *Med. Review*, quoting *Boston Med. and Surg. Journal*, October 31, p. 484.

² W. H. Bennett, quoted by Dr. Helen McMurchy, *Lancet*, October 5, 1901, also by *Med. Review*.

³ *Diseases of the Nervous System*, 1893, vol. ii. p. 786.

⁴ *Gout in its Protean Aspects*, 1883, p. 107.

vertigo to gout are very interesting. It lies along the same line of arteriole spasm which gives palpitation.' And Trousseau, in a case of violent vertigo, associated with sensation of weight in the head and succeeded by intense headache, found that 'there was slight enlargement of the liver,'¹ with some pain and tenderness in the epigastrium. Thus all the associates of paroxysmal vertigo are explicable by hyperpyraemia or by pathological vaso-motor action or glycogenic distension of the liver, secondary thereto.

In many cases, the vertiginous attack is manifestly directly dependent on the ingestion of food. Ramskill² relates a case of severe vertigo, which came on three hours after eating, hastily and with imperfect mastication, a breakfast of which sausages and Devonshire cream formed a part. Such a combination is highly carbonaceous and therefore likely to induce hyperpyraemia: the interval between the meal and the attack points to food absorption rather than to gastric irritation as the essential factor; and Ramskill himself 'goes so far as to say that it is the exception if one is able to trace any positive signs of gastric disorder.'³ Finally, Trousseau⁴ points out that, 'generally speaking, the vertiginous symptoms do not occur during, but long after, digestion, that is to say, using the vulgar expression, when the stomach is empty.'

The hyperpyraemic origin of paroxysmal vertigo (in some cases) is perhaps most clearly shown by the influence of acarbonizing agents, pathological, physiological, or therapeutic. Trousseau⁵ quotes a case of Boerhaave's, in which the patient for two years 'was always seized with vertiginous symptoms when he attempted to stand up. In vain had the ablest practitioners endeavoured to cure him. Quite suddenly he had an attack of gout, of which disease up to that time he had had no indication: from that time, he found himself free from the distressing vertigo to which he had formerly been liable.' Dr. Colin Campbell⁶ tells of a case of his own, in which a seton inserted into the back of the neck completely removed all the symptoms of Menière's disease. And I have succeeded in dispersing all symptoms in a case of recurrent paroxysmal

¹ *Clinical Medicine*, New Syd. Soc., vol. iii, p. 539.

² *Text-book of Medicine*, Fagge, 1891, vol. i, p. 771.

³ *Ib.*

⁴ *Clinical Medicine*, New Syd. Soc., vol. iii, p. 542.

⁵ *Ib.* vol. iv, p. 379.

⁶ *Brit. Med. Journal*, March 29, 1902, p. 806.

vertigo, by simply reducing the carbonaceous intake (Case LVII) ; the case was probably labyrinthine.

ATYPICAL AFFECTIONS

§ 492. Vaso-motor action may explain many enteralgias and numerous other affections, clinically heterogeneous. Every now and then, there may be picked out from the pages of the medical journals cases testifying to the paramount importance of vaso-motor action in pathology. Many of these are altogether atypical and find no place in any existing system of classification. For example, Dr. William Sykes¹ describes the case of a woman, aged 32, who, during a period of six years, suffered at various times with recurrent diarrhoea, hysterical attacks, causeless heats and flushings, followed by profuse perspirations, paroxysmal nocturnal dyspnoea of an asthmatic type, and bronchial mucorrhoea ; and he points out that all these seemingly disconnected symptoms may be correlated and explained by vaso-motor dilation of varying distribution.

§ 493. In a highly interesting clinical lecture, which is published in the 'Lancet' for June 1, 1901, Thomas D. Savill describes a series of cases of '*acroparaesthesia, erythromelalgia, sclerodactylia, and other angio-neurotic disturbances.*' He points out that 'the symptoms which these words indicate belong undoubtedly to the same category as those of Raynaud's disease': they are vaso-motor, that is to say. None of the lecturer's observations are inconsistent with the view that these cases are hyperpyraemic in origin : many are strongly confirmatory. Thus all such cases are paroxysmal, at any rate in the first instance : 'in severe cases, the attacks may be so frequent as to resemble a continuous malady, but close observation will detect that there are well-marked exacerbations. . . . There are two epochs of life which are specially prone to their development, namely, puberty and the climacteric.' The attacks are apt to be worse at an expected menstrual period, more especially if this fails to appear, at night, and in the day if the patient lies down and goes to sleep, just as occurs in asthma, some headaches, etc. The affections are commonly associated with formal neurosal acarbonizing processes and other manifestations of hyperpyraemia : in one case, there were

¹ *British Medical Journal*, 1901, March 30.

typical migraine paroxysms lasting twenty-four hours, associated with scintillating scotoma, relieved by emesis, and followed by acute tenderness of the scalp lasting several days: in another, vertigo, sometimes associated with slight interruption of consciousness, graduated into severe syncope and, finally, into 'convulsive seizures presenting all the appearances of an epileptic fit.' Most of the cases suffered from dyspepsia, probably of the variety ascribed in this work to glycogenic distension of the liver. Thyroid extract, which markedly hastens combustion, gave great relief in some: in one, 'copious libations of warm water and a practically nitrogenous diet' produced great amelioration, 'especially in the severe attacks of migraine.'

§ 494. We have seen that migraine, angina, epilepsy, gastralgia, neuralgia, Raynaud's disease, and recurrent temporary amblyopia, though frequently dependent on hyperpyraemia, may depend also on malaria (§ 489). To this list we must now add erythromelalgia. Professor A. Cavazzani and Dr. C. Bracci,¹ after describing a case of this vaso-motor affection, add that a noteworthy feature was the preceding malarial affection with enlargement of the spleen and the curative influence of quinine.

§ 495. Urticaria will be referred to under the head of cutaneous manifestations of hyperpyraemia; but this affection might with equal justice be classed in this section as a vaso-motor neurosis; and there seems no doubt that it may depend upon malaria as well as upon hyperpyraemia. Dr. George Papanikosta² describes the case of a Greek sergeant of infantry, aged 26, in whom general urticaria appeared and disappeared concurrently with the malarial paroxysms. Examination of the blood showed that the plasmodia of Laveran were present. It would seem that practically all the vaso-motor manifestations of hyperpyraemia may be exactly copied by those of malaria.

§ 496. Finally, there can be no doubt that many varieties of functional disorder of the heart depend upon peripheral vaso-motor spasm, which in turn depends upon hyperpyraemia. Gairdner says:³—'I have observed that the first sign of dis-

¹ *Il Morgagni*, January 1900, p. 30, quoted in *Med. Rev.*

² *Lancet*, January 9, 1904, p. 92.

³ Quoted by Fothergill, *Gout in its Protean Aspects*, 1883, p. 99.

turbed health which has attracted my attention and announced to me a tendency to gout, has been disorder of the heart's action. When I have had an opportunity of observing the health of any one, previously to a first attack of gout, or have had a patient who could make an observation on himself, I have rarely if ever found the disorder wanting. Its most common form is that of palpitation, fluttering, pause in the heart's action, intermission, or some indication of diminished tone or energy.' In such cases, the disturbance of action is completely relieved by the ensuing pyrexial acarbonization of the gouty attack; and convalescence is associated with distinct diminution of the tension of the radial.

The frequency, ubiquity, and variety of vaso-motor action testify to its dominant influence in organic life. This consideration, had we started our investigations from this point, would almost inevitably have carried us back to variations in the composition of the blood, for these have always been regarded as determining in great part the calibre of the arterioles.

MECHANISMS OF THE PAROXYSMAL NEUROSES COLLOCATED AND CORRELATED

§ 497. The close relationship between the different members of the class of affections termed paroxysmal neuroses has long been recognized by those physicians who are accustomed to take a macroscopic and philosophical view of disease—by 'anti-specialists,' so to speak. This is apparent in the names which have at various times been bestowed upon these disorders. Epilepsy, perhaps the most striking and distressing member of the group, has most frequently served as the standard of comparison: thus laryngismus stridulus has been termed 'laryngeal epilepsy' (Liveing), asthma 'epilepsy of the lungs,' migraine 'sensory epilepsy,' angina pectoris and tic douloureux 'epileptiform neuralgia'; but migraine has occasionally served, as in the expression 'gastric migraine' sometimes applied to recurrent gastralgia, an affection referred to by Brunton as 'headache in the stomach.'

This relationship, I have argued, depends fundamentally upon the existence of a common humoral cause, hyperpyraemia, and a common humoral effect, acarbonization of the blood or a tendency thereto. These bonds of union, however, connect

together a group of affections far larger and less homogeneous, clinically and in other respects, than the group of paroxysmal neuroses: for example, they connect the whole of the paroxysmal neuroses group with gout. But the individual paroxysmal neuroses are mutually connected by closer bonds—by the bonds of a community of mechanism. For the paroxysmal neuroses—at the least, most of those which have been already considered—are wholly or in great part vaso-motor neuroses: they consist of pathological exaggerations or modifications of physiological vaso-motor action, with or without cardiac modification. The physiological vascular conditions, of which most of the paroxysmal neuroses constitute pathological variations, are thus tersely summarized by Leonard Hill: ¹—‘A high-pressure main runs to all the organs of the body. By means of the vaso-motor nerves the stream can be turned on here or there, and any part flushed with blood, while the supply to the remaining parts is proportionately diminished.’

§ 498. For the sake of simplicity, I shall refer in this connexion only to five of the typical or representative paroxysmal neuroses, namely, migraine, asthma, angina pectoris, gastralgia, and epilepsy. Of these, extensive vaso-constriction seems common to most, if not to all, cases. This vaso-constriction may vary widely in localization, extent, intensity, rapidity of development and regression, and duration: in any case a rise of general blood-pressure must ensue unless compensation occurs. Such compensation may be by an area of vaso-dilation or by a modification of the heart-beat. Vaso-dilation may present variations parallel to the vaso-constriction it compensates. Modifications of the heart-beat may consist of increased frequency, slowing, weakening, intermittence, or stoppage. *The phenomena characteristic of each individual paroxysmal neurosis will depend upon the characters of the vaso-constriction, but, for the most part, upon the character of the compensation for the vaso-constriction, whether this be by vaso-dilation, by cardiac modification, or by both.*

This generalization enables us to depict mentally the variations of mechanism which determine the replacement of any one of these neuroses by any other—of the phenomena termed by Liveing ‘neurosal transformation or metamorphosis.’ The phenomena special to migraine, asthma, angina, and gastralgia

¹ *Text-book of Physiology*, E. A. Schäfer, 1900, vol. ii. p. 72.

depend upon the localizations of the area of vaso-dilation. In the case of a transformation of any one of these affections into any other, we have only to imagine that some factor, known or unknown, has intervened to cause a shifting of the area of vaso-dilation. Such intervening factors must be almost infinitely numerous, and include, among other things, most or all of the factors usually termed 'exciting causes' of the neuroses. To take an example, an habitual migraine sufferer commenced to have asthma, and forthwith lost his headaches: here, the intervening factor was in all probability an attack of acute bronchitis from sudden alteration of temperature. In the case of another such metamorphosis, the intervening factor may have been some obscure atmospheric alteration favourable to asthma; and so on.

§ 499. Facial neuralgia is accepted by Clifford Allbutt as closely allied to migraine (§ 467); and, in the following instance of sudden transformation of facial neuralgia into gastralgia, the intervening factor, responsible for the metastasis of the vaso-dilation, seems manifest:—'A young man,¹ subject to attacks of facial neuralgia, was seized towards the close of January, 1841, with darting pains in the right temple, which soon spread towards the opposite side. One evening *while his face was red* cold compresses were applied to his forehead: in the course of five minutes the pain in the head had abated, and at the expiration of three or four minutes more entirely disappeared. At the same time a sense of oppression was felt in the epigastrium: then suddenly agonizing pains set in, in the same region, accompanied with a sense of suffocation, painful efforts to vomit, and the escape of gas from time to time from the mouth' (Valleix). Almost identical transformations are described under the term 'retrocedent gout,' and are frequently due to the same intervening factor, namely, cold applications to the congested or inflamed part.

§ 500. In the case of a transformation of any of the above-mentioned affections, whose special phenomena depend upon vaso-dilation, into epilepsy, we may imagine that, for some reason, the habitual compensatory vaso-dilation failed or was insufficiently extensive, intense, or rapid, perhaps on account of some extra rapidity of development on the part of the vaso-constriction; and that, consequently, the general blood-pressure

¹ Valleix, quoted by Living, *Megrim and Sick-headache*, 1873, p. 202.

continued to rise until checked by a vagus inhibition of the heart-beat, of sufficient intensity to cause general convulsions through cerebral anaemia. Or, if we accept the hypothesis of spasm of the cerebral arteries as a proximate factor in some epilepsies, then we might regard this spasm as a part, detached, perhaps intensified, of the widespread vaso-constriction.

Conversely, recurrent epileptic attacks have been replaced by paroxysmal neuroses whose special phenomena depend upon an area of vaso-dilation: in these cases, we may imagine the reverse series of variations in mechanism, namely, that, under some intervening factor or factors, the rapidly rising blood-pressure, due to widespread vaso-constriction, becomes checked by vaso-dilation before vagus inhibition of the heart-beat is demanded. Gowers¹ refers to a case in which an epileptic began to suffer from migraine when his fits ceased; and Salter² says of an old-standing case of periodic epilepsy:—‘On one occasion . . . at the usual time at which he had expected the fit, he had experienced the accustomed premonitory symptoms, but instead of their being followed as usual by convulsions, this violent dyspnoea’ (typical asthma) ‘had come on. Within a few hours the dyspnoea went off, and left him as well as usual. At the expiration of the accustomed interval after this attack, the ordinary premonitory symptoms and the usual epileptic fit occurred. On several occasions . . . this was repeated, the epileptic seizure being, as it were, supplanted by the asthmatic.’ Obviously, in both varieties of attacks, the premonitory symptoms or *aurae* were synchronous with, and caused by, the vaso-motor changes responsible for the rise in blood-pressure. The asthmatic attacks were determined by compensatory vaso-dilation of the bronchial area: the epileptic attacks, by the absence or inadequacy of compensatory vaso-dilation, and by substitutive vagus inhibition of the heart-beat. Dr. Alexander Francis³ has ‘met with one case of asthma associated with epilepsy. . . . He had had asthma for seventeen years, which had become so severe that he was now unable to lie down or do any kind of work. He also suffered from epilepsy, and the fits were gradually becoming more frequent and severe. *The only time he had any freedom from asthma was immediately after an epileptic fit. The more severe the manifestation of the epilepsy,*

¹ *Diseases of the Nervous System*, 1893, vol. ii. p. 849.

² *On Asthma*, 1878, p. 44.

³ *Asthma in Relation to the Nose*, Alex. Francis, 1903, p. 47.

the greater freedom did he experience from the asthma.' (Italics mine.)

§ 501. The vaso-motor and cardio-inhibitory hypotheses enable us to understand also the mechanism of those interesting and not very uncommon cases which apparently partake of the clinical characteristics of two (or even more) of the classical paroxysmal neuroses—cases in which seem to be mingled, in various proportions, the symptoms (1) of migraine and asthma, (2) of migraine and angina, (3) of migraine and epilepsy, (4) of asthma and angina, (5) of asthma and epilepsy, (6) of angina and epilepsy, and of any of these with other neurosal disorders.¹

Some examples of such composite cases may be given.

§ 502. 1. More than one case has occurred in my own practice in which, during a paroxysm of asthma, the dyspnoea has remitted markedly for a time, the remission being synchronous with the development of intense headache of a congestive type, which in turn passed off on the full re-development of the dyspnoea (Case XXXV). Neuralgia and frontal headache are included by Salter² amongst the premonitory symptoms of asthma.

§ 503. 2. Liveing³ quotes the American author of Lobstein's 'Treatise on the Sympathetic Nerve,' to the effect that some women, having suffered from recurrent sick-headache from puberty, on arriving at middle life lose the cranial pain but retain the digestive symptoms, which then become associated with those of angina. In one case, 'there was great palpitation of the heart and embarrassment of the circulation, and most suffocative asthmatic respiration, with pain along the spine (on pressure) and sometimes in the arm and shoulder—in short, a case analogous to angina pectoris.' George Keith relates a case in which severe angina occurred habitually as the precursor of recurrent bilious attacks⁴; and Dr. Graham Steele⁵ describes a case of angina pectoris in which the paroxysms became, after three years, complicated by 'severe headache over the left eye.'

§ 504. 3. Gowers⁶ relates cases in which migrainous and

¹ Gastralgia is excluded from this part of the subject in order to avoid unnecessary complexity: it could, however, be shown to enter into composite cases; and this is true of most other neuroses.

² *On Asthma*, 1868, p. 29. ³ *Megrim and Sick-headache*, 1873, pp. 219, 220

⁴ *Fads of an Old Physician*, pp. 54, 55, 56.

⁵ *Lancet*, November 21, 1903, p. 1432.

⁶ *Diseases of the Nervous System*, 1893, vol. ii. pp. 848, 849.

epileptic attacks were inextricably tangled in their symptomatology, epilepsy commencing with migrainous visual spectra and migraine being complicated with convulsive phenomena. 'In one remarkable case of this character, the preliminary sensory disturbance of typical migraine persisted, in briefer form, as the aura of characteristic epileptic fits.'¹ R. Fuchs² points out that 'cases are recorded, in which once or twice in a lifetime an attack of migraine has terminated in a general convulsion with loss of consciousness.'

§ 505. 4. Anstie says:³—'I have certainly seen several cases of asthma in which spasmodic pain of the heart has occurred on various occasions after or during a very severe asthmatic paroxysm. One case was that of a gentleman of a highly delicate and neurotic temperament, who had suffered for fifteen or sixteen years from well-marked spasmodic asthma. . . . For some time before the outbreak of cardiac neuralgia, he had suffered repeatedly from severe facial neuralgia, and these attacks on more than one occasion culminated in facial erysipelas or what was entirely indistinguishable from that affection. He then began to suffer from cardiac pain and spasm after his asthmatic paroxysms, and these new symptoms speedily assumed the form of a very severe intermittent angina: in several of the attacks he appeared about to die.'

On the one hand, I have observed retro-sternal pain in asthmatic paroxysms, but it has, I think, most usually occurred just before or at the commencement of the attack: in one case, it might fairly be regarded as an asthmatic aura. On the other hand, I have in several instances known severe and typical anginal paroxysms, preceded, associated with, or succeeded by minor asthmatic manifestations, such as a moderate degree of wheeziness and cough: in one case, in which paroxysmal cough always followed severe anginal attacks, there was at this time distinct hyperaemia affecting the mucosae of the nose, pharynx, and larynx, which however passed off in the course of a few minutes (Case XLI).

§ 506. 5. Above, I have quoted from Hyde Salter's work on Asthma (§ 500) a case in which periodic epileptic fits were on some occasions replaced by asthmatic fits. But manifestly the

¹ *Dis. Nerv. System*, 1893, vol. ii. p. 750.

² *Die Heilkunde Rai*, 1903, quoted by *Brit. Med. Journal*, Epitome, October 31, 1903.

³ *Neuralgia and its Counterfeits*, 1871, pp. 68, 69.

replacement in this case was incomplete ; for, on each occasion, the well-recognized epileptic aura preceded, and led up to, the asthmatic fit. Such a case, if we regard the aura as an integral part of a fit of epilepsy, we are justified in classing as a hybrid between epilepsy and asthma.

A female patient of mine has suffered for twenty years from frequent attacks of epilepsy and asthma, both, however, of a mild type. The more frequent and severe the epilepsy, the less frequent and severe the asthma ; and conversely. Both the epileptic and asthmatic attacks are immediately preceded by premonitory symptoms. Usually these are distinctive ; but, not infrequently, they are indistinctive, and then the patient is at a loss to know from which variety of attack she is about to suffer.

§ 507. 6. Trousseau¹ insists that angina pectoris may be a variety of epilepsy. He says:—‘In some cases and perhaps in a pretty good number of instances according to my experience, angina pectoris is an expression of this fearful and cruel complaint.’ He calls attention to the similarity of the auras (a similarity we have seen in migraine and asthma also), the suddenness of the onset, the initial facial pallor followed by redness, and the occurrence of redness in other parts which are the seat of pain. He adds concerning angina : ‘The intellect is in general unimpaired all the time, although some exceptional instances have been recorded of individuals who had a wandering look and who muttered unintelligible words as if in a state of ecstasy.’ In one of my cases, there is no doubt that throughout the worst attacks the patient is subconscious, if not unconscious : he can rarely call to mind more than the commencement and termination of his seizures. It is, perhaps, open for us to regard cases exhibiting such mental phenomena as hybrids between angina and epilepsy.

§ 508. Mixed cases, such as those described in the above six paragraphs, must remain inexplicable so long as we continue to regard the paroxysmal neuroses as disorders of individual organs, such as the brain, heart, and lungs ; but, if we enlarge our horizon and include therein the general circulation and the ubiquitous system of vaso-motor nerves, the difficulties will be found to shrink. For it would be unreasonable to expect the initial vaso-constriction to be equally extensive, to develop

¹ *Clinical Medicine*, New Syd. Soc., vol. i. pp. 602, 605, 606.

with equal rapidity, or to affect the same regions, in all cases. Neither can we expect the compensatory vaso-dilation, which is so prominent a proximate cause of symptoms, to be invariably and sharply restricted to the one organ, or even to the one locality: there is no reason, for example, why the coronary arteries should not share in the vaso-dilation of the bronchial arteries responsible for the asthmatic paroxysm, and so introduce into the clinical picture of asthma the retro-sternal pain so often observed; and so on.

Again, if both vaso-constriction and vaso-dilation are liable to vary in degree and extent, it is highly probable that there will be found (1) cases in which the latter affords inadequate compensation for the former; and (2) cases in which the former is over-compensated by the latter. In both events, modification of the cardiac action will be demanded: in the first such modification will consist of inhibition, in the second of compensatory acceleration or augmentation.

§ 509. Conformably with these anticipations:—

1. Many¹ cases of migraine, asthma, angina pectoris, gastralgia, etc., are recorded, in which slowing of the heart-beat was a marked symptom. Such cases, according to the views here adopted, escape more narrowly than the majority epileptic complications or transformations; and we are not surprised to find that occasionally mental or convulsive phenomena are superadded. 2. Not a few cases of migraine, asthma, angina pectoris, gastralgia, etc., occur in which the pulse-rate is distinctly accelerated. I have myself seen this modification in all except the last; and the acceleration, in some cases of migraine and asthma, has been already referred to (§§ 356 and 386).

¹ *Megrin and Sick-headache*, Liveing, 1873, pp. 311, 329, 330, 331, 332, 214, 217, 219, 230; also *On Periodical Headache*, Suckling, p. 3.

CHAPTER XIII

§§ 510–581

The theory of pathological prepotency as applied to the paroxysmal neuroses—
 Factors in the paroxysmal neuroses other than humoral: secondary or functional factors: exalted irritability of the vaso-motor system: some extrinsic factors: heredity: acquired intrinsic factors; the ‘memory of the body’: nasal mucosa: eye-strain—Results of prolonged recurrence of the paroxysmal neuroses: humoral results or results as regards supply: functional results—
 Conditions which may be left on the stoppage, through means other than acarbonization, of the efficiently acarbonizing paroxysmal neuroses: substitutive physiological acarbonization: substitutive pathological acarbonization: unrelieved hyperpyraemia—General principles of treatment of the paroxysmal neuroses: physiologically prepotent cases: pathologically prepotent cases—
 Summary.

§ 510. We have seen that healthy organisms differ materially from each other in the manner of physiological acarbonization. Some depend in relatively high degree upon regulation of the carbonaceous income, through physiological distension of the liver by glycogen: others, upon a high rate of katabolic expenditure or combustion, whether inherent or maintained by constant physical exercise: others, upon a high grade of anabolic expenditure, especially fat-formation; others again, upon free haemorrhagic expenditure, or a tendency to menstruate profusely. Thus there is no fixed standard for any of these physiological functions: deficiency or excess of one is apt to be compensated by excess or deficiency of another: in each case the organism strives to attain efficient physiological acarbonization by means of its individual physiological capacities. The preponderances of acarbonizing factors may be expressed as *prepotencies* of the different physiological acarbonizing capacities. Thus we may have prepotency of the hepatic regulating capacity: prepotency of combustion which constitutes the katabolic expenditure: prepotency of fat

formation, the chief form of anabolic expenditure ; and prepotency of menstruation or expenditure through direct loss. And all these without going beyond the limits of the physiological domain or health. Such constitutional individualities seem to me, in great degree, fundamentally responsible for 'temperament.'

Now in Chapter IX we reached the conclusion that the paroxysmal neuroses, in some cases, may be regarded as ultra-physiological, or pathological, reinforcements of physiological acarbonization, which is inadequate to deal with the carbonaceous income. This conclusion involves the following inferences concerning such cases:—that the pathological process arises only when the physiological processes have been strained to their utmost limits : that it may be wholly prevented by reducing the carbonaceous income ; and that the carbonaceous income remaining after such reduction will be sufficient to satisfy the legitimate demands for physiological acarbonization, that is, the demands of the organism for the production of the different forms of energy (force, heat), and for the different forms of anabolism (fat-formation, secretion-formation, etc.). That these inferences are correct is shown at once by the numerous cases in which a paroxysmal neurosis may be immediately prevented from further recurrence by a slight restriction of the carbonaceous income (achieved in several ways, but most rapidly by restriction of the carbonaceous intake), and by the fact that such restriction of income is followed by no loss of energy or strength but the reverse, and sometimes by no loss of weight, occasionally even the reverse.

In that the reduced carbonaceous income is capable of fully satisfying the physiological demands of the organism, both katabolic and anabolic, such cases may be regarded as *physiologically prepotent* : the pathological process is strictly a reinforcement, or auxiliary, called in to disperse a supply of carbonaceous material in the blood which is unneeded ; and the treatment of the pathological process will consist simply in getting rid of the unneeded supply.

§ 511. Were all cases thus physiologically prepotent, the treatment of neurosal acarbonizing processes would be a simple matter : it would consist, as just stated, in mere regulation of supply. But physiological prepotency by no means obtains in all cases. In many, it is found that reduction of the supply

of carbonaceous material in the blood (in whatsoever way achieved), *although never without conspicuously favourable influence upon the frequency or severity of the recurring paroxysms*, is not successful in completely preventing paroxysms, unless it is carried to such an extent as to interfere materially with the strength and nutrition of the patient. Such cases we can only explain by assuming that the pathological process, instead of constituting a mere reinforcement adapted to disperse a supply of carbonaceous material in the blood which is beyond the requirements, as well as beyond the unaided capacities, of physiological acarbonization, is, in reality, overlapping, and therefore usurping a portion of the duties of, physiological acarbonization. Such a relation between the pathological acarbonizing process and the physiological acarbonizing processes may be expressed by the term *pathological prepotency*.

It may of course be contended that all cases which exhibit pathological acarbonization in any circumstances are in a sense pathologically prepotent. This would be true; but I propose in this work to use the term in the more restricted sense above implied—to denote a condition in which the organism is unable to ingest, digest, and absorb, without the occurrence of pathological acarbonization of some kind, sufficient carbonaceous material to supply its purely physiological requirements. It is manifest that physiological and pathological prepotency will graduate by imperceptible gradations into each other.

The theory of pathological prepotency is of immense importance, indeed it is absolutely essential, to the tenability of the general theory of hyperpyraemia. Without it, the latter must inevitably fall to the ground when applied to a large section—*how large I do not know*—of the disorders which we are regarding as manifestations of hyperpyraemia, more especially those included under the term ‘paroxysmal neuroses.’ A clear conception of the meaning of the term is, therefore, indispensable; and we shall, I think, best attain to this through a consideration of those paroxysmal neuroses which exhibit a tendency to periodicity.

§ 512. We have seen that each attack of those paroxysmal neuroses which operate effectively as acarbonizing processes is followed by a period of immunity from fresh attacks (§ 338);

and that such immunity wanes progressively thenceforth and ultimately ceases. This waning immunity has been ascribed to a progressive increase in the carbon contents of the blood—to a progressive increase of pyraemia. And it has been argued that the succeeding paroxysm occurs when the carbon contents of the blood have risen sufficiently to call forth the pathological vaso-motor action which constitutes, or, as in certain cases of major epilepsy, initiates, the paroxysm—when, in other words, physiological pyraemia has passed over into pathological hyperpyraemia.

Assuming the paroxysms to be fully efficient in promoting acarbonization, it is obvious that the duration of the immune interval will depend fundamentally on two factors, namely (1) the rate of increase of pyraemia; and (2) the facility with which the vaso-motor system responds by pathological action to pyraemic conditions. An increase of either factor will diminish, a diminution of either will increase, the duration of the interval. Hence the condition of the vaso-motor system as regards pathological irritability or inirritability would determine, for each individual case, the degree of pyraemia which constitutes hyperpyraemia. In cases in which the vaso-motor system is highly irritable, it is easy to conceive that paroxysms would be determined by a degree of pyraemia which, under a less irritable vaso-motor system, would be physiological. In such cases, the paroxysmal neuroses, though still acarbonizing processes, would cease to be conservative, or at any rate salutary. Instead of dispersing an excess of fuel in the blood which is acting as an incubus, they would be wasting the supply which is no more than is required for physiological purposes,—instead of recurrently reducing an actual hyperpyraemia to pyraemia, they would be recurrently reducing pyraemia to an actual hypopyraemia, thus forcing the organism to be drawing at frequent intervals upon the fuel reserves in the tissues, carbonaceous, if not also partly carbonaceous (nitrogenous tissues).

§ 513. It follows that acarbonizing treatment alone can hardly be expected to restore such cases to robust health. For, even when the recurring paroxysms can be completely held in abeyance thereby, the immunity is apt to be dearly purchased, in that it can only be maintained by continuance of the conditions, amongst which will be a fuel supply which is

miserably inadequate for continued nutrition. Manifestly, for the completely satisfactory treatment of cases exhibiting marked pathological prepotency, the factors of the pathological prepotency will have to be sought out and removed, or modified if irremovable. Now these factors are numerous and complex, for they embrace all the factors of the paroxysmal neuroses other than the humoral factor.

These factors will all be found to be factors which conduce to an error of *function*, as distinguished from factors which conduce to excess of *supply*. Thus the factors of the paroxysmal neuroses will fall naturally into two fundamental divisions, namely, supply factors and functional factors. Pathological prepotency will depend solely on the functional factors. Hence, in the treatment of pathologically prepotent paroxysmal neuroses, attention will have to be directed mainly, though rarely solely, to the functional factors.

FACTORS IN THE PAROXYSMAL NEUROSES OTHER THAN HUMORAL: SECONDARY OR FUNCTIONAL FACTORS

§ 514. It might perhaps be contended that the tendency of this work so far is to reduce the causation of certain disorders to a condition of absurd simplicity—that it is, *primâ facie*, unreasonable to ascribe so many diverse morbid affections to the one factor, hyperpyraemia. But any such contention would involve several fallacies.

In the first place, hyperpyraemia is a wide and comprehensive term, including possibly many different chemical departures from physiological pyraemia; nor have we attempted to restrict the humoral factors of the paroxysmal neuroses to hyperpyraemia. We have seen, indeed, that one toxaemia, the malarial, is capable of giving rise to the typical phenomena of, at any rate, nine of the paroxysmal manifestations of hyperpyraemia, namely, migraine, angina, epilepsy, gastralgia, neuralgia, Raynaud's disease, recurrent temporary amblyopia, erythromelalgia, and urticaria; and it may be that many other toxic conditions have similar potentialities.

But, apart from all humoral conditions, it is obvious that there are numerous other factors concerned in the causation of the paroxysmal neuroses. Indeed, the theory of hyperpyraemia does not tend to reduce the number of the co-operating factors

in any paroxysmal neurosis. On the contrary, it adds yet another to the list, while leaving ample room for all the already accredited factors and for many more as yet undiscovered or unthought of.

Though doubtless in many cases more dominant in causation, the factors other than humoral may for convenience be spoken of as the secondary factors of the paroxysmal neuroses. Early in this work (§ 341), we reached the conclusion that the affinities of the paroxysmal neuroses are those of blood relations, their antagonisms those of mutual rivalry. It is to the diversity of the secondary factors that we must ascribe the possibility of such rivalry. There is a common task, the dispersion of hyperpyraemia: the mode of its accomplishment will depend upon the pathological capacities of the individual organism; and organisms will be endowed with widely diverse pathological capacities in accordance with the wide diversity of the secondary factors. Thus, in physiologically prepotent cases, the secondary factors will determine the nature of the paroxysmal neurosis, its existence being determined by an actual hyperpyraemia. But, in pathologically prepotent cases, the secondary factors will do more: they will determine the existence, as well as the nature, of the paroxysmal neurosis; for there will be no actual, but merely a relative hyperpyraemia. And whether any given case is to be physiologically or pathologically prepotent, will depend upon the weakness or strength of the secondary factors.

In attempting to classify the secondary factors of the paroxysmal neuroses, we are soon faced with the difficulties which tend to embarrass all classification: whatever system is adopted, the groups are found to overlap. Probably a primary division into extrinsic factors or factors in the environment, and intrinsic or personal factors, would be as convenient as any; but this would not be fundamental, since many personal factors depend upon, or have resulted more or less recently from, the environment. Here, however, I shall attempt no scientific classification, but shall content myself with alluding to some of the best known conditions which have been shown to conduce to the paroxysmal neuroses, but which can hardly operate humorally, that is, by favouring hyperpyraemia or toxaemia of any kind.

§ 515. EXALTED IRRITABILITY OF THE VASO-MOTOR SYSTEM. Considering that the mechanism of the paroxysmal neuroses

is primarily vaso-motor, one of the first questions which naturally arise is whether an exalted irritability of the vaso-motor system is not an essential factor in many of these affections, especially of course in those which are pathologically prepotent in a marked degree. A simple exaggeration of the responsiveness of this system to some or all of its accustomed stimuli would help to explain many of the phenomena of the paroxysmal neuroses.

It would help to explain the undoubted fact that exposure of the surface of the body leads, in some cases, to paroxysms of migraine, asthma¹ (West), angina pectoris² (Fagge), epilepsy³ (Trousseau), Raynaud's disease⁴ (Munro) and probably other allied disorders. Cold promotes cutaneous vaso-constriction; and this may constitute the essential feature of the paroxysm, as in the local syncope of Raynaud's disease, or the initial step in the series of vascular or cardiac changes which are responsible for the most characteristic features of the affections. But we may suppose that, in most cases where cold is the precipitating influence, the underlying humoral condition hyperpyraemia is already present and the paroxysm impending; for, usually, thermal influences are powerless within a certain time (varying with the individual case) after an efficiently acarbonizing paroxysm, or after hyperpyraemia has been dispersed by treatment or intercurrent disease. In other words, external cold, through constituting an added factor of vaso-constriction, assists in the mechanism, and therefore precipitates the attacks, of the paroxysmal neuroses which depend fundamentally upon hyperpyraemia.

In the case of persons endowed with exalted vaso-motor irritability, intense cutaneous vaso-constriction is apt to succeed a lowering of the external temperature so slight as to be almost inappreciable to the average person. This is a conspicuous phenomenon in many cases of Raynaud's disease; but it is observable also in some cases of migraine, asthma, and other paroxysmal affections. And as with the thermal stimulus, so doubtless with other stimuli, amongst these the humoral stimulus. A vaso-motor system which is abnormally irritable would respond to a proportionately lower degree of carbonaceous

¹ *Diseases of Infancy and Childhood*, West, 1884, p. 369.

² *Text-book of Medicine*, Fagge, 1891, vol. ii. p. 22.

³ *Clinical Medicine*, New Syd. Soc., vol. i. p. 40.

⁴ *Raynaud's Disease*, T. K. Munro, 1899, p. 29 *et seq.*

accumulation in the blood: put otherwise, what is hyperpyraemia for such a vaso-motor system would be physiological pyraemia, perhaps even hypopyraemia, for one more stable.

Cutaneous vaso-constriction, manifested subjectively by chilliness, is not uncommon in moderate degree following meals in healthy persons. In some pathological states this symptom may be greatly exaggerated. George S. Keith,¹ referring to the case of a youth whose health had broken down from over-study and who was extremely emaciated and feeble, says: 'Any food he tried to take brought on pain and chilliness to a degree I had never met with before.' I have seen two cases of rheumatoid arthritis in which intense cutaneous vaso-constriction, following meals, was the source of almost as much annoyance to the patient as the arthritic trouble. And it may be added that exaggerated sensibility to cold and heat is common in this disease (compare § 854).

With such a condition of the vaso-motor system, neurosal paroxysms would probably be induced by pyraemic conditions which would be physiological with a less irritable system. On this view, the indication for treatment of the paroxysmal neuroses would be the reduction of vaso-motor irritability, rather than the reduction of the carbon contents of the blood. Here the nitrites, which tend to cause vaso-motor paresis, naturally suggest themselves; and we are reminded that Gowers regards nitro-glycerine as the most useful of all drugs in rendering less frequent the paroxysms of migraine (§ 362). It seems a reasonable supposition that nitro-glycerine, given in small frequently repeated doses, might, by reducing irritability of the vaso-motor system, render it tolerant of a higher degree of pyraemia, and thus enable patients liable to recurrent neurosal paroxysms to ingest a larger amount of carbonaceous material not only with impunity but with advantage. This anticipation seemed to be borne out in some degree in Case XI.

But the reduction of exalted vaso-motor irritability by such means as the prolonged administration of the nitrites, even if possible in some cases, would seem to amount after all to the promotion of a kind of artificial inirritability: such treatment ignores the existence of factors which can, I think, be shown to be often responsible for exalted vaso-motor irritability, and of which some are undoubtedly removable.

¹ *Fads of an Old Physician*, 1897, p. 168.

§ 516. Exalted irritability of the vaso-motor system may depend upon inadequacy of the inhibitory influence which the cerebral cortex normally exerts over the vaso-motor (amongst other lower) centres (Schäfer¹). And certain considerations render it probable that deficient cerebral inhibition is a factor in some cases of the paroxysmal neuroses. Gowers says: ²— ‘Convulsions occur in young children with great readiness, and have many causes. The special liability of infants is probably due to the condition of development of the nervous system. At the time of birth only parts of it are structurally complete. . . . But the lower centres are farther advanced than the higher ones, and are, in consequence, imperfectly controlled. This is probably the chief reason why reflex disturbance so readily occurs in early childhood. By far the most potent cause of convulsions in children is the constitutional condition termed “rickets.” The essential element in rickets is defective development. . . . At the time at which this constitutional state chiefly occurs, the structural development of the nervous system is complete. But it is probable that functional capacity is only fully developed after structural perfection, and the parts last developed must suffer from the general delay in development more than those parts that have been longer perfect and longer in full use. The lower motor centres in the spinal cord, medulla oblongata, and even in the cerebral cortex, are under less than the normal amount of control; they pass into a condition of over-activity, are excited by peripheral impressions with undue readiness, and thence is produced the series of symptoms of excessive reflex action, laryngismus stridulus, carpo-pedal contractions, tetany, and convulsions. It is probable that the morbid tendency is exalted by an inherited neurotic disposition.’

What is true of the temporary inadequacy of cerebral inhibition associated with childhood would be true of the permanent inadequacy associated with idiocy; and a high percentage of idiots suffer from epilepsy. Further, as already argued, post-hemiplegic epilepsy may be due to inadequate cerebral inhibition. This is rendered the more probable by the fact that it is the hemiplegia of childhood which is most frequently followed by

¹ *Text-book of Physiology*, E. A. Schäfer, vol. ii. pp. 711, 712.

² *Diseases of the Nervous System*, 1893, vol. ii. p. 769.

epilepsy, and that it is the hemiplegia of childhood which is most prone to lead to mental defect. As Gowers says,¹ 'the development of the whole brain seems to be retarded by the lesion, and the intellectual power is permanently below par.'

It is not meant to be inferred that, in all cases of post-hemiplegic epilepsy, the fits are due to inadequate inhibition of vaso-motor action. Gowers says :²—'In half the cases convulsions attended the onset of the hemiplegia.' In these the fits are doubtless due directly to the organic lesion : they are for the most part one-sided ; and 'the spasm can often be observed to commence locally in the hand or face'³ (Gowers). But 'in other cases there is an interval after the onset of the paralysis before the recurring convulsions. . . . In about a sixth of the cases the interval is more than five years. . . . It is not very rare, in cases in which the hemiplegia comes on during the first year of life, for the patient to be free until puberty, and then at thirteen, fourteen, fifteen, and sixteen the fits commence and continue. No doubt in these cases their occurrence is due to the influences which determine the frequent commencement of idiopathic epilepsy at this period'⁴ (Gowers). In such cases, at any rate, it seems reasonable to suppose that the fits are vaso-motor in mechanism and depend upon hyperpyraemia ; and that the original hemiplegic lesion operates by damaging the inhibitory functions of the cerebrum and thus increasing vaso-motor responsiveness to pyraemia.

Sherrington says that an increase of this inhibitory function 'may be associated with a temporary deprivation of volitional power, such as the condition known as hypnosis';⁵ and it is known that, by repeated hypnotic suggestion, some of the features of the hypnotic condition may be impressed upon the waking state. It is conceivable, therefore that the power of cerebral inhibition might be gradually increased through hypnotic education. Conformably, Dr. Richard Arthur says:⁶—'I am able to recall, both from my own practice and from the records of others, cases of migraine, asthma, epilepsy, gastralgia, angina pectoris, neuralgias, tic-douloureux, pleurodynia, etc., which have been cured or markedly benefited by hypnotic suggestion.' Bernheim⁷ describes a case of tic-douloureux

¹ *Epilepsy*, Gowers, 1901, p. 163. ² *Ib.* p. 156. ³ *Ib.* p. 23. ⁴ *Ib.* p. 157.

⁵ *Text-book of Physiology*, E. A. Schäfer, vol. ii. pp. 711, 712.

⁶ *Australasian Medical Gazette*, November 20, 1903, p. 530.

⁷ *Suggestive Therapeutics*, H. Bernheim, 1889, p. 397.

almost cured by suggestion in ten days ; and I know of one case of undoubted epilepsy in which the fits have quite ceased apparently as a result of hypnotism.

§ 517. But simple exaggeration of vaso-motor irritability, though seemingly present to some extent in most cases, would be inadequate alone to account for the occurrence of the paroxysmal neuroses. For the condition present is more than a simple increase of vaso-motor irritability : it is an increase of irritability which tends to result in the special variety of vaso-motor action peculiar to each of the paroxysmal neuroses. And the paroxysmal neuroses can, I think, be shown to depend upon numerous factors of extremely diverse nature and situation.

§ 518. SOME EXTRINSIC FACTORS.—The extrinsic factors of the paroxysmal neuroses may usually be regarded in the light of excitants of attacks. Not only are they numerous and diverse in their nature and strength, but their influence varies widely with the condition of the patient. We have seen that the immunity conferred by a paroxysm is at its maximum immediately thereafter, decreasing thenceforward progressively ; and, in explanation, we have assumed a progressive inter-paroxysmal increase of pyraemia. Decreasing immunity implies increasing susceptibility to exciting factors. Hence the intensity of the excitant required to evoke a paroxysm will vary widely. Towards the end of the inter-paroxysmal period a very slight degree of excitation will be sufficient. It is, indeed, questionable whether at the termination of the interval any excitation at all is necessary—whether, figuratively speaking, the carbonaceous accumulation is not then capable of exploding without external assistance. But, having regard to the insignificance of the excitants required at that time, we must recognize that such are probably ubiquitous, and that we can hardly hope to exclude their operation entirely.

Many writers have dwelt upon the insignificance of the excitants which are often capable of precipitating neurosal paroxysms. ‘Dr. Charles Féré,¹ of the Bicêtre, Paris, writing in the “*Journal de Névrologie*” of November 5, 1902, points out that though it is well known that mechanical irritation may be the cause of starting an epileptic attack, it is not generally known that the sudden normal or physiological stimulus of a

¹ *Lancet*, December 13, 1902, p. 1644.

sensory nerve may provoke an epileptic fit.' Goodhart,¹ speaking of certain respiratory neuroses, says :—' It must be said that although a certain number of cases are inexplicable explosions, yet many, perhaps most, have a local exciting cause—a cause insufficient, it may be, to produce any disagreeable effect under healthy conditions of the nervous system.'

On the other hand, at the commencement of the interparoxysmal period, an intense degree of excitation will presumably be required to induce an attack. And we may suppose that some excitants are so potent as to be capable of inducing attacks in the presence of a pyraemic condition which is approximately or absolutely normal. Excitants so potent would of course determine marked pathological prepotency.

§ 519. Extrinsic factors may be thermal, mechanical, chemical, etc. ; or they may consist of some obscure atmospheric condition. The action of exposure of the surface to cold has been already referred to.

The emanations of various kinds from animals, inanimate bodies, flowers, and so on, are dominant factors in the class of affections termed hay-fever, hay-asthma, cat- and horse-asthma, rose-asthma, rose-cold, etc.—affections associated by the closest ties with the ordinary variety of asthma : indeed, we may regard all these varieties of asthma as differing from ordinary asthma mainly in the fact that they own a proximate extrinsic factor which is clinically conspicuous.

It is in the cases in which the extrinsic factor is clinically conspicuous, that we have the clearest illustration of the necessity for a co-operation of factors in the causation of disease. The existence of the extrinsic factor in hay-fever and hay-asthma is not open to question ; and yet it seems certain that, at least in some cases of these affections, hyperpyraemia is equally essential. The following is an illustrative case :—

A medical man for the greater part of his life had been subject to hay-fever and hay-asthma : at first, he suffered from coryza with considerable inflammatory reaction and paroxysmal sneezing ; later, his attacks consisted of paroxysmal asthma. The attacks of either kind were invariably induced by hay, more especially by hay which had remained for some time in the hay-loft and was dry. About the

¹ Clifford Allbutt's *System of Medicine*, vol. v. p. 291.

age of 50, he had an attack of acute gout, and he has suffered from recurrent attacks of this disorder ever since. Now at the age of 60, *and ever since his first attack of gout*, hay has absolutely no effect upon him : he can bury his face in it and inhale strongly without the slightest unpleasant result.

It is reasonable to suppose that, in this case, the recurrent pyrexial acarbonization of acute gout removed the tendency to hay-asthma through removal of the hyperpyraemic factor, although there are certainly alternative explanations : it may have been, for example, that the hay-asthma ceased through the intervention of unknown factors, and that the cessation of the asthmatic acarbonization permitted the development of gout.

§ 520. But, as is well known, hay-fever and hay-asthma are favourably influenced by simple change of air : removal to the seaside usually, a sea voyage invariably, disperses the complaints for the time being. Here, there can be no reasonable doubt that it is the extrinsic factor which is struck out. In the following case, the disorder is seen to have been susceptible of relief by either method :—

A gentleman suffering from severe hay-fever invariably convalesced at once whenever he left Brisbane and took up his residence on the coast about twelve miles distant. But business precluded such frequent absences ; and it was found that the enforcement of a diet scale from which were excluded sugar and some of the other more highly carbonaceous food-stuffs, together with regular physical exercise, kept him quite comfortable though not entirely free from coryza. This happened even in the city of Brisbane, where he had been accustomed to suffer most severely.

A similar sequence of events was observed in a case in which hay-fever had graduated into hay-asthma. In such cases, the extrinsic factor may be regarded as determining a certain degree of pathological prepotency for the affection in question.

§ 521. It is well known that asthma—what is called pure spasmodic asthma—is, in an extreme degree, dependent upon obscure atmospheric conditions ; Salter's masterly monograph is full of examples which show that this paroxysmal neurosis may disappear instantly on a change of location, and may remain permanently absent, so long as the favourable

atmospheric environment is preserved. The following is an especially pertinent case :—

A gentleman of 40, whose official duties necessitate constant travelling throughout the length and breadth of Queensland, has suffered on and off for three years from paroxysmal asthma. He remains absolutely well while he is in the interior, when he increases rather rapidly in weight ; but he invariably commences to suffer from nocturnal asthma whenever he re-crosses the coastal ranges, no matter in what latitude. At first I was inclined to believe that the difference was to be accounted for by difference of habits, more especially as regards physical exercise. For while on the coast, he would be either on shipboard or in an office, in either case taking little or no exercise and living rather well ; and, while in the interior, he would be living less well and either riding long distances on horseback or spending much time in a bush coach, a means of locomotion by no means divorced from physical exercise. But this explanation fell to the ground ; for he found that he remained free from asthma in the towns of the interior while taking no exercise at all ; and that in the coastal towns he was affected in spite of considerable exercise. So far, the history of this case seemed fatal to the whole theory of hyperpyraemia, at least as applicable to this individual case. But the effect of dietetic treatment showed that any such conclusion would have been erroneous. For, on restricting his carbonaceous intake, more especially that of his evening meal, and taking a moderate amount of exercise between this meal and bedtime, this patient remained absolutely free from all tendency to asthma, nocturnal or other, in any of the coastal towns, even in those which were most prejudicial to him under indiscriminate eating. I should add that this patient had been treated by cauterization of the upper and posterior part of the nasal septum on several occasions, with no more than temporary benefit ; also that, after about a year of dietetic restriction, he seemed to lose his asthmatic tendency, and now lives upon an ordinary mixed diet even on the coast.

Such cases are explicable only on the view that, under certain conditions of the environment, doubtless atmospheric, asthmatic acarbonization is apt to become to some extent prepotent over physiological acarbonization, and usurps a portion of the latter's duties ; and that, the environment being altered, the physiological processes resume full sway. But that such pathological prepotency is merely relative as regards the carbon contents of the blood, is shown by the effect of carbonaceous restriction and increased katabolic decarbonization *under the mal-environment*. In other words, a pyraemia which is

normal under a non-asthmatic environment becomes excessive under an asthmatic environment.

§ 522. Reflecting upon conservative acarbonizing processes, such as hay-asthma, which manifestly own an exciting extrinsic factor, it naturally occurs to us to imagine that the organism, burdened with hyperpyraemia, takes advantage of the presence in its environment of the extrinsic irritants, just as certain plants take advantage of the chance contact of pollen-bearing insects for fertilization—in more general terms, that the organism is accustomed to utilize its opportunities as well as its capacities.

§ 523. HEREDITY.—It has long been observed of the paroxysmal neuroses that they are, in many cases, hereditary, and this in a marked degree. To a large extent this heredity is indirect, that is to say, the neurosis of the parent may appear in a different form in the offspring; but it is often direct, and this perhaps in an even greater degree.

Living¹ says of *migraine* that, although it ‘often exhibits a certain tendency to transformation in the course of hereditary transmission, and among different members of the same family, yet, in the great majority of instances, it is transmitted without any such change, and very often exactly the same type is preserved. Thus, if it is a blind megrim or transient hemianopia in the father, it is often a blind megrim in the son; if sick-headache in the mother, it is often sick-headache in the daughter, and so on.’ Suckling² regards *migraine* as the most hereditary of all complaints; and Gowers says:³—‘*Migraine* is strongly hereditary: in more than half the cases inheritance can be traced, and it is usually direct.’ Asthma is often directly hereditary. Out of 217 cases, Salter⁴ found ‘distinct traces of inheritance in 84: in 133 not.’ Of epilepsy, Gowers says:⁵—‘An inherited tendency (indicated by the presence in ancestors or collateral relations of epilepsy itself, or of insanity) is traceable in rather more than a third of the cases (35 per cent). . . . There is a family history of epilepsy in two-thirds of the inherited cases.’ And it is probable that something similar is true of the less common paroxysmal neuroses.

¹ *Megrim and Sick-headache*, 1873, p. 32.

² *On Periodical Headache or Migraine*, p. 3.

³ *Diseases of the Nervous System*, 1893, vol. ii. p. 837.

⁴ *On Asthma*, 1868, p. 116.

⁵ *Diseases of the Nervous System*, 1893, vol. ii. p. 731.

§ 524. The recognition of the hyperpyraemic factor in the paroxysmal neuroses naturally suggests that the heredity so often exhibited by these affections is to be in part explained by an hereditary tendency to hyperpyraemia. This is doubtless true: the functional factors of hyperpyraemia may, as has been argued, be hereditary in many cases (§ 224), and possibly even the food factor may present hereditary elements, such as hereditary tastes, leading to hereditary food habits. But the factors concerned in hyperpyraemia have been sufficiently dwelt upon already. What we are now considering are the factors of the paroxysmal neuroses other than hyperpyraemia—those factors which determine neurosal, as distinguished from, and in preference to, other forms of pathological acarbonization and unrelieved hyperpyraemia.

§ 525. It seems probable that this hereditary factor in the paroxysmal neuroses consists of a peculiarity of structure, macroscopic, microscopic, or molecular. Such may concern a variety of tissues and lead to a variety of results.

Of epilepsy, we may imagine the transmitted peculiarity to be some modification of the vaso-motor nervous tissues, resulting in a tendency to widespread and precipitate vaso-constriction, which leaves no time or room for adequate compensatory vaso-dilation. In addition to such special nervous proclivity, perhaps assisting it, there may be some imperfectly adjusted anatomical condition, which, under the stress of physiological usage, becomes a permanent source of irritation; for there can be no doubt that reflex sources of irritation are often factors in the paroxysms of the ordinary, so-called idiopathic, variety of epilepsy; and the adoption of a vaso-motor theory of epilepsy does not render less tenable the co-operation of such reflex influences. One such reflex influence is possibly eye-strain, another some unknown condition of the nasal mucosae: these will be considered later.

Similarly with hereditary migraine, in addition to a proclivity to extensive vaso-constriction, there may be some anatomical peculiarity, some macro- or microscopic fault connected with the eye or nasal passages, which determines the situation of the compensatory vaso-dilation. Headaches from eye-strain are commonly easy to distinguish from migraine; yet typical periodic migraine is known to have been permanently cured through the correction by glasses of a refractive

error which could hardly have been other than congenital. And the same typical neurosis has ceased to recur on the removal of spurs from the nasal passages, and on the correction of other morbid anatomical conditions in all probability largely congenital.

The hereditary factor in asthma may consist of some structural peculiarity of the mucosae, or of the nervous or vascular supply of the mucosae, concerned—a peculiarity rendering these membranes prone to a pathological degree of vaso-dilation. The same is probably true of hay-fever and hay-asthma, affections which Beard, Wyman, Morell Mackenzie, and others have shown to be undoubtedly hereditary.¹ In speaking of these two affections, I have referred hitherto to only two co-operating factors, hyperpyraemia and the extrinsic irritant. But these cannot exhaust the etiology of these disorders: otherwise all who suffer from hyperpyraemia would, at certain seasons and in certain districts, be liable to suffer, and it is certain that many such persons escape. Without doubt we must include a certain vulnerability of the mucous membranes concerned. In support whereof it has been shown that some persons intensely susceptible to hay-fever are, after intra-nasal treatment, able to visit with impunity the very districts which previously had invariably induced severe coryza. Such vulnerability is probably often congenital, and may be, in some cases, hereditary.

§ 526. But there can be no doubt in the great majority of cases of asthma, whether dependent or not upon a conspicuous extrinsic factor, that the *macroscopically healthy* nasal mucosa is most conspicuously, but in an entirely unexplained manner, connected with the pathological vaso-motor action which constitutes the disease. This is demonstrated, infallibly to my mind, by the marvellous success which, in a large proportion of cases, attends the practice, introduced by Dr. Alexander Francis, late of Brisbane, of cauterizing the mucosa covering the upper and posterior part of the nasal septum. This subject will be considered separately later. This factor has been referred to here under 'heredity'; but, since its nature is entirely unknown, we cannot, of course, deny that it may often be acquired: indeed, the history of many cases shows that such is highly probable.

¹ *Hay-fever*, by W. C. Hollopeter, 1898, pp. 52, 53, 54.

§ 527. ACQUIRED INTRINSIC FACTORS.—No one will question the statement that personal proclivity to the paroxysmal neuroses is often acquired: this is conspicuous in asthma. I have already pointed out, on the authority of Hyde Salter (§ 328), that whooping-cough, bronchitis, and measles are 'beyond a doubt the commonest of all the causes of asthma'; and to these I have added influenza and dengue. And, though all these affections are pyrexias, and therefore probably lead to asthma by inducing post-pyrexial hyperpyraemia, just as do other pyrexias, such as typhoid and malaria, yet most of them possess in addition a localized modifying influence upon the respiratory mucosae which may direct the ensuing pathological acarbonization into the respiratory channel (compare § 328). On this view, pyrexias uncomplicated by respiratory affections would be more likely to be followed by pathological acarbonizing processes other than asthma; and conversely.

I have already ascribed some neurosal paroxysms (some epileptic fits and some migraines) to the initiation of points of reflex irritation arising from congenital anatomical defects; but many points of reflex irritation are acquired, unaided by congenital malformation, and such seem capable of initiating neurosal paroxysms. At any rate, neurosal paroxysms have ceased to recur on the removal of such sources of irritation.

§ 528. This applies to epilepsy. A few cases are recorded in which epilepsy has ceased to recur on the expulsion of intestinal worms or on the removal of foreign bodies or polypi from the ear, nasal passages, or elsewhere. Tomes¹ related a case in which the removal of some decayed molars resulted in the cessation of recurrent epilepsy. Jousset reports two cases in which nasal lesions seemed responsible for epilepsy. 'One² was a man of 26, who complained of impaired nasal respiration with occasional pricking in the nose, followed by mild epileptic attacks with loss of consciousness for a few seconds. . . . On examination of the nose, a marked deviation of the septum was found, correction of which greatly diminished the frequency and severity of the attacks. The other was a woman of 30, who for a long time had suffered from occasional epileptic attacks and in whom was discovered a unilateral hypertrophic rhinitis. Reduction of the enlarged turbinates by means of the

¹ *Text-book of Medicine*, Fagge, 1891, vol. i. p. 760.

² *American Year-book of Medicine and Surgery: Surgery*, 1903, pp. 554, 555.

galvano-cautery and the use of the nasal douche completely relieved the epilepsy.'

Dr. Joseph Dreyfus¹ relates a case of recurrent major epilepsy which was apparently dependent on a lump of inspissated wax in the right auditory meatus, and refers to similar cases by Schurig and Kupper. He also points out that the presence of an acarus in the auditory canal of the dog may cause convulsive attacks.

Dr. W. N. Robertson reports the following case:—

On October 23, 1896, a boy of 7 had been suffering from epileptic fits every hour for the last fortnight: during the previous fortnight he had had three or four daily. He had post-nasal adenoids, which were removed by Dr. Francis under chloroform. Two fits occurred on the table. During the next four days, he had two or three mild fits each day. On November 13 he ceased to have fits and remained free for four years. Then the fits returned. When seen by Dr. Robertson he was having eight daily. His hypertrophied tonsils, together with some remaining adenoid and scar tissue, were removed. He was then given bromide and enjoyed another period of freedom, which however was much shorter than the first.

§ 529. In migraine and asthma also, acquired sources of reflex irritation are stated to have been found in morbid conditions of the anterior and posterior nares, such as polypi and adenoid growths, in enlargement of the tonsils, in decayed teeth, in disease of the middle and external ear, in ovarian, uterine, rectal, and other disorders. In some cases, the evidence connecting asthma with nasal disorder is peculiarly conclusive. Dr. Alexander Francis² refers to six cases in point. In the first, asthma of five and a half years' duration commenced immediately after a fall on an oil-drum which 'broke the bridge of his nose.' In the second, asthma commenced immediately after a horse-kick resulting in the same fracture. In the third, asthma developed very rapidly after an intra-nasal operation necessitating plugging. And in the fourth, fifth, and sixth, 'mechanical irritation of the nasal mucous membrane instantly induced an asthmatic paroxysm, which was quickly relieved by painting the part with a solution of cocaine.'

The same author has published nine cases of headache,

¹ *Lyon Médical*, June 10, p. 188, quoted in *Med. Review*.

² *Asthma in Relation to the Nose*, Alexander Francis, 1903, pp. 23, 24.

mostly periodic or recurrent, in eight of which the middle turbinates were enlarged and causing pressure on the septum. In these, relief of the pressure, through freeing the turbinates, resulted in a practical cure of the headaches. These cases will be referred to again, since the relief afforded is susceptible of an alternative explanation.

In headaches, whether typically migrainous or other, and in asthma, it would seem that the chances of relief from the removal of sources of peripheral irritation are much greater than in epilepsy. This follows, I think, from the fact that epilepsy, more than any other recurrent neurosal disorder, tends to be self-propagative, that is, to establish pathological prepotency through the 'memory of the body' (§ 531).

§ 530. Of cases completely cured by the removal of some source of reflex irritation, such as a polypus or an enlarged turbinated body, it might naturally be inferred that the humoral factor is quite without influence. But this would be erroneous, as I have demonstrated by a long series of observations. These observations go to show that many recurrent neuroses which are susceptible of cure or relief by treatment which can act presumably only on secondary factors, are often capable of being held in complete abeyance for long periods by treatment or circumstances which can act presumably only on the primary or humoral factor, that is, by reducing the carbon contents of the blood; and this, despite the continued operation of the aforesaid secondary factors. The following is an illustrative case:—

A clergyman who had suffered from practically lifelong migraine remained absolutely free during a rather long attack of typhoid fever. He had also been free on a few occasions for a month or so at a time, when his duties demanded constant and severe physical exercise. Fifteen years after his attack of typhoid, Dr. Hawkes operated on him for enlargement of the middle turbinateds, which was evidently of long standing, with the result that his migraine ceased immediately and had not recurred four years later. This result was attained without increased physical exercise, without any increase of weight, and without dietetic restriction. And the only possible inference is that the abnormal nasal condition had for long years so operated as to render migrainous acarbonization to some extent prepotent over physiological acarbonization.

§ 531. THE 'MEMORY OF THE BODY.'—This is one of the best recognized of the acquired intrinsic factors, and might

well have been included under that head. It is, however, so important that I have deemed it worthy of separate consideration.

It seems certain that a strong proclivity towards any special form of neurosal paroxysm may be acquired through the mere recurrence of the paroxysm, no matter in whatsoever way this was initiated. Gowers¹ says of epilepsy:—‘Each fit apparently leaves a change in the nerve-centres, facilitating the occurrence of other fits.’ Hence, as Gowers points out, the cause of the disease must be sought in the cause of the first fit; and the inference is that the disease is liable to persist after the original cause has ceased to operate. In this view there is nothing inconsistent with the theory of hyperpyraemia. We may imagine that, as time elapses, convulsive acarbonization, becoming increasingly facile, is evoked by continually decreasing degrees of hyperpyraemia, until eventually a pyraemic condition suffices, which is well within the ordinary physiological acarbonizing capacities of the organism. In such a case, the convulsions which may in the first instance have constituted an acarbonizing reinforcement, rendered necessary by perhaps a mere temporary hyperpyraemia, will have ended by usurping a portion of the duties of physiological acarbonization: in other words, convulsive acarbonization will have become to some extent prepotent over physiological acarbonization. And a similar line of argument, leading to similar conclusions, may be applied to recurrent paroxysmal neuroses other than epilepsy, to recurrent pathological acarbonizing processes other than the paroxysmal neuroses, and to some of the manifestations of unrelieved hyperpyraemia. Increased proclivity, through mere recurrence, was ascribed by Hunter to ‘the memory of the body.’

Hence it is that the transformations or metamorphoses of the neuroses, though they loom large in this work, are found, when contrasted with the recurrences of the *unchanged* neuroses, to be actually infrequent phenomena. Any organism affected with hyperpyraemia is liable to enter upon some special form of pathological acarbonization, the form being determined by the operation of secondary factors; and this special form will tend to recur thenceforward without alteration, partly no doubt through the continued operation of the secondary factors which originally determined it, but also—and this is

¹ *Diseases of the Nervous System*, Gowers, 1898, vol. ii. p. 731.

sometimes the sole cause—through a progressively accentuated ‘memory of the body.’ So we may account for the facts that in the subject of periodic migraine the special features of the paroxysm, even to the smallest detail, may be preserved over a period of many years or during life, that the asthmatic as a rule remains asthmatic, the epileptic, epileptic, and so on; although, in all cases, the patient may have periods of freedom through the intervention of some substitutive acarbonizing process of higher potency, physiological or pathological, and in a few the form of the recurrent disorder may become permanently changed through some alteration in the concurrence of secondary factors. Thomas Savill observes:¹— ‘A patient may have migraine at one time, severe flushings at another, and syncopal attacks at another, though I have generally found that there is a tendency to a recurrence of the same disorder.’ In this quotation, only one of the alternating disorders happens to be an acarbonizing process; but many examples will be found in the pages of this work in which two or more formal acarbonizing processes, mostly neurosal, e.g. migraine, asthma, angina, epilepsy, alternated in the same patient.

§ 532. Hence it is clear that in the complete etiology of any of the paroxysmal neuroses we must include a long series of negative factors. For example, a patient will be epileptic because, amongst numerous other reasons, he is not migrainous, does not suffer from asthma or from various other neurosal acarbonizing processes. Similarly with sufferers from migraine and asthma, they will suffer from these affections because, amongst a host of other reasons, they have escaped epilepsy and other acarbonizing processes.

The importance of this point of view becomes obvious when we come to investigate such questions as the relative frequency of certain diseases in the two sexes and in different geographical districts. Why, for instance, is asthma twice as common in the male sex as in the female? Probably in great part because, as Salter says,² ‘the causes of asthma are such as men are more exposed to than women’; but also, in some part, because women are more subject to other forms of neurosal acarbonization, such as sick-headaches, epilepsy, and gastralgia. And conversely, a portion of the proneness of women to the last-named disorders is due to the fact that they are less exposed to

¹ *Lancet*, June 1, 1901, p. 1518.

² *On Asthma*, 1868, p. 114.

the extrinsic causes of asthma, and therefore suffer less frequently from this respiratory acarbonizing process.

§ 533. But the paroxysmal neuroses are only one branch of the large class of pathological acarbonizing processes. Hence persons affected by any neurosal acarbonizing process so suffer because, *inter alia*, they have escaped other pathological acarbonizing processes, such as recurrent anorexia, bilious attacks, and acute gout—affections which are not prominently nervous or which, at least, are not commonly included in the class of paroxysmal neuroses. Further, it is obvious that we can hardly hope to attain the full explanation of the special proclivity of one sex or certain countries to any special hyperpyraemic affection, without a complete and accurate statistical statement of the hyperpyraemic and other acarbonizing affections of both sexes and all countries. And a similar argument may be applied with added force to the individual: hence the supreme importance of pathological life histories in all cases.

§ 534. After striking out the hyperpyraemic factor (which is often comparatively easy), the curability of the paroxysmal neuroses will be inversely as the potency of the tendency to recurrence. This, as might be anticipated, will vary with a number of conditions. Other things being equal, it will vary directly with the frequency of the recurrences and the length of time over which these have extended. Frequently recurring and old-standing neuroses will be dispersed with difficulty, if they are dispersable at all; and it may be that this rule applies with special force to cases which are hereditary. On the other hand, attacks of infrequent, especially I think irregular, recurrence and of recent origin, may be dispersed, in some cases, with extreme facility. Naturally, much depends upon the form of the recurring affection. Affections not prominently nervous, like recurrent anorexia, dyspepsia, and bilious attacks, even when long recurrent, are often amongst the most curable of disorders by the rational treatment of hyperpyraemia: the more prominently nervous and complex migraines are more resistant; while epileptic fits are probably the least curable of any.

§ 535. The extreme facility with which the organism in some cases receives a tendency to recurrent epilepsy is peculiarly well illustrated in the case related by Gowers (quoted in § 422), in which the first fit was due to accidental asphyxia, but in which fits continued to recur thereafter in the complete

absence of recurrence of this initial cause. The extreme potency of the tendency to recurrence of epilepsy, when once initiated, is well seen under conditions, such, for example, as prolonged pyrexias, which practically preclude hyperpyraemia. Louis Lenoir¹ has recently reinvestigated somewhat minutely the influence of typhoid fever upon old-standing recurrent epilepsy. He concludes that epileptic convulsions proper (major epilepsy) are diminished, but that epileptic vertiginous attacks, or 'attenuated fits,' are, if anything, somewhat increased. The diminution, often the entire cessation, of frank convulsions during pyrexia is an old and well-established observation. As regards an increase in the number of minor seizures, my own experience, so far as it goes, is not confirmatory; but I am fully prepared to admit that, in some cases, the number of these is *undiminished*.

A truly analogous phenomenon may be observed in some cases of migraine treated by Whitehead's method of wearing a tape seton. During the slight but prolonged septic pyrexia so induced, attacks of migraine proper, consisting of severe headache with complete anorexia, followed perhaps by vomiting, are largely, sometimes completely, in abeyance; but 'attenuated' attacks, consisting for the most part of the accustomed premonitory symptoms referable to the nervous system and sense organs, such as drowsiness, visual and other disturbances, are liable to recur periodically for a time at least. The same has occurred in cases treated by restriction of the carbonaceous intake.

As has so often been argued, hyperpyraemia can hardly co-exist with pyrexia of any duration or severity: hence acarbonizing epileptic convulsions and acarbonizing migrainous anorexia and vomiting are not demanded; but the inveterate tendency to recurrence is manifested by the persistence of the epileptic and migrainous 'rhythms.' A physiological parallel is the persistence of the 'menstrual rhythm'² throughout pregnancy (Harry Campbell) when, from the increased anabolic decarbonization, the presumed 'object' of the periodic discharge of blood is lacking.

But in both cases—that is to say, in the case of the prepotent pathological acarbonization of pyrexia and in the prepotent physiological acarbonization of pregnancy—the persistence

¹ *British Medical Journal*, July 27, 1901, Epitome.

² *Causation of Disease*, Harry Campbell, 1889, p. 53.

of the rhythms of the antecedent recurrent acarbonizing processes (epileptic, migrainous, and menstrual) must be regarded as an indication of deep-rooted habit. In the physiological example, the habit, *being of manifest advantage to the race*, is doubtless a result of natural selection and extends back to countless generations: in the pathological examples, the habit may be hereditary, congenital, or only acquired from the environment (using this term in its widest sense) by the individual less or more recently. Other things being equal, the duration of the habit, racial as well as individual, will determine its stability or irremovability. Accordingly, it seems hardly conceivable that we could interrupt the recurrence of the menstrual *rhythm* during the reproductive period of human life: it seems unlikely that we could interrupt the recurrence of the epileptic and migrainous *rhythms* that are hereditary, congenital, or very old-standing; but it seems not at all improbable that we might succeed in cases that are of comparatively short duration. Conformably, I have quoted from West a case in which sharp pyrexia supervened upon epilepsy of comparatively recent origin, and in which the tendency to this recurrent neurosis was apparently completely dispersed (§ 328); and in the Appendix will be found several cases in which the tendency to migraine, asthma, etc., seemed to have been removed.

§ 536. The potency of the tendency to recurrence may be gauged by the facility with which the organism responds by its accustomed paroxysm to slight exciting factors. When once a paroxysmal neurosis is firmly established, attacks may be precipitated by impressions, originating in a variety of places, and acting in a variety of ways, directly or indirectly, upon almost any portion of the vaso-motor mechanism. The impression may arise peripherally: exposure of the surface to cold may, as we have seen, precipitate attacks of almost any of the paroxysmal neuroses. But the impression may originate in the cerebrum. This may be regarded as a central origin; although it is open for us to regard the cerebrum as peripheral in its relation to the vaso-motor centre. We have seen the influence of mental emotions, such as fear and anger, in precipitating paroxysms; and it is certain that mere suggestion may, in some cases, start an accustomed neurosis. John N. Mackenzie¹ 'cites the case of a subject of hay-fever to whom

¹ *Hay-fever*, W. C. Hollopeter, 1898, pp. 39, 40.

he handed an artificial rose. Immediately an attack of rose-cold ensued. A patient, mentioned by Morell Mackenzie, while gazing upon a picture of a hay-field, was seized with an attack of hay-fever.' And in some asthmatics, in whom eating is rapidly followed by dyspnoea, the mere smell, or even the thought, of food has been known to induce an attack.

§ 537. The tendency to recurrence, which depends upon prolonged recurrence, seems to be a fundamental tendency of the organism. Yet it must not be assumed that the paroxysmal neuroses *invariably* tend, through prolonged recurrence, to gain in acarbonizing power and to become more and more prepotent over physiological acarbonization. Much depends upon the nature of the neurosis. Probably epilepsy, as a rule, tends to become increasingly prepotent in acarbonization; and this may account for the fact that epilepsy tends to persist to the end, a pathological acarbonizing process, *sui generis*, uncomplicated by other manifestations of hyperpyraemia. But there is another and an opposite tendency, which holds good of perhaps the majority of the neurosal acarbonizing processes other than epilepsy, namely, that as time passes they tend to become less efficient as acarbonizing processes—to wear out, so to speak—and to graduate into the manifestations of unrelieved hyperpyraemia (compare § 868).

The treatment of the paroxysmal neuroses, in so far as they depend upon 'the memory of the body,' is well put by Munro in referring especially to Raynaud's disease. This writer says: ¹ 'In Raynaud's disease, the vaso-motor centres have the tendency not so much to cease acting as to act with abnormal readiness. To cure this habit, it is of the utmost importance to avoid everything that favours the occurrence of an individual paroxysm. Every prolongation of the interval between the attacks is a step towards the subjugation of the habit. As the patient learns to avoid the conditions that favour the attack, he may expect to find the paroxysms occurring, not only less frequently, but also less easily, less promptly, and less severely. Each of these is a gain, and the patient's comfort and liberty are increased. When the attack occurs less frequently, the vaso-motor mechanism tends to get out of practice. When it occurs less easily, the patient can submit himself to conditions more trying than formerly, so that his liberty is increased,

¹ *Raynaud's Disease*, T. K. Munro, 1899, pp. 218, 219.

whilst the vaso-motor mechanism, having withstood these conditions, is hardened to resist others more severe. When the attacks occur less promptly, the patient may have time before its full development to adopt measures to render it abortive; and when it occurs less severely, the patient's suffering is less, and he is encouraged to persevere in his struggle. *This is true of countless neuroses.*' (Italics mine.)

§ 538. NASAL MUCOSA.—To Dr. Alexander Francis, late of Brisbane, we are indebted for what seems to me the most important of the advances which have been made in the practical therapeutics of asthma.¹ The technique of his therapeutic procedure is thus described by the author:—'After painting one side of the septum nasi with a few drops of solution of cocaine and resorcin on a pledget of cotton wool attached to a probe, I draw a line with a galvano-cautery point from a spot opposite to the middle turbinated body, forwards and slightly downwards, for a distance of rather less than half an inch. In about one week's time, I repeat the operation on the other side, and afterwards do it on alternative sides at intervals of ten days or a fortnight, as occasion requires. On each occasion, I select a fresh spot to cauterize.'

The results of this practice, including cases treated by Dr. W. N. Robertson of Brisbane, are as follows:—

Complete relief	313 cases
Great improvement	143 „
Slight or temporary improvement	40 „
No improvement	24 „
Total treated	520 „

These results are sufficiently startling. Undoubtedly, the first sentiment they tend to arouse is one of scepticism. Nevertheless, those members of the profession who are personally acquainted with the author, more especially those who have lived and worked in the same city and who have seen and followed up many of his cases, will not, I think, hesitate to accept his general results. For myself I do so with but little reservation. So well assured am I of the efficacy of the treatment, that I advise all asthmatics, whose complaint does not at once yield to a moderate dietetic restriction with moderate physical exercise, to submit to it without further delay.

¹ *Asthma in Relation to the Nose*, Alex. Francis, 1903, pub. Adlard and Son, London.

§ 539. The rationale of the result is obscure. The author soon found himself forced to abandon the view that the cautery destroys a sensory irritation in the nose, which is the starting-point of the reflex action, 'because, among other abundant and convincing evidence, as a rule the quickest and most satisfactory results were obtained in cases where the nose was apparently normal.'¹ He considers that 'asthma depends absolutely upon an unstable condition of the respiratory centre':² that some part of the nasal mucous membrane has a controlling influence upon the respiratory centre, and that the area is situated on the septum nasi;³ and that cauterization of this area is capable of restoring the stability of the respiratory centre.

These views are an almost necessary result of the author's preconception that the mechanism of the asthmatic dyspnoea consists in constriction of the bronchioles by means of contraction of their own muscular fibres. But those who accept the view that the asthmatic dyspnoea depends upon swelling of the mucosa of the bronchioles through vaso-dilation of the bronchial arteries will perhaps believe that cauterization of the septum nasi, if it increases the stability of any cerebral centre, increases the stability of the vaso-motor centre. For myself, I prefer for the present a less specific supposition, namely, that cauterization of the septum nasi has a restraining influence upon the pathological vaso-motor action which constitutes the mechanism of the asthmatic paroxysm.

§ 540. Taken in connexion with Dr. Francis's discovery, the mechanism of the paroxysmal neuroses here becomes of extreme practical importance. If the dyspnoea of asthma depend upon muscular constriction of the bronchioles, then cauterization of the septum nasi, whether it act by increasing the stability of the respiratory centre or otherwise, would in all probability be restricted in its beneficial operation to asthma alone. But if, as argued in this work, asthma is a vaso-motor neurosis and constitutes but one member of a long series of vaso-motor neuroses, all more or less closely allied to each other in their mechanism, then there seems no *à priori* reason why cauterization of the septum nasi should not be widely extended as a therapeutic measure.

Even now, there are more than indications that cauterization

¹ *Asthma in Relation to the Nose*, Alex. Francis, 1903, p. 29.

² *Ib.* p. 25.

³ *Ib.* p. 29.

of the septum nasi exerts a restraining influence upon exaggerated or disordered vaso-motor action of many varieties, over and above the variety which constitutes the mechanism of the asthmatic paroxysm. It has been argued that the phenomena of migraine, angina pectoris, epilepsy, and many other paroxysmal affections depend upon exaggerations of physiological vaso-motor variations, with or without the co-operation of compensatory cardiac changes; and that the physiological process of menstruation itself depends upon a special variation of vaso-motor action, namely, an increase of peripheral vaso-constriction or physiological tone, combined with, and to a large extent compensated by, pelvic, especially uterine, vaso-dilation. Now in none of these cases is there any question as to the stability of the respiratory centre; and yet it can, I think, be shown that local treatment, applied to the nasal mucosa, by preference perhaps to that which covers the septum nasi and by the galvano-cautery, is capable of exerting a conspicuous influence in several of these conditions.

§ 541. The factors in dysmenorrhoea are numerous and complex, but there is one factor common to all cases because essential to menstruation, namely, vascular distension or increase of localized blood-pressure in the pelvic organs. The internal organs of generation may be macroscopically healthy, there may be diseased or tender adnexa, or there may be stenosis or flexion of the cervix causing painful contractions of the uterus upon its sanguineous contents. In any of these cases, reduction of the vascular distension, and therefore of the rate of the blood-flow, will by so much reduce for the time being the pain experienced. The vascular distension, being the result of the special menstrual variation of vaso-motor action, may be reduced by modifying the vaso-motor action: for example, it may be reduced directly by reduction of the pelvic vaso-dilation or indirectly by reduction of the widespread vaso-constriction.

These deductions may be placed alongside the observations of Fliess—observations recently confirmed by Schiff.¹ 'On either side of the nasal septum, there are spots which constantly become congested, swollen, and highly sensitive during menstruation. Dysmenorrhoea can often be cut short by cocaineizing these localities, and can be permanently relieved

¹ *American Year-book of Medicine and Surgery: Surgery*, 1903, p. 423.

by the use of the thermo-cautery. Schiff reports 200 observations upon forty-seven subjects. All the women suffered from severe dysmenorrhoea, due in many instances to diseased adnexa. . . . Twelve patients were permanently relieved by the use of the thermo-cautery.'

We have seen the influence of similar procedures in asthma: presently we shall see it in some cases of angina, epilepsy, and migraine. Considered in these connexions, we can, I think, only conclude that cauterization of the septum nasi relieves pain in these cases by modifying the vaso-motor action which is essential to both eumenorrhoea and dysmenorrhoea.

§ 542. It has long been known that anginal and asthmatic seizures are prone to alternate. Further, it is by no means infrequent for seizures to occur which present some of the features of both these affections. As we have seen (§ 505), many asthmatic paroxysms are preceded, accompanied, or succeeded, by severe retro-sternal pain; which pain has been observed to shoot down the arm in some cases. Such alternations or mutual replacements and hybrid seizures are readily explicable by variations in the localization of vaso-dilation. On this view, cauterization of the septum nasi might be expected to relieve the cardiac pain, as well as the bronchial dyspnoea. This question is being investigated by Dr. W. N. Robertson, who already reports the following cases:—

Mr. M——, aged 30, suffered from asthma complicated by great pain over the cardiac region. Cauterization of the septum nasi gave prompt relief from the asthma, and the cardiac pain left him before he rose from the operating chair.

Mr. W——, aged 32, had suffered from asthma in infancy. Five years ago, the asthma returned and was speedily relieved by intranasal cauterization (1902). Two years later (1904) the asthma returned, but precordial pain now accompanied the paroxysms. Both the asthma and the precordial pain were relieved at once by the same local treatment. Four months later, there had been no recurrence of either symptom.

Mr. P. R——, aged 63, had suffered for six weeks from regular attacks of angina every morning between 4 and 4.30. He also suffered at other times on exertion. The attacks were mild but characteristic, and yielded readily to nitrites. Cauterization of the septum nasi gave prompt relief. After the first cauterization, he hurried to catch a train, and, while doing so, felt as though an attack

were coming on. To his surprise, however, it failed to appear. The same occurred on several occasions, but one month later he had had no attack. A month later still he had had 'a few little twinges of pain,' but nothing like the old attacks. Six months afterwards he remained in excellent health.

Mrs. M——, aged 30, had suffered on and off for three years from attacks, during which she felt 'as if a hat-pin were being stuck into her heart,' and as if 'her heart was being crushed.' The attack left a soreness in the cardiac region lasting two or three days. Three cauterizations of the septum nasi gave great relief. Three months later, she had had only one 'dart of pain,' and she expressed herself as feeling better than at any time during the last three years.

Mr. H——, after an attack of influenza, had several vertiginous attacks associated with, and doubtless dependent on, bradycardia. These attacks ceased and in their place he suffered from several slight (and one severe, but short-lived) anginal paroxysms. On one occasion while seated in the operating chair, he was suffering from a little cardiac pain and uneasiness. These symptoms ceased on the preliminary application of cocaine to the septum nasi. Immediately, however, on the application of the cautery, though this caused no pain locally, he had a violent, but momentary, anginal paroxysm.

These cases are mostly incomplete. They seem sufficient, however, to show that local treatment of the septum nasi is capable of exerting a marked and rapid influence upon the pathological vaso-motor action which constitutes the mechanism of some anginal seizures.

§ 543. The occasional replacement of asthma by epilepsy, and conversely, has been referred to (§ 500); and the occurrence has been explained on the view that in both affections there is a widespread vaso-constriction, compensated in the former by bronchial vaso-dilation, in the latter by vagus inhibition of the heart-beat. It would not be surprising, therefore, for cauterization of the septum nasi to exert a favourable influence in some cases of epilepsy. The following case in point is described by Dr. Alexander Francis: ¹—

'No. 399 (March 15, 1902) seemed a neurotic wreck. He had asthma for seventeen years which had become so severe that he was now unable to lie down or do any kind of work. He also suffered from epilepsy, and the fits were gradually becoming more frequent and severe. The only time he had any freedom from asthma was immediately after an epileptic fit. The more severe the manifestation of the epilepsy, the greater freedom did he experience from

¹ *Asthma in Relation to the Nose*, Alex. Francis, 1903.

asthma. He derived almost immediate relief from his asthmatic symptoms after his septal mucous membrane was cauterized, and, without any medicinal treatment, his epileptic seizures quickly became less severe and frequent. In January 1903 he reported that he had had no further trouble with asthma and *his epileptic fits had completely ceased.* (Italics mine.)

The following case in point is reported by Dr. W. N. Robertson:—

Mr. F. C——, aged 31, had suffered for seventeen years from asthma. He also suffered from epilepsy. When he had asthma, he had no epilepsy: when epilepsy, no asthma. Cauterization of the septum nasi (March 1902) gave prompt relief from the asthma with at first aggravation of the epilepsy. Then there followed relief from both affections. In June 1903 he remained very well, but had a slight recurrence of epilepsy for which his septum nasi was again cauterized. His subsequent history is unknown.

§ 544. I have as yet but one case which goes to show that cauterization of the nasal septum may exert a restraining influence upon the special variety of pathological vaso-motor action which constitutes the mechanism of the migraine paroxysm.

Mr. P. G. D——, aged about 40, had suffered from headaches for fifteen years: the attacks came on at least once a fortnight, but sometimes more frequently: the pain always affected him over one or other eye, usually over the right. His eyes had been examined frequently, but the spectacles prescribed gave no relief. Dr. Alexander Francis examined his nose, and, finding no pressure by the middle turbinated on the septum, cauterized the latter. That was on August 4, 1903. On October 15 following, there had been absolutely no recurrence of the headache.

I may, however, again refer to the series of nine cases of recurrent headache relieved by the above rhinologist by freeing the septum nasi from pressure of the middle turbinated (compare § 529). It is, perhaps, significant that, in such cases, the pressure is necessarily exerted upon the exact area, the cauterization of which affords such marked relief in many cases of asthma. Dr. W. N. Robertson tells me of a case of frequently recurring headache in which painting the middle turbinated with cocaine never fails to give great temporary relief from

pain. He is quite willing to admit, however, that this result may be due to the influence of the drug upon the adjoining septum, which indeed could hardly escape.

In concluding, I would submit that the clinical evidence adduced, fragmentary though it be, is sufficient to show that local treatment applied to the septum nasi is sometimes capable of exerting a marked influence upon some of the best-known manifestations of pathological vaso-motor action, and that this influence is for the most part, though not invariably in the first instance, of a salutary nature.

§ 545. EYE-STRAIN.—Under the head of 'Heredity,' incidental reference has already been made to the influence of eye-strain from uncorrected ametropia in epilepsy and migraine. Here this question will be considered at greater length, since recent investigations tend to the belief that the anatomical basis of eye-strain, negligible under conditions of savagery or of earlier and cruder civilizations, is a fruitful source of pathological action of various kinds under the conditions of advanced civilization, which necessarily involve prolonged use of the eyes at near range.

'G. M. Gould and Bennett¹ publish a preliminary report to demonstrate the enormous proportion of epileptic patients who suffer from morbid optical conditions. They examined the eyes of 71 epileptics of very varying ages, the majority being young or middle-aged adults, all sane and able to read, but otherwise unselected. Of these, only 3 had eyes for practical purposes optically normal. Of the remaining 68, no fewer than 67 had astigmatism, and of these, 33 (50 per cent.) had asymmetrical astigmatism, a defect which, according to the authors, almost inevitably produces the most injurious results upon the cerebral functions. The incidence of this latter condition in the patients examined is twenty or more times as great as in ordinary patients. Only 9 out of 71 patients were isometropic. The authors draw no deductions as yet, but maintain that sewing, reading, etc., with uncorrected asymmetrical or other astigmatism and anisometropia, may well be shown to share in the causation of epilepsy as of many other neuroses.'

§ 546. The first named of the above writers has adopted in his 'Biographic Clinics' what seems to me a peculiarly forceful method of bringing under the notice of the medical profession

¹ *Brit. Med. Journal*, referring to paper in *American Medicine*, September 13, 1902.

his views as to the wide and diverse pathological potentialities of eye-strain. In the work¹ referred to, and subsequently in the columns of the 'British Medical Journal'² and 'Lancet,'³ he discusses the origin of the chronic and almost lifelong ill-health of De Quincey, Carlyle, Darwin, Huxley, Browning, and Wagner. All these illustrious men suffered, through the greater part of their lives, from a series of nervous, gastric, and bilious symptoms. They all remained in fair health so long as they were taking severe physical exercise: they all relapsed when they returned to their life studies and occupied themselves mainly in reading and writing: they all suffered intensely when proof-reading. From these and other facts Gould infers that they all suffered from eye-strain due to uncorrected ametropia; and that the relief which they experienced under outdoor physical exercise was the result of the cessation of ocular accommodative effort and reflexes—of the incidental relief of eye-strain, in short.

§ 547. The medical life histories of all six, as sketched by Gould, point to prolonged hyperpyraemia, one of the chief fundamental functional factors of which was, I am inclined to think (in some of them at any rate), deficiency of fat-forming capacity. As a result of this deficiency, they were constrained to depend for physiological acarbonization to a more than average extent upon the exaggerated combustion involved in physical exercise. Upon the abatement of physical exercise necessitated by a return to study, the manifestations of hyperpyraemia appeared; and the intensity of these manifestations was proportionate, not to the mental strain involved, but to the unremitting nature of the work, that is, to the absence of physical exercise. Though the hyperpyraemic manifestations in each case presented certain differences, they were all common manifestations.

All suffered from biliousness or dyspeptic symptoms, and from nervous symptoms, such as insomnia, depression, lassitude, and vertigo: most of them were subject to migraine or headache (chiefly of the sick variety). The majority had some additional hyperpyraemic manifestation. Thus De Quincey suffered from gastralgia: Carlyle, from anginal symptoms: Browning from a tendency to asthma: Wagner, from rheu-

¹ *Biographic Clinics*, Geo. M. Gould, 1903, P. Blakiston, Son, and Co., Philadelphia, U.S.A.

² *Brit. Med. Journal*, September 19 and 26, 1903, pp. 663, 757.

³ *Lancet*, August 1, 1903, p. 306.

matism and recurrent erysipelas, the latter being preceded by depression and irritability and succeeded by return of his bright animal spirits (compare § 667) ; and Darwin succumbed to angina pectoris and atheroma (compare Chapter XXIV).

§ 548. All, as already mentioned, found physical exercise the only therapeutic measure upon which they could depend. Gould says :¹—‘No one . . . seems to have adequately pondered, at least not to have asked for the significance of, the irresistible necessity these men were under to walk or exercise. . . . All his life De Quincey walked many miles a day, walked in day and darkness, in sunshine or in rain, and in the worst time of trials he would walk round and round a ring, like a poor dumb driven animal, forty rounds to the mile, from 400 to 500 times a day. At the age of 70 he was still active and vigorous, outwalking younger men.’ ‘Carlyle² found that the sole and absolute condition of ability to read and write, as well as live, was continuous and prolonged exercise in the open air.’ Darwin, up to the age of 22, ‘had done nothing but waste, “worse than waste,” time and opportunity in hunting, walking, riding, athletics, rat-catching with dogs, etc., so that even his most kind and indulgent father said he would be a disgrace to himself and to his family.’³ During these years he remained in perfect health, except for a period of two months, when, on account of bad weather, ‘he was obliged to keep indoors without amusements other than reading. Then he became ‘inexpressibly gloomy and miserable’ and suffered from pain about the heart and palpitation. Huxley said :⁴—‘You can’t think how well I am, so long as I walk eight or ten miles a day, and don’t work too much. . . . The only thing my demon can’t stand is sharp walking.’ Browning wrote :⁵—‘You don’t know how absolutely well I am after walking.’ And Wagner said :⁶—‘We sedentary animals scarcely deserve to be called men. How many things we might enjoy if we did not always sacrifice them to that damnable “organ of sitting still” !’

§ 549. Careful dieting, even severe restriction of food, had a marked salutary influence in three of these cases. Darwin was much improved by restricted diet under Bence Jones⁷ and Andrew Clark :⁸ Huxley, under the latter physician, remained

¹ *Biographic Clinics*, Blakiston, Son, and Co., 1903, pp. 30, 31. ² *Ib.* p. 61.

³ *Ib.* p. 89.

⁴ *Ib.* p. 110.

⁵ *Ib.* p. 113.

⁶ *Lancet*, August 1, 1903, p. 307.

⁷ *Biographic Clinics*, Blakiston & Co., 1903, p. 87

⁸ *Ib.* p. 87.

in satisfactory health for two years as a result of 'cutting down food';¹ and, in the case of Wagner, a course of hydrophathy, which involved a diet mainly of dry bread, milk, and water, 'worked wonders' for a time.

§ 550. Some of the cogency of Gould's argument depends upon the fact that the mechanism of biliousness has been overlooked. As he says:²—'What is it to be bilious? I have asked many men and more books, and no two answers are alike, no two reconcilable.' If, however, the theory of hyperpyraemia is accepted, this negative source of strength will henceforth be lacking. Nevertheless, the adoption of the humoral (hyperpyraemic) hypothesis *does not by any means involve the abandonment of the hypothesis of Gould*. Many of the illustrious patients of whom he writes may well have suffered from ametropia; and the eye-strain so induced may quite possibly have been responsible for a state of increased vaso-motor irritability, and so for conditions of pathological prepotency. In this event, much of the relief from symptoms, which in their case followed physical exercise in the open air, would have been due to the incidental relief from eye-strain, and the abolition of eye-strain by properly correcting spectacles might have done much, if not all, to relieve their almost lifelong miseries.

§ 551. Many observations directly support the view that eye-strain is capable of causing increased vaso-motor irritability, and so of leading to exaggerated or disordered vaso-motor action. Thomas D. Savill, in a clinical lecture on hysterical skin symptoms and eruptions, quotes Dr. Stelwagon to the following effect:—'The action of nervous influence, direct or indirect, is shown in a case' [of urticaria] 'reported by Oliver, where the eruption was due to eye-strain, persisting or recurring when a change in lenses was necessary; his patient had been the subject of frequently recurring attacks for years, but, after suitable fitting of glasses for diminishing vision, full relief ensued; if not worn constantly, the eruption would return, to disappear upon resuming their use; later, the return was again persistent and was found due to vision changes requiring new lenses; on one occasion, a mistake was made by the optician and the eruption again appeared.'³ There is no question that the mechanism of urticaria is essentially vaso-

¹ *Biographic Clinics*, Blakiston & Co., 1903, p. 112.

² *Ib.* p. 145.

³ *Lancet*, January 30, 1904, p. 274.

motor and consists of dilation of certain cutaneous arterioles followed by exudation of serum and leucocytes (Malcolm Morris).¹

The above-quoted case, in all respects save the detail of location of the vaso-dilation, is strictly comparable with the following:—‘A healthy, clear-headed, intellectual man was given two pairs of spectacles for his myopic astigmatism, a stronger or higher correction for use at the theatre, driving, etc., a weaker correction for reading and daily or constant use. For a year, his wife and daughter observed, without telling him, that whenever he wore the strong or accommodation-exciting glasses, he “caught cold,” with coryza, hoarseness, etc., which at once disappeared when the weaker lenses were used. He used the stronger ones but few times a year. When certain of the strange coincidence, his wife told her husband. In the past ten years, the cold has been produced in this way a hundred or more times. Now, if his weaker glasses get “crooked” or maladjusted, miscorrecting his axis of astigmatism by a few degrees, his cold promptly appears, to vanish in an hour after the visit to the optician’ (George M. Gould).² In such colds, the vaso-dilation is doubtless the dominant, if not the sole, local factor: there is probably but little true inflammatory or catarrhal reaction.

§ 552. In the following case, the exaggerated vaso-dilation of the internal genitalia, responsible for dysmenorrhoea, was clearly shown to be due to eye-strain. Mr. Alban Doran,³ in dwelling upon the necessity for following up the after-history of operation cases in order to verify reported recoveries, refers to a case of severe dysmenorrhoea in which it was proposed to remove the ovaries. The symptoms, however, were relieved by the patient wearing spectacles suitable for the correction of her hypermetropia.

§ 553. It must, I think, be admitted that, in many cases, typical recurrent migraine has been abolished by the correction of ametropia by appropriate glasses, the necessary inference being that eye-strain was an essential factor of the migraine. Now the most prominent symptoms of typical migraine may be roughly divided into cephalic and digestive.

¹ *Diseases of the Skin*, Malcolm Morris, 1894, p. 63.

² *Brit. Med. Journal*, September 26, 1903, pp. 757, 758.

³ *Lancet*, January 30, 1904, p. 103.

But, as already argued, either class of symptoms may be absent: we may have, on the one hand, recurrent migrainous headache with practically no loss of appetite or digestive power: on the other, recurrent anorexia, dyspepsia, or biliousness, with complete absence of headache. In both cases, the symptoms are, according to the views here adopted, determined by vaso-dilation, which is a part of an extensive vasomotor 'storm': in the former, the vaso-dilation affects some part of the tense cranial area, giving rise to pain: in the latter, it affects the hepatic artery, causing active congestion, and later, glyco-genic distension, of the liver. Consequently, there is reason to anticipate that recurrent anorexia, dyspepsia, and biliousness will be found in some cases to own an essential factor in eye-strain from uncorrected ametropia.

This anticipation is strongly supported by an increasing accumulation of clinical evidence at my disposal, most of which I have collected since the publication of Gould's 'Biographic Clinics.' This subject is of immense importance and deserves the fullest consideration; but it is one that I regard myself as incompetent to deal with satisfactorily. Moreover, though I am conscious that my conception of the theory of pathological prepotency is clear, yet I am even more conscious that my command of language is inadequate to render that conception readily intelligible. Therefore it seems to me that I shall minimize the risk of misinterpretation by giving in some detail a fully illustrative case—the personal experience of Dr. A. J. Turner, whose name so frequently appears in these pages. There are, I am aware, objections to the inferences to be drawn from personal experiences, but these have always seemed to me outweighed by the compensating advantages. At any rate, in the present instance, the scientific accuracy and caution of the physician-patient are so widely known and appreciated throughout Australia as to call for no insistence. The subjoined history, given in Dr. Turner's own words, fully demonstrates, to me at least, the indispensability of both the humoral or supply factor and the neuro-vascular or functional factor (in this case grossly exaggerated by unconscious eye-strain) in the causation of what may be termed recurrent hepatic anorexia. Therein is fully emphasized, not only the influence on the attacks of those conditions, namely, external temperature, exercise, and diet, which, as already

argued, influence the pyraemic state, but also the influence on the attacks, of eye-strain and the relief of eye-strain, which, I am now arguing, influence the responsiveness of the vaso-motor system to the pyraemic state.

CASE OF DR. A. J. TURNER, RELATED BY HIMSELF.

§ 554. I am 42 years of age : height 5 ft. 8 $\frac{1}{4}$ ins. : weight varying from somewhat below eight stone in summer to about a stone heavier in winter. Of slight build : habits temperate and active both mentally and physically. I do a very easy medical practice with occasional intervals of busy work. My favourite recreations are gardening and entomology : at one time, I did much microscopy, but not lately. My entomological work has had an increasing fascination for me the last few years. It involves great accuracy of observation, which entails much eye-strain, but does not entail mental fatigue : indeed, I have regarded it as a mental relaxation. Habitual blood-pressure 100 mm. Hg.

§ 555. MEDICAL HISTORY.—I cannot remember any periodic attacks of any kind during childhood and youth ; and I have only had one headache in my life. As a student, I used to have cold hands in winter in spite of woollen gloves : the backs of my hands would then be purplish with salmon-pink patches ; and, on seeing for the first time a case of Raynaud's disease during a spasm, I was greatly struck by the exact resemblance presented by the hands to my own. As far as I can remember, the condition in my case was habitual, not periodic ; and I am now inclined to regard it as evidence of undue excitability of the vaso-motor system. In 1888 I arrived in Australia and spent eight months practising in Sydney. During this period, I had an extreme susceptibility to catarrhs, which would follow the slightest chill. In 1889 I arrived in Brisbane. Here I lost the tendency to catarrh and no other recurrent attacks took their place. After this, there was an interval of seven or eight years before my present troubles began.

§ 556. HISTORY OF ATTACKS.—These commenced, I think, in the summer 1898-1899 ; at any rate, I had some bad attacks in September of the latter year. About the same time in the following year, I was in North Queensland and had much microscopic work to do. My appetite then became very poor this I attributed to general overstrain. In December 1900 I returned to Brisbane and soon had a typical attack which was apparently brought on by eating an 'Irish stew' consisting chiefly of potatoes. It was then that I commenced dieting under Dr. Hare's advice. Previously, I had regarded my trouble as a 'primary dyspepsia,' and had endeavoured to excite appetite by gentian and to promote digestion by hydrochloric acid

and pepsin. I tried to overcome the anorexia, but usually the anorexia overcame me.

In January 1901 I left for England. During the voyage I was perfectly free, ate largely, and put on fat. In England I had occasional slight symptoms, but no well-marked attack. The voyage out was also marked by a large appetite, indulged without harm.

In February 1902 I returned to Brisbane in very good health, but was soon suffering again. Before the winter, I had apparently lost all the advantage gained by my long holiday. In May I recovered; and, during the winter months which followed, I gained about a stone in weight. In September my troubles began once more. In spite of careful dieting and regular exercise, I could not keep free of my enemy. My only resource was to take two or three days in the bush every month. My weight declined. In May again, I began to regain weight, and I kept well again until September 1903, when the old symptoms returned. About this time, Dr. Hare suggested that eye-strain might be a factor in my case. Accordingly, I had my eyes tested on October 15, and commenced my experience with glasses on the 17th. Up to this time, treatment had failed to do more than modify attacks. They were becoming serious (1) because they interrupted my work, owing to the loss of energy and occasionally the great physical weakness which they entailed: (2) because of the progressive loss of weight every summer; and (3) because the regularity of their recurrence and their obstinacy suggested that they might be the forerunner of serious organic disease.

§ 557. SYMPTOMS OF THE ATTACK.—At first my attacks would come on suddenly and unexpectedly, several hours after a meal, or I would awake with one in the morning. My condition was one of simple anorexia, accompanied by a sensation of fulness, heaviness, or repletion in the epigastrium. In other respects I kept in good health, could ride a bicycle, etc., on the first day of the attack. The attack would last three days, and on the third day I would be very weak, faint from want of food yet unable to eat, and the slightest exertion would be a weariness. Rather quickly, within a few hours, the anorexia would disappear, and, after one good meal, I would feel quite well again.

Occasionally, during the attack I would drink a cup of tea or take a little milk or minced meat: sometimes this gave temporary relief, but this was apt to be followed by aggravation of the symptoms. On one occasion, the sensation of repletion was so marked that I took an emetic, but my stomach was quite empty.

From the commencement of the attack, I would have cold hands and feel chilly in warm weather (cutaneous vaso-constriction): indeed, my sense of temperature became so unreliable that I used to ask people whether it was a cold or a hot day. The secretion of urine

was increased during the attacks, sometimes very markedly. There was no interference with the biliary function.

My later experience showed that by attention to epigastric sensations I could often anticipate and sometimes ward off the symptoms. The premonitory symptoms were those of a fully developed attack in slight degree. A meal always relieved the epigastric sensations at first, but, unless very sparing, much aggravated them a few hours later. These sensations were accompanied by tenderness of the epigastrium, which was sometimes intense: in the severest attack, the same tenderness was observable over the costal margin on the right side. This symptom forcibly suggested a swollen tender liver. Inability to sleep was characteristic of the worst attacks: this appeared to be due to the epigastric discomfort.

§ 558. CONDITIONS INFLUENCING THE OCCURRENCE OF THE ATTACKS.—These conditions were temperature, diet, exercise, country holidays, and sea voyages.

From May to September (cool season) I was almost free from attacks, ate a fairly liberal diet, and gained weight (nearly a stone) during the first part of the winter, retaining the increased weight until the commencement of the warm season. I would not be entirely free, for occasionally I would have slight symptoms which were easily controlled by a slight restriction of diet. The only change in my habits was a somewhat increased exercise, but during some periods in winter I might be taking no more or less exercise than during some periods in summer. In England, I had a similar freedom (not quite complete), but there were changes in my mode of life that may have had influence.

The relations to temperature were not quite exact. I was usually rather worse than usual at the beginning of May, when it was already cool, and would during that month develop a hearty appetite and gain weight rapidly, being able to eat even milk-puddings, cake, and jam, which during summer were invariably harmful. During two successive Mays, I can trace this rapid improvement as coinciding with periods of relief from eye-strain. *But, as a rule, I worked my eyes quite as hard in winter as in summer.* My period of deterioration would begin in September, when the weather, no longer bracing, was still pleasantly cool, and I would be as bad or worse then than in the hottest months. *The relation of temperature to the attacks was marked and unmistakable, if the summer and winter seasons as a whole are contrasted.*

§ 559. As to the influence of *diet* on the attacks, there is equally no doubt. By missing a meal or by reducing my diet to a very small amount, I would often succeed in avoiding an attack, or in making it much less severe. I also found that excess in carbohydrates was especially harmful; and, amongst these, sugar in any form appeared to produce the most rapid bad effects. As I am naturally fond of

porridge, potatoes, puddings, jams, cakes, etc., I repeatedly transgressed and was convinced of their harmfulness against my will by innumerable experiences. I always took a liberal allowance of proteid (meat), and, without being certain that a large excess of this was never harmful, I am certain that a liberal allowance was not. Of fats, I took a fair proportion: at one time I tried to put on weight by increasing the amount of fat consumed, but found that this was as harmful as an increase of carbohydrates.

I had at one time great hopes of curing myself by dieting, but failed. Sometimes I kept well for a few weeks on a rigid diet (restricting carbohydrates to a minimum). But usually the attempt to escape attacks in this way led to loss of weight, a slight increase in the diet led to an attack, and again to a loss of weight. Again, attacks of real hunger would lead me to eat considerably more than usual, sometimes—but by no means always—with impunity. There was some disturbing factor which I could not understand; and the diet which was to keep me at an equilibrium of weight was not to be found. Though I sometimes ate better than at others, I never once during the last two summers gained two pounds—I doubt if I ever gained one pound—in weight.

§ 560. As with diet, so with exercise, a distinct influence over the attacks was exerted. I kept up bicycling through the last hot season with benefit. When it was prevented by wet weather for several days, I usually had an attack. One of my warning symptoms was a restless desire for physical exertion of some kind; but usually this impulse came too late to be of service in averting the attack. I have, however, more than once, I believe, prevented an attack by taking a brisk ride of five or ten miles on a bicycle.

The beneficial effects of exercise were, however, limited. When pushed to the point of fatigue, it appeared to have a prejudicial effect. This happened most often in the hot weather and when I was run down by previous attacks. When an attack had once developed, exercise was useless. On the first day of the attack, I was, indeed, capable of taking a fair quantity, but it did me no good. On the second and third days, I was physically weak. Exertion seemed then to be simply drawing on my reserves of energy, which rapidly became very small, reappearing when the attack was over.

§ 561. BUSH HOLIDAYS practically always gave me relief. Sometimes the relief would be immediate: at others, I would have to be very careful of my diet the first day. After that, I had a good appetite, ate freely, and put on weight. I often developed a craving for the articles of food which most disagreed with me at home—porridge, puddings, potatoes, jam, and even treacle—and ate them freely with impunity. I was much puzzled to account for the effect of these excursions. Analysing the factors, I noted:—

§ 562. (1) Cool weather. A change to a cooler place did me most good, but, on several occasions, I derived great benefit although the weather was as hot as, or hotter than, in town.

(2) Exercise. I took much walking exercise while collecting entomological specimens. But this did not fully explain the matter, as I would often take equivalent bicycling exercise in the suburbs without the same benefit.

(3) Relief from strain and worry of practice, etc. This I could exclude, as frequently I had had a very easy time in town, occupied almost wholly by my hobbies, and yet suffered. During these times, of course, I did most work involving eye-strain.

(4) Eye-strain. This factor escaped my notice. I used my eyes a good deal in collecting, but escaped all the hardest lens work. I always resumed this work on my return to town, and my attacks soon returned.

SEA VOYAGES gave me remarkable and complete relief. They were taken in hot weather, and the factors of low temperature and exercise could be completely excluded. Relief of eye-strain seems the only satisfactory explanation.

§ 563. EYE-STRAIN.—My eyesight was good and I always worked my eyes hard and was seldom conscious of fatigue in them. Ordinary reading and writing never caused eye fatigue. Reading in the train did sometimes, and lens work always did after an hour or two.

On examination, I was found to have hypermetropia in both eyes, some astigmatism in the left eye, but none in the right. The right eye, which I had always used in lens work, gave no evidence of astigmatism when interrogated with cylinders. I did not think there was any connexion between my eye-defect and my symptoms, but was ready enough to try the experiment of glasses.

I was ordered R. +1D sph. L. +1D sph. +0.25 D cyl. axis, at first in pince-nez frames for near work. With these glasses, I could see as well at a distance as without, for a brief moment, when things went hazy. For reading, they enabled me to see well, but not comfortably. I wore them for all near work for a few days, subjecting them to the severe test of reading in the train. I soon had an attack, which I did not attribute to the glasses. But at length, after reading in the train, I had a very severe attack, accompanied by nausea and great discomfort in the eyes, together with a tendency to spasm. I was now advised to have the same lenses in spectacle frames and wear them constantly. I soon experienced the same symptoms. I then adopted different tactics, keeping my eyes closed as much as possible, carefully avoiding looking at things when going about, and doing no near work. Under this system, my general health greatly improved, appetite returned, and I put on a little of the

weight I had lost. I was sanguine of good results and did not yet realize that my improvement was due simply to not using my eyes. But, when I began to see rather better with the glasses and to use them for seeing, my symptoms returned with aggravated force. I could eat hardly anything, lost weight rapidly, got very weak, and found, after about nine days' constant wear, that I must either give up my practice or my glasses. I chose the latter. I lost six pounds in weight in the course of this experiment.

§ 564. While using these glasses, I noted several times an *immediate* effect in causing tenderness of the liver. The following is one of the most striking of these instances :—I had been on a lowly carbonaceous diet and losing weight steadily for several days, coincident with an increased use of my glasses. Notwithstanding, I was encouraged by the fact that I could see rather better with the glasses than at first, and by the hope that my difficulties with them would soon be over. I awoke in the morning at an early hour, thinking myself rather better, had a cup of weak tea, and employed myself in the garden for over an hour picking beans and gathering flowers—work which requires a great deal of eye-focussing. I managed this pretty well with my glasses and was rather pleased with my success. Unfortunately, though faint from want of food and with a long day's work before me, I found it impossible to touch a morsel of breakfast. At the same time, my epigastrium was acutely tender to pressure. I lay down with my eyes shut for an hour and could then eat a small breakfast. For the rest of the morning, I kept my eyes closed with very brief intervals of sight. I was then able to eat a good lunch and was the better for it.

I regard this attack, which occurred when the alimentary system was practically empty of food, as a purely vaso-motor one, rapidly induced and quickly subsiding. The usual attacks of three days' duration I explain as due to a glycogenic distension of the liver, due to an increase in the activity of the glycogenic function, secondary to vaso-dilation of the hepatic artery. This would explain their duration and the consequent weakness of the muscles from their lack of nutriment (dextrose), a weakness which disappeared immediately when the glycogenic block was relieved and carbohydrates once more entered the blood. The following is an illustrative instance :—I went away just as an attack was commencing, and the weather happened to be hot. I could eat no breakfast before starting. Later in the day, I was better. During that and the next day, I was fairly free from symptoms and ate more of farinaceous and sweet foods than I should have done at home. The second night, I was restless and slept badly, with frequent risings to pass water. I arose before daybreak, had some tea and two buttered scones, had a brisk bicycle ride to the station, and ate a sugar banana. At this

time I felt all right. While sitting quietly in the train *about two hours after my breakfast* and suspecting no evil, I felt the commencing symptoms. These had developed about one hour later into one of the severest attacks I ever experienced, accompanied by acute epigastric and hypochondriac tenderness and lasting the usual three days.

Briefly, I regard the attacks as vaso-motor disturbances of reflex origin, the excitant stimulus being the eye-strain, which through the vaso-motor centres caused a dilation of the hepatic artery, accompanied by peripheral vaso-motor constriction. When the irritation was extreme, as in the instance given when wearing glasses, the effect was immediate, even on an empty stomach and low diet: then it rapidly subsided. In the ordinary attacks the stimulus caused trouble only when the liver had some food material (probably carbohydrate) to deal with: these attacks might be avoided by rigid diet or brought on by too liberal diet; and once the glycolytic distension (secondary to vaso-motor dilation) was established, they would last until the glycolytic block was disposed of, a process lasting usually three days.

§ 565. After abandoning the glasses, my eyes were extremely irritable and constantly in a state of spasm, so that I had to keep them closed nearly all day. From this condition I very slowly made a very partial recovery. Nevertheless, I lost my liver trouble and gradually regained the weight I had lost: never before had I gained two pounds in town at this time of year.

I was surprised to find that, when the spasm and discomfort of my eyes was at its worst, my liver was behaving well. It was when I was unconscious of eye trouble and was using my eyes with effort—effort which was unconscious at the time—that my liver got bad. This explains my failure to recognize my eye-strain before my experience with glasses. This vaso-motor reflex does not depend on sensory irritation, but somehow results from the unconscious effort of accommodation.

§ 566. SEQUEL.—Later, I had my eyes tested in Sydney with identical result, namely, + 1D sph. both eyes, with 0.25 D cyl. left eye. I was advised + 0.5 D with the sph. for constant wear. I took to these immediately without discomfort and have worn them since constantly. Occasionally, I use the old formula (+ 1D) for near work; sometimes they worry me, sometimes they seem easy. I have had several slight attacks, but, by moderate restriction of diet and rest of the eyes, have always dispersed them within twenty-four hours. They are nothing like so severe as those I used to have. My weight keeps constant at a little over eight stone.

§ 567. There can be no doubt that, whatever would have happened eventually, the use of the glasses first prescribed in

this case increased, for the time being, the eye-strain of the patient. The inverse relation between the eye and liver symptoms was an independent and unsuggested observation on his own case by Dr. Turner: when writing out his case, he was unaware of any such observation having been previously made. It appears, however, that, according to Gould, Dr. Turner's case is merely an individual example of a general law. Gould says: '—The almost universal rule is that, the more severe the reflexes, the more certainly the eyes themselves do not complain; or conversely, the more the eyes are injured by ametropia, the less the reflexes are shunted to other organs.'

Unless the vaso-motor hypotheses advanced in this work are fundamentally fallacious, the obvious conclusions to be drawn from a careful consideration of all the details of the above case consist of the following:—

1. The patient suffered from frequently recurring glycogenic distension of the liver in a pathological degree.
2. Such distension was proximately due to dilation of the hepatic artery.
3. Such vaso-dilation was part of a widespread vaso-motor storm, consisting largely of vaso-constriction, of which the hepatic vaso-dilation might be regarded as in part correlative.
4. Such widespread vaso-motor storm depended upon an exalted irritability of the vaso-motor system, involving, *inter alia*, a grossly exaggerated responsiveness to pyraemic conditions, and constituting one form of pathological prepotency.
5. Such exalted irritability of the vaso-motor system depended very largely, if not mainly, upon unconscious eye-strain, chiefly from prolonged lens work.

§ 568. That the deficiency of fat-formation in this case depended, in great part at least, upon deficiency of supply, that is, of carbonaceous material in the blood-stream available for fat-construction, and not solely upon deficiency of function, that is, of fat-construction capacity,—is shown, I think, somewhat clearly by one of the carefully observed experiences of the patient. In order to add to his store of fat, it was only necessary to eliminate the peripheral irritation, eye-strain,

¹ 'The Rôle of Eye-strain in Civilization,' Geo. M. Gould, *Brit. Med. Journal*, September 26, 1903, p. 757.

upon which apparently depended most of the exaggerated responsiveness of the vaso-motor system to pyraemic conditions. This he achieved by keeping his eyes closed for many hours of the day and avoiding all near work at other times. The results of this manœuvre may be tabulated as follows:—

1. Cessation of the exaggerated responsiveness of the vaso-motor system to pyraemic conditions.
2. Cessation of exaggerated hepatic glycogenesis.
3. Increased delivery of sugar by the liver to the general blood-stream.
4. Cessation of recurrent glycolytic distension.
5. Increased digestion in, and absorption from, the alimentary canal, through removal of the constantly recurring hepatic block.
6. Increased supply of nutritive material of all kinds to the general circulation.
7. General increase of nutrition.

We have now seen that urticaria, certain catarrhs, dysmenorrhoea, recurrent hepatic anorexia, and migraine, all affections in which a pathological degree of vaso-dilation in different localities is an essential factor, may depend upon eye-strain from uncorrected ametropia; and there seems a possibility that some cases of epilepsy may arise from this cause. It would not be surprising, therefore, if there should be found cases of asthma and angina pectoris owning a similar causation. Hitherto, however, I have searched for such in vain.

RESULTS OF PROLONGED RECURRENCE OF THE PAROXYSMAL NEUROSES

§ 569. *Assuming the paroxysmal neuroses in question to be efficient acarbonizing processes, the results which may follow their prolonged recurrence will be of two orders, namely, humoral results, or results as regards supply, and functional results.*

HUMORAL RESULTS OR RESULTS AS REGARDS SUPPLY.—These will vary according as the neurosis in question is physiologically or pathologically prepotent. In the first case, the neurosis recurrently reduces an actual hyperpyraemia to pyraemia. In so far as it thus recurrently disperses an excess of fuel in the blood, which, being beyond the necessities

and capacities of physiological function, is acting as an incubus, it has a salutary influence on the organism. And many sufferers continue through life in perfect physical health except as regards their one recurrent disorder.

In the second case, the neurosis is recurrently reducing pyraemia to an actual hypopyraemia. In so far as it is thus recurrently wasting the fuel supply, which is no more than is required for the performance of physiological function, its influence on the organism is insalutary. The recurrent hypopyraemia was well shown in Dr. Turner's case (§ 568). On the second and third days of each attack of anorexia, there was a sensation of extreme muscular weakness; but this always entirely disappeared almost immediately after the first meal. As a result of frequently recurring hypopyraemia, the blood is frequently drawing upon the carbonaceous reserves in the tissues. At first, doubtless, the purely carbonaceous reserves (glycogen, fat) are withdrawn: later, probably, the partly carbonaceous reserves (nitrogenous tissues) are attacked: thus the actively functioning tissues are disintegrated and physiological function is weakened proportionately. Persons so affected may be reduced to the extremes of denutrition, as shown by emaciation, retarded combustion, and muscular and nervous prostration, with the ulterior consequences to which such conditions render them especially prone. One form of neurasthenia—the form which, I think, is marked by habitual low tension pulse—is a common result of the prolonged operation of pathologically prepotent paroxysmal neuroses (compare § 789). And it is more than probable that the malnutrition so engendered enters largely into the predisposition to some microbic infections and into vulnerability generally. Having argued that uncorrected ametropia is one of the commonest causes of biliousness, George Gould says: 'The rôle that biliousness and dyspepsia have played in civilization and are still to play . . . is as serious a part as those of any, possibly of all, infectious diseases combined. That, I know, seems exaggeration at first sight, but not when one reconsiders the fact that denutrition is the fundamental preparation of the "soil" for the reception of most organic and infectious diseases.'

¹ 'The Rôle of Eye-strain in Civilization,' G. M. Gould, *Brit. Med. Journal*, September 19, 1903, p. 665.

It is obvious that we could have no more efficient safeguards against actual hyperpyraemia than the frequent recurrence of such pathologically prepotent paroxysmal neuroses. Hence these affections will be preventive of affections, such as gout which depend upon actual hyperpyraemia of some duration (compare §§ 607 *et seq.*), of the manifestations of unrelieved hyperpyraemia, such as persistent high blood-pressure (see Chapter XIX), and of the degenerative affections, vascular, cardiac, and renal, which result eventually from prolonged unrelieved hyperpyraemia (see Chapter XXIV). Nevertheless, as we shall see later, paroxysmal neuroses of prolonged recurrence are often found to have been present in the life history of cases of gout, persistent high blood-pressure, and vascular, cardiac, and renal degenerations. Then we may perhaps conclude that these diseases have arisen in spite of the paroxysmal neuroses which were physiologically prepotent and, moreover, inefficient as acarbonizing processes (compare § 591).

§ 570. FUNCTIONAL RESULTS.—These will depend upon the frequent unphysiological use of tissues, structures, and organs, nervous, vascular, and other: generally, they will be ultimately degenerative, but their exact nature will, of course, depend upon the nature of the neurosis. They will be again referred to in Chapter XXIV. Meanwhile, it may be pointed out that one common result may be a tendency to the perpetuation of the neurosis in question, through a progressively accentuated 'memory of the body.' Unlike the humoral results of the paroxysmal neuroses, the functional results will not vary with physiological or pathological prepotency, except that, being dependent to a great extent upon the number of recurrences, they will tend to be most marked in those cases which are pathologically prepotent.

CONDITIONS WHICH MAY BE LEFT ON THE STOPPAGE, THROUGH MEANS OTHER THAN ACARBONIZATION, OF THE EFFICIENTLY ACARBONIZING PAROXYSMAL NEUROSES

§ 571. There is no question that, in many cases, neurosal paroxysms may be prevented from recurring by means which can operate only upon the secondary factors—those factors which determine the nature, and assist in determining the

occurrence, of the neurosis in question. Thus migraine has ceased on the correction of ametropia : asthma, on the removal of nasal polypi and on cauterization of the septum nasi : hay-asthma, on removal to the coast : epilepsy, through prolonged use of the bromides ; and angina pectoris, on intra-nasal cauterization. In these circumstances, there arises the question as to what has become of the humoral factor.

§ 572. SUBSTITUTIVE PHYSIOLOGICAL ACARBONIZATION.— On the view here adopted, namely, that pathologically prepotent neuroses usurp a portion of the duties of the physiological acarbonizing processes, it is clear that the dispersion of the former may leave the latter fully competent for their work. In such cases, there has been of course no actual, but merely a relative, hyperpyraemia : physiological acarbonization has not been lacking in capacity, but merely in opportunity. Hence, in these cases, the removal of the secondary factors essential to the neurosis will conduce to no hyperpyraemic condition : for there will have been merely a transference of work from a pathological to a physiological process : in other words, the patient will become well. The exaggeration of physiological acarbonization which ensues will often be conspicuous, but it will vary somewhat widely with the physiological capacities of the individual.

Perhaps, as a rule, the most conspicuous exaggeration of physiological acarbonization consists of an increase of fat-formation (anabolic decarbonization). In, I think, the majority of Dr. Francis's cases, relieved of asthma by cauterization of the septum nasi, there ensued a rather rapid increase of weight : in one case known to me, the patient gained two and a half stone in twelve months.

In other cases, the substitutive physiological acarbonization seems to consist mainly of an increase in the rate of combustion. I have seen many patients who, while asthmatic, suffered in the intervals of their paroxysms from the manifestations of retarded combustion, such as cold hands and feet with languid circulation, but in whom all such manifestations disappeared on removal to some district where they ceased to suffer from asthma. Such variations are, of course, open to more than one explanation. But, in many cases, the increase in combustion is beyond question, since it depends upon an amount of physical

exercise which was previously impossible. This was so in the following case:—

The patient had at one time been an ardent cyclist, but, from the pressure of business engagements, had been compelled to abandon his favourite pursuit. He then developed rather severe paroxysmal asthma, which became increasingly frequent and ultimately almost continuous. Intra-nasal cauterization resulted in rapid abatement of the disorder, so that almost immediately the patient was enabled to resume his regular cycling exercise. This undoubtedly served to maintain, if it did not initiate, the cure.

Again, the exaggeration of physiological acarbonization demanded by the suppression of an accustomed neurosis may take the form of an increase, or re-establishment, of the menstrual flow (haemorrhagic decarbonization). In one of my cases, rendered completely free from asthma by mere change of residence, the menstrual loss, from being very slight and lasting barely three days, increased to a somewhat profuse flow lasting six days. And a similar result followed in a case of migraine in which the use of spectacles had terminated completely the recurrent sick-headaches.

§ 573. SUBSTITUTIVE PATHOLOGICAL ACARBONIZATION.— On the view here adopted, namely, that the paroxysms of the physiologically prepotent paroxysmal neuroses constitute ultra-physiological or pathological reinforcements of physiological acarbonization which is inadequate to deal with the carbonaceous income, it is clear that the dispersion of the former may leave the latter incompetent for its work. In such cases, there has of course been not merely a relative, but an actual, hyperpyraemia: physiological acarbonization has been lacking in capacity, not merely in opportunity. Hence the removal of secondary factors, essential to the neurosis, will conduce to a humoral alteration which will constitute for the individual in question a condition of hyperpyraemia. This will eventuate, in many cases, in some substitutive form of pathological acarbonization.

Such substitutive pathological acarbonization may be neurosal. Salter records a case of periodic asthma of twelve years' duration, cured for the time being by residence in London; but 'from the time the asthma disappeared he became liable to occasional violent fits of spasmodic colic.'¹

¹ *Megrim and Sick-headache*, Ed. Liveing. 1873, p. 201.

Here we may suppose that the change of residence struck out from the patient's environment some factor, doubtless atmospheric, which was essential for the development of periodic asthmatic acarbonization; and that the still present hyperpyraemia, under a rearrangement of secondary factors, became recurrently dispersed by gastralgie acarbonization. I know of more than one case in which hay-asthma, always present when the grass is seeding, is completely replaced at all other seasons of the year by periodic migraine. I have seen intensely severe headaches of a migrainous type supervene on the suppression of epileptic fits by bromide of potassium. And Hobart Amory Hare insists upon the danger, in old epileptics, of inducing a maniacal outburst through suppressing the convulsions by heavy doses of the bromides (§ 810). The phenomena of the transformations or metamorphoses of the neuroses, so frequently referred to by Liveing and contemporary writers, must, for the most part, be regarded as the substitution of one form of neurosal acarbonization for another.

But the substitutive pathological acarbonizing process need not be conspicuously neurosal in character. In a case of hay-asthma, completely relieved by removal to the coast, the hyperpyraemia became recurrently dispersed by simple bilious attacks. Bilious attacks, indeed, seem especially common on the coast: Harley says¹ that many persons cannot live at the seaside for beyond a fortnight or three weeks without suffering from them. In one of Dr. W. N. Robertson's cases, cauterization of the septum nasi resulted in cessation of asthma, but immediately thereupon recurrent bilious attacks commenced. In a case of migraine, reported cured by appropriate glasses, the attacks, I afterwards discovered, had been replaced by recurrent epistaxis. In another, there was recurrent haemorrhoidal haemorrhage. In another case, intra-nasal treatment completely removed a severe paroxysmal asthma of long recurrence, but a few months later the patient experienced his first attack of acute articular gout, and this in turn became recurrent. Finally, it is manifest that pathological acarbonization takes such varied forms, that it must be always difficult to exclude it completely.

§ 574. UNRELIEVED HYPERPYRAEMIA.—If there are cases in which the dispersion of an efficiently acarbonizing

¹ *Diseases of the Liver*, George Harley, 1883, p. 244.

paroxysmal neurosis, through removal of some essential secondary factor, eventuates in some substitutive pathological acarbonizing process, then is it in the highest degree probable *à priori* that cases will sometimes occur in which such dispersion eventuates in a condition of unrelieved hyperpyraemia. For it may be that the paroxysmal neurosis dispersed was an expression of the only pathological acarbonizing capacity possessed by the organism in question. The clinical manifestations of unrelieved hyperpyraemia have yet to be considered. Meanwhile, I may state my firm conviction that the danger referred to is not an imaginary one, though it may be that it is not present in more than a small proportion of cases. It seems to have been partly appreciated by Liveing; for he points out that the abrupt cessation of an habitual migraine may be a forerunner of apoplexy;¹ and apoplexy is one of the terminal results of high blood-pressure, a common manifestation of unrelieved hyperpyraemia (§ 727). Later, I shall argue that unrelieved hyperpyraemia may supervene upon the abrupt cessation of any pathological, and of, at any rate, one physiological (menstruation), acarbonizing process.

GENERAL PRINCIPLES OF TREATMENT OF THE PAROXYSMAL NEUROSES

§ 575. It is unnecessary to point out that paroxysmal neuroses, depending upon toxic conditions, such as malaria, sepsis, etc., demand the special treatment, antitoxic or other, adapted to these conditions. Here, however, I am referring only to cases in which some degree of pyraemia is the sole humoral factor. Now it is clear that the indications for treatment will vary according as the humoral condition is one of actual or relative hyperpyraemia, that is, according as the neurosis is physiologically, or pathologically, prepotent. To distinguish between these two classes is, therefore, of great practical importance; but the full rules for such differentiation are yet to make. Probably, in many cases, we shall have to decide solely by the results of treatment—acarbonizing treatment, that is to say. Apart from this, the association of certain conditions with the paroxysmal neurosis under investigation points strongly to physiological prepotency.

¹ *Megrim and Sick-headache*, Ed. Liveing, 1873, p. 26.

§ 576. The first of these is the co-existence of corpulency or a distinct tendency thereto. It has frequently been insisted in these pages that the paroxysmal neuroses (perhaps excluding epilepsy) are far more readily dispersed by a carbonizing treatment in the corpulent than in the lean; and we have ascribed this fact to the assistance afforded by a well-developed fat-forming capacity (anabolic decarbonization). But this is probably not the sole reason; for it seems hardly possible that paroxysmal neuroses in the corpulent can be to any extent prepotent over physiological a-carbonization: at any rate, it is manifest that they cannot be so over anabolic decarbonization.

§ 577. The second associated condition, pointing to physiological prepotency, is the co-existence of hyperpyraemic manifestations *which do not depend upon exaggerated vaso-motor irritability*. The qualification is essential because it seems not unlikely that a condition of exaggerated vaso-motor irritability, responsible for pathological prepotency, might express itself in several forms concurrently. With this reservation, then, it seems clear that paroxysmal neuroses, associated with other hyperpyraemic manifestations, are more likely to be physiologically than pathologically prepotent. In other words, a pyraemic condition, which is excessive as regards more than one capacity of the organism, is more likely to amount to an actual hyperpyraemia than a pyraemic condition which is excessive as regards only one capacity.

The above considerations would seem to involve the following definitions of these two varieties of hyperpyraemia:—An actual hyperpyraemia is a pyraemia which is excessive as regards many or all of the physiological capacities or functions of the organism, the main fault lying, therefore, presumably with the humoral condition: a relative hyperpyraemia is a pyraemia which is excessive only as regards one, or perhaps a small minority, of these physiological capacities or functions, the main fault lying, therefore, presumably with the capacity or capacities (function or functions) in question.

Perhaps the hyperpyraemic manifestations most commonly associated with the paroxysmal neuroses are certain dermatoses, such as acne, eczema, and rosacea (urticaria, a conspicuously vaso-motor affection, may be omitted in this connexion for the reasons stated), haemorrhoids, gout, high blood-pressure persisting through the inter-paroxysmal periods, and certain

degenerative affections of the circulatory and renal systems. Paroxysmal neuroses so associated should for the most part be physiologically prepotent and therefore more amenable to acarbonizing treatment than uncomplicated paroxysmal neuroses. And this, I believe, will be found to be generally true. In the Appendix will be found several cases in which headaches, migrainous and other, and asthma, were associated with rosacea, acne, and haemorrhoids; and in these the neurosal affections were for the most part comparatively easy of management by acarbonizing measures.

It has been argued that pathologically prepotent neurosal acarbonizing processes are necessarily an efficient safeguard against actual hyperpyraemia; and I shall argue that articular gout depends upon a somewhat prolonged actual hyperpyraemia (§ 607). Hence neurosal acarbonizing processes which antecede, and are dispersed by, articular gout will, in all probability, be physiologically prepotent and inefficient as acarbonizers.

§ 578. The same will probably be true of neurosal acarbonizing processes which are associated with inter-paroxysmal high blood-pressure, a condition which, I shall argue, depends upon unrelieved hyperpyraemia (§ 727). Such paroxysmal neuroses will be again considered (§§ 744 *et seq.*).

In Chapter XXIV, I shall argue that renal cirrhosis is one of the terminal results of prolonged unrelieved hyperpyraemia. On this view, neurosal acarbonizing processes associated with renal cirrhosis would be physiologically prepotent in all probability. And this would be true, whether such neurosal acarbonizing processes had anteceded and led up to the renal cirrhosis, or whether they had arisen only after the development of the renal cirrhosis. In the first case, the subsequent development of renal cirrhosis might be accepted as an indication that the anteceding neurosal acarbonizing processes had been inefficient to disperse hyperpyraemia. In the second case, it might be argued that an organism, which had endured unrelieved hyperpyraemia so long as to be suffering from 'hyperpyraemic renal degeneration' without having received assistance in its efforts to attain acarbonization from neurosal acarbonizing processes, is obviously an organism which has no special proneness to neurosal acarbonization: such an organism on the contrary, would have to be regarded as one which is in

high degree resistant to neurosal acarbonization. Hence neurosal acarbonizing processes, arising in such circumstances, would presumably depend upon a high grade of hyperpyraemia; and we should anticipate, consequently, that such would be peculiarly amenable to acarbonizing treatment. Conformably, some cases are detailed in the Appendix in which recurrent headaches, asthma, etc., arose during the course of renal cirrhosis, and in which such complications were dispersed with comparative ease by restriction of the carbonaceous intake, increase of physical exercise, etc. (Cases LXXXIV and LXXXVI.)

Consistent with these anticipations and confirmatory observations is, I think, the experience of Dr. Alexander Francis in the following respect. Dr. Francis informs me that as a general rule, to which of course there are many individual exceptions, the salutary influence upon asthma of cauterization of the septum nasi is less conspicuous in the case of patients in easy circumstances than in the case of those who live by physical labour. It is, I think, obvious, other things equal, that the pyraemic would probably be the more dominant factor in the former, the responsiveness of the vaso-motor system the more dominant factor in the latter. Consequently, measures adapted to operate directly on the vaso-motor system would be more likely to be beneficial in the latter than in the former. In the former, on the other hand, the most urgent therapeutic necessity would be acarbonizing treatment.

§ 579. PHYSIOLOGICALLY PREPOTENT CASES.—In cases which are physiologically prepotent, and in which, consequently, there is an actual hyperpyraemia preceding the paroxysm, the main indication for treatment will be acarbonization of the blood. To strike out the secondary factors only would be to fasten down a more or less efficient safety-valve without providing other means of relief or guarding against a continuance of the accumulation. To attain acarbonization, we may proceed in any of the ways already mentioned. On the one hand, we may regulate the carbonaceous income, either by restricting the intake (supply) or by restricting the carbonizing process (function): on the other hand, we may seek to increase the various physiological processes of carbonaceous expenditure. Usually we shall be well advised to operate by some combination of these means; and such combinations will, of course, vary with

each individual case, especially, perhaps, with the presumed origin of the hyperpyraemia in each individual case.

§ 580. PATHOLOGICALLY PREPOTENT CASES.—In cases which are pathologically prepotent, and in which, consequently, there is a mere relative hyperpyraemia preceding the paroxysm, the main indication for treatment will be the removal of the secondary factors, or their modification if they are irremovable. But, even in these cases, acarbonizing treatment will by no means be entirely useless. The secondary factors may be undiscoverable: if discovered, they may be susceptible of modification only, not removal; or they may consist solely in ‘the memory of the body.’ In all these cases, acarbonizing treatment will be of great assistance to other therapeutic measures: of this, probably the best illustration is to be found in the *greatly increased power of the bromides in epilepsy under acarbonizing treatment of any kind.*

SUMMARY

§ 581. In this chapter, I have sought to divide the hyperpyraemic paroxysmal neuroses into two fundamental classes, namely, those which are physiologically, and those which are pathologically, prepotent.

In the former, there remains a margin of carbonaceous material or fuel in the blood over and above the amount required to satisfy the physiological demands of the organism—there is an actual hyperpyraemia, that is to say; and it is the dispersion of this excess which constitutes the function of the neurosal paroxysm. Consequently, the paroxysm, assuming it to result in efficient acarbonization, is salutary, at any rate as regards the condition of the blood.

In the latter, there is no real excess of fuel: the paroxysm depends upon an exaggerated responsiveness of the vaso-motor system to pyraemic conditions; and this functional super-irritability may be said to determine a relative hyperpyraemia. Consequently, the neurosal paroxysms exert no salutary influence, but are altogether deleterious, not only as regards function, but as regards the condition of the blood and general nutrition.

The distinction between the two conditions is arbitrary, since all intermediate gradations are to be found. Neverthe-

less, it is of high importance, since not only the treatment, but the whole subsequent evolution of the case, may depend upon the degree in which the two opposing conditions are operative, respectively. In physiologically prepotent cases, acarbonizing treatment will be essential, it may be all that is necessary; and treatment which operates merely by striking out some essential secondary factor may be actually prejudicial to the interests of the patient ultimately. In pathologically prepotent cases, acarbonizing treatment will be sometimes advantageous but never adequate; while treatment which operates by striking out some essential secondary factor may be necessary, successful, and free from all danger of subsequent injury.

The factors concerned in pathological prepotency are presumably identical with the secondary or functional factors of the paroxysmal neuroses, but their influence is more powerful than in physiological prepotency.

INDEX TO AUTHORITIES

- ADAM, James : asthma, i. 222 ; epilepsy, i. 210, 223, 346 ; vision, ii. 209
- Airy : migraine, i. 228
- Alden, W.A. : pyorrhoea alveolaris, i. 39
- Alexander, H. de M. : melancholia, ii. 213, 228, 229
- Alibert : cutaneous disease, ii. 242
- Allbutt, Clifford : arterial disease, ii. 293, 303 ; atheroma, ii. 297, 298, 335 ; blood-pressure, i. 312, ii. 149-151, 159, 160, 170, 171 ; diet, i. 29, 43, ii. 379 ; gastralgia, i. 377, 378 ; headache, ii. 131 ; neuralgia, i. 405 ; neurasthenia, ii. 201
- Allen, Chas. Lewis : neurasthenia, ii. 203
- Andral : glycosuria, i. 195
- Anstie : angina pectoris, i. 322, 327 ; asthma, i. 408 ; digestive phenomena, ii. 131 ; migraine, i. 173, 254, 277, ii. 199, 288 ; neuralgia, i. 384-386, 392, 394, ii. 80, 81
- Arthur, R. : hypnotic suggestion, i. 420
- BABCOCK : insanity, ii. 220
- Balfour : gout, ii. 5
- Ball : haemorrhoids, i. 76 ; uric-acid calculi, ii. 53
- Banks : cancer, ii. 122
- Bannatyne : gout, ii. 4 ; rheumatoid arthritis, ii. 263, 268, 269, 272, 275
- Banting : cutaneous disease, ii. 253
- Barié, M. : chromidrosis, ii. 240
- Barlow : arterio-sclerosis, ii. 301
- Barnes : insanity, ii. 215, 216, 219, 226, 228 ; menstruation, i. 363
- Bartels : Bright's disease, ii. 313
- Baruch, Herman B. : angio-neurotic oedema, ii. 238 ; secretion of urine, ii. 176
- Bauer, Prof. J. : acids in stomach, i. 42 ; cardiac disease, ii. 310 ; cutaneous disease, ii. 253 ; diet, i. 157, ii. 107 ; digestion, i. 37 ; dyspepsia, i. 69 ; liver, i. 71 ; metabolism, i. 19 ; phthisis, ii. 271 ; pyrexia, i. 197, 198, ii. 175
- Bazin : cancer, ii. 119
- Beard : hay-fever, i. 427
- Beatson : cancer, ii. 123, 124
- Beaver : cancer, ii. 124
- Becher : urea, i. 19
- Beddoes, T. B. : cephalalgia, i. 225 ; eczema, ii. 237 ; epilepsy, i. 226
- Bedford, G. : obesity, i. 237
- Beevor : albumen in urine, ii. 320 ; periodic neurosis, i. 348
- Beneke, F. W. : diet, i. 157
- Bennett, W. H. : eye-strain, i. 443 ; hydrops articularum, i. 399
- Benson : migraine, i. 291
- Bergouignan, Paul : cardiac disease, ii. 309
- Berkhart : asthma, i. 5, ii. 73 ; obesity, i. 237
- Bernard, Claude : gout, ii. 10 ; liver, i. 11, 55-57, 60, 79
- Bernheim : tic-douloureux, i. 420
- Berry : venesection, i. 314
- Bidder : secretion of bile, i. 51, 52
- Binet : phthisis, i. 200, ii. 114
- Boas, J. : cancer, i. 203
- Boerhaave : vertigo, i. 400
- Bonnaire : epilepsy, i. 248
- Bonnet : epilepsy, i. 210
- Borden : bronchitis, ii. 191
- Boubée : gout syrup, ii. 261
- Bouchard : acute rheumatism, ii. 77 ; cancer, ii. 119 ; cutaneous disease, ii. 249 ; deficient combustion, i. 174 ; diabetes, ii. 103 ; gout, i. 258, ii. 2, 7 ; liver, i. 83 ; migraine, i. 216, 232 ; obesity, i. 239
- Bourneville : epilepsy, i. 190, 248
- Bouveret : polyuria, ii. 175
- Boyd, Stanley : cancer, ii. 123
- Bracci, C. : erythromelalgia, i. 402
- Bramwell, Byron : psoriasis, ii. 237
- Breckett, E. G. : hydrops articularum, i. 399
- Bretonneau : epilepsy, i. 343
- Bristowe : gout, ii. 3 ; migraine, i. 227 ; uric acid, ii. 44, 56
- Broadbent : anaemia, ii. 153 ; angina pectoris, i. 327, ii. 300 ; atheroma, ii.

- 308; blood-pressure, i. 157, 173, 286, 294, 363, 365, ii. 113, 145, 148, 149, 151, 152, 154, 170, 171, 307, 328; convulsions, i. 346, 347, ii. 163, 164, 166, 181, 182; diabetes, ii. 161; diet, ii. 367; epilepsy, i. 222, 224, 338, 341, 342; gout, ii. 158; headache, ii. 155; hemiplegia, ii. 305; insanity, ii. 224; melancholia, ii. 226-228; neuralgia, ii. 200; obesity, ii. 156; plumbism, i. 172, ii. 162; purgation, i. 180, ii. 162; radial artery, ii. 304; rigor, i. 351; urine, ii. 175
- Brockbank: gall-stones, i. 84
- Brockway: asthma, i. 263, 307
- Brodie: asthma, i. 301; vaso-motor mechanism, i. 292
- Browne, Crichton: epilepsy, i. 336
- Bruce, Lewis C.: acute mania, ii. 219
- Bruce, Mitchell: gout, ii. 160; gouty heart, ii. 307, 308
- Brunet, D.: hemiplegia, ii. 305
- Brunton, Lauder: angina pectoris, i. 317, 328; arsenic, ii. 371; bile secretion, i. 63; blood-pressure, i. 343, ii. 150; diet, ii. 367; glycosuria, i. 354-356; headache, i. 262, 263; malaria, i. 294; migraine, i. 180, 187, 210, 277, 285, 403; ocular tension, i. 293; oxidation, i. 308; purgatives, i. 179, 180
- Brush: arterio-sclerosis, ii. 291, 293
- Bryant: venous valves, i. 58
- Buchanan, Major D. J.: tropical liver, i. 72
- Budd, Wm.: cancer, ii. 119; gall-stones, i. 83; gout, ii. 27
- Bullowa, Jesse G. M.: asthma, i. 306
- Burian: uric acid formation, ii. 28
- Burman: insanity, ii. 230
- Burnett: epilepsy, i. 342
- Burthe: renal cirrhosis, ii. 329
- Buxton: cancer, ii. 127, 128
- Buzzard: epilepsy, i. 223
- CALMÉIL:** secretion of urine, ii. 176
- Calmette: Raynaud's disease, i. 395
- Camerer: uric acid, ii. 51, 52
- Campbell, Colin M.: insanity, ii. 218; vertigo, i. 400
- Campbell, Harry: blood in starvation, i. 153; blood-pressure, ii. 170-172; bronchitis, ii. 75, 190, 192, 194; cited, i. 12; diet, i. 42 *n*, 43, 126; dyspepsia, i. 67; environment, i. 31, 32; epilepsy, i. 261; gastric juice, i. 41; glaucoma, i. 293; gout, ii. 7, 32, 87; heat production, i. 88; hypertonus, i. 276 *n*; menstruation, i. 146, 434; migraine, i. 225, 228, 232, 261; pyorrhoea alveolaris, i. 38; rheumatoid arthritis, ii. 268; urinary excretion, ii. 184
- Cantani: diet, i. 157, 181, ii. 47, 49, 367
- Carpenter: gastric juice, i. 177
- Carr, J. W.: supraemia, i. 40
- Carter: acute rheumatism, ii. 77; graduation of disease, ii. 130
- Cash: oxidation, i. 308
- Cavazzani, Prof. A.: erythromelalgia, i. 402
- Celsus: gout, ii. 8
- Chapman: emmenagogues, i. 370
- Charcot: cancer, ii. 119; dyspepsia, ii. 278; gout, ii. 7, 10, 16, 17, 22, 27; migraine ophtalmique, i. 397; rheumatoid arthritis, ii. 270; uric acid, ii. 53
- Cheadle: infantile eczema, ii. 250
- Chevers, Norman: diabetes, ii. 100
- Chiozzi: nerve-cell inanition, ii. 231
- Chittenden, Russell H.: incubus of food, ii. 360; palate, i. 164; uric acid, ii. 28, 53
- Clark, Sir Andrew: restricted diet, i. 445; asthma, i. 11, 297; phthisis, ii. 112; urticaria, ii. 248
- Claude: renal cirrhosis, ii. 329
- Clemans: angina pectoris, i. 395
- Cohnheim: blood-pressure, i. 11; cancer, ii. 128; renal cirrhosis, ii. 327-330
- Coley: cancer, ii. 125
- Comby, J.: arthritism, i. 46, ii. 279
- Cooper, Lillian: migraine, i. 188; urolithiasis, ii. 54
- Cornish, Surg.-Gen.: diabetes, ii. 99
- Cornish, Sydney: migraine, i. 243
- Cotton, F. J.: hydrops articulo-rum, i. 399
- Craig, Maurice: acute mania, ii. 228
- Crile: arterial dilation, i. 312; asphyxia, i. 343
- Crocker, Radcliffe: cutaneous disease, ii. 239, 242, 250, 254 *n*
- Croftan: renal degeneration, ii. 324
- Crofton: uric acid, ii. 47
- Crombie, Surg.-Lt.-Col. A.: blood-pressure, ii. 152; diabetes, ii. 100; respiratory exchange, i. 91; rheumatoid arthritis, ii. 265
- Cullen: gout, ii. 5
- DA COSTA: epilepsy, i. 338
- Dapper: renal cirrhosis, ii. 332
- Darwin: cited, ii. 248; theory of natural selection, i. 4
- Dawson, Bertrand: gastralgia, i. 379, haematemesis, i. 364

- Dawson, Mr. E. Rumley : haematemesis, ii. 84
- Day : migraine, i. 259
- Delipine : uratic deposits, ii. 58
- Demarquay : asthma, i. 225, 304 ; leprosy, ii. 238 ; migraine, i. 225
- de Montyel, Maraudon : epilepsy, i. 351
- de Mussy, Noel Gueneau : hay-fever, ii. 69
- Dewey, Edward Hooker : anorexia, ii. 366
- Dixon : asthma, i. 301
- Donkin : epilepsy, i. 215, ii. 132, 141 ; migraine, i. 250 ; rickets, i. 215
- Doran, Alban : dysmenorrhoea, i. 447
- Dostal : renal degeneration, ii. 324
- Draper, W. H. : lithic acid, ii. 47
- Dreyfus, J. : epilepsy, i. 429
- Dubois : phthisis, ii. 108
- du Boismont, B. : haemorrhoids, ii. 83 ; phthisis, ii. 109
- Du Bois-Reymond, Prof. : megrim, i. 218 ; vaso-constriction, i. 277, 282 ; vaso-dilation, i. 278
- Duckworth : cancer, ii. 119 ; cutaneous disease, ii. 246-248, 252 ; diabetes, ii. 295 ; gout, i. 46, 201, ii. 5, 15, 17, 19, 27, 160, 176, 179, 260, 281, 282, 370 ; hay-fever, ii. 69 ; liver, i. 359 ; renal cirrhosis, ii. 330 ; uric-acid excretion, ii. 21, 39 ; varix, ii. 311
- Dufour, M. Henri : erythema, ii. 240 ; sugar in blood, i. 105
- Duncan : menstruation, i. 142 ; pregnancy, i. 194
- Dupuytren : Raynaud's disease, i. 396
- Durante : cancer, ii. 128
- Duringe, M. : gout, ii. 8
- EBSTEIN : gout, ii. 18
- Ehrlich : diabetes, ii. 104
- Eliot, George : cited, ii. 40
- Ellis, Havelock : menstruation, i. 148
- Emmett : phthisis, ii. 109
- Engelmann, G. J. : menstruation, i. 148 ; puberty, i. 142
- Eschweiler : tumours, ii. 125
- Esquirol : epilepsy, i. 223, 248, 340
- Eulenburg : facial neuralgia, ii. 81 ; hemicrania, i. 290
- Ewart : cutaneous disease, ii. 235, 246 ; gout, i. 6, 44, 183, ii. 2, 4, 6, 13, 15, 16, 24, 25, 370 ; gouty bronchitis, ii. 75 ; paroxysmal neuroses, i. 210 ; phthisis, ii. 111 ; uric-acid excretion, ii. 21, 38, 54
- Ewing, James : plumbism, i. 172 ; renal cirrhosis, ii. 331
- Eykman : metabolism, i. 91
- FABRE : epilepsy, i. 236
- Fagge, Hilton : ague, i. 293, ii. 174, 175 ; angina pectoris, i. 318, 319, 321, 323, 417, ii. 299 ; apoplexy, i. 293 ; asthma, i. 233 ; cutaneous disease, ii. 246, 254 ; diabetes, ii. 100 ; dyspepsia, i. 67, 68 ; epilepsy, i. 241, 259, 335, 340, 341, 346 ; epistaxis, ii. 84, 86, 92 ; fever, i. 241 ; gout, ii. 1, 260 ; hay-fever, ii. 66 ; hyperaemia, i. 297 ; insanity, ii. 221, 229 ; migraine, i. 212 ; menstruation, i. 374 ; renal cirrhosis, ii. 317, 327, 329-331 ; urea, i. 88, 197 ; uric-acid excretion, ii. 56
- Falconer : gout, ii. 9
- Fearnley, W. J. : asthma, i. 236 ; cutaneous disease, ii. 243 ; diabetes, i. 256 ; glycosuria, i. 255 ; haemorrhoids, i. 77 ; rigor, i. 295
- Feder : urea, i. 18
- Fentem, Thomas : hemicrania, i. 244
- Fenwick, Soltan : periodic vomiting, ii. 131
- Féré, Charles : epilepsy, i. 248, 421 ; migraine, i. 228
- Fergusson, J. : convulsions, i. 339
- Ferrier : vaso-motor mechanism, i. 292
- Fleiner : arterio-sclerosis, ii. 295
- Fleury : epilepsy, i. 210 ; neurasthenia, ii. 203
- Fliess : dysmenorrhoea, i. 439
- Flint, Austin : carbonic acid, i. 97, 129
- Floyer, Sir John : paroxysmal neuroses, i. 326 ; pulse-rate, i. 302
- Folin : uric acid from kidneys, ii. 20
- Fordyce : gout, ii. 10 ; migraine, i. 232
- Fosbrooke : rheumatoid arthritis, ii. 273
- Foster, M. : blood in starvation, i. 153 ; blood-pressure, i. 280, 354 ; convulsions, i. 345 ; diet, i. 50 ; digestion, i. 42 ; fat-formation, i. 107 ; glycosuria, i. 50, 71, 353 ; heat production, i. 86-88, 90, 93 ; liver, i. 55, 57, 58, 60, 63 ; metabolism, i. 18, 19, 23, 24 ; muscle glycogen, i. 104 ; thirst, ii. 330 ; urea, i. 156 ; urinary excretion, ii. 173, 184, 185 ; vaso-motor mechanism, i. 292
- Fothergill, J. M. : dyspepsia, i. 44 ; erysipelas, ii. 81 ; gout, i. 327, ii. 5, 13, 14, 17, 262 ; haemorrhage, ii. 89, 90 ; liver, i. 359 ; migraine, i. 212 ; neuralgia, i. 389 ; pyrexia, ii. 79 ; paroxysmal neuroses, i. 326 ; teeth, i. 38 ; vertigo, i. 399
- Fox, Tilbury : cutaneous disease, ii. 250
- Foxwell, Arthur : asthma, i. 303 ; blood-pressure, ii. 147
- Fraenkel : arterio-sclerosis, ii. 301 ; asthma, i. 297 ; pyrexia, i. 197

- Francis, Alexander : asthma, i. 406, 427, 429, 437, 438, 441, 466 ; epilepsy, i. 229
- Frank : menstruation, ii. 83
- Fraser : epilepsy, i. 249
- Frerichs : arterio-sclerosis, ii. 295 ; diabetes, ii. 101 ; glycosuria, i. 356
- Frew, William : convulsions, i. 367 *n*
- Fuchs, R. : migraine, i. 408
- Fuller : neuralgia, i. 389
- Fürbringer : glycosuria, i. 356
- Futcher, T. B. : arterio-sclerosis, ii. 296 ; gout, ii. 20 ; renal degeneration, ii. 316
- GAIRDNER : angina pectoris, i. 327 ; gout, ii. 262 ; heart disorders, i. 402
- Galen : blood-vessels, ii. 156 ; cancer, ii. 117 ; fever, i. 252 ; venesection, ii. 86
- Gardanne : boils, ii. 242 ; haemorrhoids, ii. 83
- Garrod : albumen in urine, ii. 320 ; cutaneous disease, ii. 245, 272, 273 ; diabetes, ii. 100 ; dyspepsia, ii. 15, 278 ; gout, i. 11, 202, ii. 1, 5, 8, 9, 13, 19-21, 26, 27, 40, 258-260 ; haemorrhoids, ii. 89 ; renal cirrhosis, ii. 316 ; rheumatoid arthritis, ii. 265, 266, 268, 275 ; secretion of urine, ii. 180 ; uric acid, ii. 42, 43, 45, 49 ; uric-acid excretion, ii. 57, 185 ; uricaemia, ii. 58, 182, 322, 323
- Geddes : anabolism, i. 132
- Gendrin : haemorrhoids, ii. 83
- Gilbert, E. G. : haematuria, ii. 91
- Giles : insanity, ii. 215 ; menstruation, i. 132, 135, 137, 362, 363, 374
- Gillespie, A. Lockhart : heat production, i. 95
- Goodhart : asthma, i. 299, 376 ; bronchitis, ii. 76 ; epilepsy, i. 333 ; neurasthenia, ii. 202 ; Raynaud's disease, i. 376 ; respiratory neuroses, i. 422 ; rheumatism, ii. 77 ; sneezing, i. 376 ; swooning, ii. 132 ; uro-lithiasis, ii. 59
- Gould, G. M. : biliousness, i. 445, 446 ; erysipelas, ii. 81 ; eye-strain, i. 443, 444, 447-458, ii. 33, 70
- Gowers, Sir William : acute pain, i. 319 ; albumen in urine, ii. 320 ; amaurosis, i. 240 ; amblyopia, i. 398 ; arterio-sclerosis, ii. 301 ; convulsions, i. 341, 349, 419 ; epilepsy, i. 190, 215, 233, 234, 236, 241, 249, 251, 330, 331, 334, 336, 337, 339, 340, 347, 348, 351, 425, 431, 433, ii. 132, 133, 141, 225 ; fainting, i. 345 ; gout, ii. 10 ; hemiplegia, i. 420 ; hysteria, ii. 229 ; migraine, i. 188, 285, 291, 292, 406, 407, 418, 425 ; neuralgia, i. 385-389, 391-393 ; oculo-motor paralysis, i. 397 ; oedema, i. 293 ; vertigo, i. 399
- Graves : asthma, i. 309 ; cutaneous disease, ii. 246, 252 ; epilepsy, i. 253 ; gastralgia, i. 223, 377, 378 ; migraine, i. 232, 284 ; neuralgia, i. 391 ; venesection, i. 253, 238
- Gray, George : prickly heat, i. 99
- Griesinger : insanity, ii. 230
- Gross : cancer, ii. 117
- Grube (of Neuenahr) : arterio-sclerosis, ii. 294
- Guelineau : angina pectoris, i. 322
- Guerin : menstruation, i. 129
- Gulland : vaso-motor mechanism, i. 292
- Gunn : periodic neurosis, i. 348
- HADDON, John : colds, ii. 71
- Haig : asthma, i. 235 ; blood-pressure, ii. 154 ; diet, ii. 367 ; epilepsy, i. 264, 265, 334, 342, ii. 133 ; glycosuria, ii. 46 ; gout, ii. 111, 112 ; heart-beat, i. 280 ; liver, i. 359 ; migraine, i. 10, 187, 210, 254, 262, 284, ii. 313, 319 ; putrefaction, i. 361 ; pyrexia, ii. 175 ; recurrent febricula, ii. 80 ; rigor, i. 277 ; uric acid, ii. 51, 52 ; uric-acid excretion, ii. 21, 37-39, 41-44, 54, 55, 178, 179, 181-183, 185, 189 ; uricaemia, i. 263, ii. 45 ; uricaemia, i. 180, ii. 47
- Halford, Sir H. : abscess of liver, i. 143
- Hall, I. Walker : gout, i. 201, ii. 259 ; renal degeneration, ii. 323
- Hall, Marshall : mania, ii. 221, 226 ; paroxysmal neuroses, i. 326
- Halliburton, Prof. W. D. : muscle glycogen, i. 104, 105 ; uric-acid excretion, ii. 50
- Hamilton : malarial epilepsy, i. 350
- Hammond, G. M. : migraine, i. 47
- Hare, Hobart A. : asthma, i. 307 ; drugs, ii. 371, 372 ; epilepsy, i. 248, 343, 350, 462, ii. 112 ; insanity, ii. 219, 225 ; pyrexia, i. 198
- Harley : biliousness, i. 62-65, 69, 80, 462 ; gall-stones, i. 83 ; jaundice, i. 189
- Hawkes : angina pectoris, i. 317 ; asthma, i. 214, 217, ii. 319 ; cancer, i. 203, 258, ii. 119, 120 ; catarrh, ii. 70, (nasal) ii. 188, 189 ; cutaneous disease, ii. 243, 244 ; diet, ii. 380 ; dyspepsia, i. 47 ; eczema, ii. 239 ; epilepsy, i. 190 ; gastralgia, i. 379 ; haemoptysis, ii. 94 ; hay-fever, ii. 66, 72 ; malaria, i. 295 ; migraine, i. 244, 250, 254, 268, 284, 430 ; neuralgia,

- i. 382; obesity, i. 239; paralysis, ii. 163; puerperal pyraemia, i. 294; recurrent febricula, ii. 80; renal cirrhosis, ii. 317; rheumatism, ii. 78; rheumatoid arthritis, ii. 271; secretion of urine, ii. 176; syncope, ii. 132
- Hayem, Georges: body temperature, i. 117; plumbism, i. 172; warm skin, i. 124
- Head: ganglion nerve-cells, i. 390
- Heape: uterine changes, i. 132
- Heberden: angina pectoris, i. 322, 323; migraine, i. 235
- Heidenhain: asphyxia, i. 334
- Held: ganglion specimens, i. 390
- Hensen: glycosuria, i. 354
- Herb, R. G.: epilepsy, i. 342
- Hermann: menstruation, i. 362
- Herter, C. A.: body temperature, i. 92, 117, 118; faeces, i. 51, 52; putrefaction, i. 361; urine (post-epileptic), ii. 55
- Hertz: ague, ii. 175
- Hill, Leonard: blood-pressure, i. 274, 275, 285, 348, 354, 404, ii. 94, 149, 169, 205, 228; epilepsy, i. 332, 336, 347; tonic spasm, i. 344; vaso-motor mechanism, i. 292
- Hippocrates: body temperature, i. 171; cited, i. 11; convulsions, i. 346; epilepsy, i. 248, 340; fever, i. 252; gout, ii. 8; haemoptysis, ii. 86; purpose of disease, ii. 353
- Hirsch: haemorrhoids, i. 76
- Hochstetter: venous valves, i. 58
- Holder: menstruation, i. 148
- Holland, Sir Henry: epilepsy, ii. 14; gout, ii. 10; paroxysmal neuroses, i. 260
- Home: gout, ii. 26
- Hood, Sir C.: insanity, ii. 230
- Hood, P.: cutaneous disease, ii. 236
- Hopkins, F. Gowland: uric-acid excretion, ii. 20, 50
- Hoppe-Seyler: typhus, i. 198
- Horbaczewski: uric-acid excretion, ii. 28, 50
- Huchard, M.: bronchitis, ii. 195, 196, 198; cardiac disorder, ii. 309
- Hueppe, Prof. F.: diet, i. 31, 100
- Hunt: cutaneous disease, ii. 242
- Hunter, John: 'memory of the body,' i. 431, ii. 346
- Hunter, William: septic conditions, i. 40; vaso-motor mechanism, i. 292
- Huppert: albumen in urine, ii. 320
- Hutchinson, Jonathan: arthritis, ii. 270; cited, i. 12; disease partnership, ii. 361, 362; Raynaud's disease, i. 396
- Hutchinson, Robert: diet, i. 26, 28; fat-formation, i. 175; uric-acid excretion, ii. 38
- Huxham: gout, ii. 9
- Hyde: gout, ii. 4; rheumatoid arthritis, ii. 265, 267, 272, 274
- IRION, J. W.: eczema, ii. 241
- JACKSON, Hughlings: convulsions, i. 347; petit mal, i. 341
- Jackson, J. M.: renal tuberculosis, ii. 329
- Jacobi: malarial epilepsy, i. 350
- Jacquet: body temperature, i. 92, 117, 118
- Jamieson: cutaneous disease, ii. 242; menstruation, ii. 239
- Jenner, Sir Wm.: convulsions, i. 215
- Jipson, N. W.: asthma, i. 305
- John: blood-pressure, ii. 157
- Johnson, George: radial artery, ii. 304; renal cirrhosis, i. 273, ii. 318, 319, 328; stop-cock action, i. 11; vaso-constriction, ii. 229, 233
- Jolles: uric-acid crystals, ii. 321
- Jones, Bence: restricted diet, i. 445; secretion of urine in gout, ii. 180
- Jones, Handfield: angina, i. 327; menopause, i. 145
- Jones, Llewellyn: rheumatoid arthritis, ii. 271-273
- Jones, Maenoughton: insanity, ii. 215; menstruation, i. 133, ii. 84
- Jores (of Bonn): arterio-sclerosis, ii. 291
- Jousset: epilepsy, i. 428
- Jürgensen: body temperature, i. 94, 95, ii. 154
- KAPLIN, David M.: asthma, i. 306
- Kappler: cancer and diabetes, i. 203
- Keith, Geo. S.: angina pectoris, i. 263, 407; cancer, ii. 122; chilliness, i. 418; diarrhoea, i. 75; diet, i. 59, ii. 365; drugs, ii. 370; erysipelas, ii. 81; haematuria, ii. 90; insanity, ii. 212, 219; pyrexia, i. 241; tertian ague, ii. 76, 77; vision, ii. 208
- Kellog: uric-acid poisoning, ii. 283
- Kelynack: cancer and phthisis, ii. 121
- Kidd, Percy: phthisis, ii. 110, 111
- Kingscote: asthma, i. 251
- Klein: nasal mucosa, i. 301
- Klemperer: gout, ii. 260; renal diabetes, i. 196; uric acid, ii. 323
- Kolisch: renal degeneration, ii. 324
- Kovalesky: gout and neuroses, ii. 10
- Kraus, F.: pyrexia, i. 198
- Külz: hepatic glycogen, i. 60
- Kupper: epilepsy, i. 429
- Kussmaul: epilepsy, i. 343, 347

- LABARRAQUE: gout, ii. 10; jaundice, i. 188; megrim, i. 208, 293; pulse, i. 280; secretion of urine, ii. 176
- Labbé: malarial neuralgia, i. 394
- Laking, Sir Francis: cancer, ii. 124
- Lancereaux: epistaxis, ii. 90; hæmoptysis, ii. 87; menstruation, ii. 83, 84
- Lane, Mr.: epilepsy, i. 341
- Langerhaus: cells in pancreas, ii. 104
- Lannois: epilepsy and fever, i. 248
- Lartigue: gout pills, ii. 261
- Lauret: epilepsy and fright, i. 340
- Laycock: gout, ii. 7; teeth, i. 38
- Lebert: cancer and menopause, ii. 117
- Lecorché: cancer, ii. 119; excretion of uric acid, ii. 180; gout, ii. 19, 20
- Lemonnyer: asthma, i. 230
- Lenoir, Louis: epilepsy and fever, i. 434
- Lepasse, M. de: migraine, i. 225
- Le Roy, Bernard R.: cyclic vomiting, i. 202
- Le Souef, Mr.: rut, i. 136
- Leube: glycosuria, i. 195; uric-acid crystals, ii. 321
- Levison: uric acid, ii. 45, 46, 321; uric-acid excretion, ii. 38, 44, 53, 54
- Levy, Magnus: gout, i. 201, ii. 259, 260; body temperature, i. 92, 118
- Lewis, W. Bevan: epilepsy, ii. 40
- Leyden: pyrexia, ii. 175, 197
- Liebermeister: fall in combustion, i. 227; temperature, i. 94, 95; ii. 37, 154; urea, i. 88, 197
- Liebig: arsenic, ii. 371; cited, i. 115; diet, i. 33; muscular waste, i. 221
- Liveing, Edward: angina pectoris, i. 318, 407; arterio-sclerosis, ii. 294; choroidal hæmorrhage, i. 293; diuresis, ii. 56; epilepsy, i. 338; epistaxis, i. 252, 288, 364; gastralgia, i. 378, 382; gout, i. 202, ii. 10; hyperæmia, i. 289, 290; insanity, ii. 225; jaundice, i. 188; laryngismus stridulus, i. 403; migraine, i. 5, 212, 216, 218, 223, 234, 235, 237, 242, 261, 284, 288, 326, 392, 425, ii. 248; neural transformations, i. 206-210, 404, 462, 463; pulse-rate, i. 302
- Lobstein: angina, i. 407
- Loewy: asthma, i. 240; metabolism, i. 91; pyrexia, i. 198
- London, B.: gout, ii. 15, 30; hæmaturia, ii. 90; urethritis, ii. 68
- Love, Wilton: epilepsy, i. 249
- Luff: gout, ii. 25; uric acid, ii. 23, 49, 323
- Lugaro: nerve-cell inanition, ii. 231
- Lyman, Henry M.: gout, ii. 13
- MABON: insanity, ii. 220
- Macalister: rheumatoid arthritis, ii. 274
- MacCaskey: cancer, ii. 121
- McCrorie: arterio-sclerosis, ii. 335
- MacCulloch: brow ague, i. 293
- MacDonald, Greville: asthma, i. 314
- Mackenzie, James: blood-pressure, ii. 147, 162; Bright's disease, ii. 314, 315; epistaxis, ii. 92; menstruation, i. 363, 367, 373, ii. 83; migraine, i. 210
- Mackenzie, John N.: hay-fever, i. 435
- Mackenzie, Morell: hay-fever, i. 427, 436
- Maclagan: heat production, i. 92
- McMurphy, Helen: catarrh, ii. 66; diuresis, ii. 179; menstruation, i. 129, 135, 138, 198, 365-368, ii. 174, 209, 215, 239; nitrogen output, i. 130; tonsillitis, ii. 190
- Magnon, Mons. V.: epilepsy, i. 343
- Mahomed: Bright's disease, ii. 312; renal cirrhosis, ii. 318
- Maisonneuve: epilepsy and fright, i. 340
- Major: brain wasting, ii. 230
- Malim, J. W.: rheumatoid arthritis, ii. 270
- Manché: hepatic glycogen, i. 60
- Mangelsdorf: epilepsy, i. 190; migraine, i. 187
- Manson: tropical liver, i. 69
- Mantegazza: menstruation, i. 148
- Marcet: asthma, i. 219
- Marchal: boils, ii. 247
- Maress: uric-acid excretion, ii. 50, 53
- Marey: blood-pressure, i. 11, 275, 280, 365, ii. 150, 154, 175
- Marian: blood-pressure, ii. 157
- Martin: arterio-sclerosis, ii. 291; manometer, ii. 158
- Maudsley: mania, ii. 225, 227
- Mead: gout, ii. 13
- Menville: hæmorrhoids, ii. 83
- Meyer, Adolph: insanity, ii. 231
- Mills, Chas. K.: migraine, ii. 131
- Minskowski: uric-acid formation, ii. 28
- Mitchell, J. K.: massage, ii. 205
- Mitchell, Weir: anaemic obesity, i. 162; blood-pressure, ii. 150; cataract, ii. 208; fat-formation, i. 112; neurasthenia, ii. 204-206
- Moebius: headache, i. 32; ophthalmoplegia, i. 397
- Mohr: renal cirrhosis, ii. 332
- Moleschott: diet, i. 155
- Möllendorff: hemicrania, i. 279; hyperæmia, i. 289, 290; menstruation, i. 362; migraine, i. 11, 277, 278, 282, ii. 55
- Monakow: paralysis of insane, ii. 229

- Raynaud: gangrene, i. 396; local syncope, i. 11; vaso-constriction, i. 395, ii. 157
- Rayner, Henry: gout, ii. 5; melancholia, i. 220
- Redtenbacher: ague, ii. 174
- Reider: uratic deposits, ii. 58
- Reissman, C.: diabetes, ii. 104
- Rendu: epistaxis, ii. 87; hepatic crises, i. 360
- Reprev: metabolism, i. 20; pregnancy, i. 97
- Reubner: heat-production, i. 113
- Reynolds: epilepsy, i. 222, 223, 340
- Ribbert: cancer, ii. 128
- Richter: epilepsy, i. 326, 338
- Riegel: asthma, i. 240
- Ringer: ague, ii. 174; urea, i. 88, 197
- Ritter: excretion of bile, i. 51
- Ritti: Raynaud's disease, i. 396
- Riva-Rocci: manometer, ii. 297
- Roberts, Frederick: asthma, i. 309; gastralgia, i. 378
- Roberts, Leslie: arsenic, ii. 371
- Roberts, Sir William: diet, i. 29; excretion of urine, ii. 177; gout, ii. 2; lithic acid, ii. 49; quadriurate theory, i. 11, ii. 23, 26; palate, i. 164; renal cirrhosis, ii. 315; uro-lithiasis, ii. 57
- Robertson, Ford: nerve-cell nutrition, ii. 231, 232
- Robertson, W. N.: angina, i. 440; asthma, i. 236, 311, 437, 442, 462; epilepsy, i. 429
- Robin: phthisis, i. 200, ii. 114
- Robson, Mayo: gall-stones, i. 83; gastrotomy, i. 380
- Rogers, John, Jun.: cancer, ii. 126, 128
- Rokitansky: cancer, ii. 121
- Romberg: asthmatic aura, i. 298; epilepsy, ii. 112
- Rosenstein: convulsions, ii. 163
- Rossolino, G. J.: facial paralysis, i. 397
- Roughton, E. W.: sapraemia, i. 40
- Russell, James W.: migraine, i. 260, ii. 14; ophthalmoplegia, i. 397
- Russell, Wm.: asthma, i. 298, ii. 314; biliousness, i. 357; blood-pressure, ii. 170, 171; hypertonus, i. 276, 278; orthopnoea, ii. 307; radial artery, ii. 303, 304; renal cirrhosis, ii. 302, 328
- Ruysch, Frederick: headache, i. 245
- SAINTON: plumbism, i. 396
- Sajous: sugar in blood, i. 105
- Salisbury diet, ii. 49
- Salter, Hyde: asthma, i. 5, 47, 191, 213, 214, 217, 219-221, 223, 224, 226, 227, 230-232, 235, 236, 238, 251, 259, 260, 272, 296, 298, 300, 303-305, 307-309, 311-313, 315, 338, 406-408, 423, 425, 428, 432, 461, ii. 14, 40, 248; chronic bronchitis, ii. 190, 193; diuresis, ii. 56; dyspepsia, i. 47; haemoptysis, i. 364; neuralgia, i. 391; polyuria, i. 302, ii. 181
- Sanderson, Sir J. Burdon: pyrexia, i. 198
- Sankey: mania, ii. 211
- Saundby: cutaneous disease, ii. 246, 247; diabetes, i. 194, ii. 99-101; glycosuria, i. 60, 195, 354; lithaemic kidney, ii. 312; renal cirrhosis, ii. 302, 315, 316, 318, 324, 325; uric acid, ii. 324
- Savage, F. J.: asthma, i. 306
- Savage, Geo. Hy.: insanity, ii. 214, 216-218, 220-224, 226, 227, 230-233
- Savill, T. D.: atypical affections, i. 401; alternating disorders, i. 432; epilepsy, i. 330; gout, ii. 7; urticaria, i. 446
- Schäfer, Prof.: blood-pressure, ii. 95; combustion fluctuations, i. 95; diet, i. 33, 164; fat-formation, i. 107; gelatin, ii. 383; glycaemia, i. 355; glycosuria, i. 105, 165, 196, 354; heat production, i. 93; liver, i. 73; liver glycogen, i. 79, 353; metabolism, i. 14, 15, 17; muscle glycogen, i. 104; nerve excitation, i. 320; urea, i. 16, 18
- Scharling: carbon output, i. 97
- Schiff: dysmenorrhoea, i. 439, 440; epilepsy, i. 336; glycosuria, i. 354
- Schlöss, Heinrich: epilepsy, i. 269
- Schmidt, C.: acids in stomach, i. 42; secretion of bile, i. 51, 52
- Schrader: nitrogen output, i. 130
- Schroeder: gall-stones, i. 84
- Schultze: uric acid, ii. 44
- Schur: uric-acid formation, ii. 28
- Schurig: epilepsy, i. 429
- Schwab, Sidney: neuralgia, i. 389
- Scudamore: erysipelas, ii. 81; gout, ii. 3, 10
- Seengen: diabetes, ii. 101; glycosuria, i. 195
- Séglas: epilepsy, i. 248
- Senn: cancer, ii. 128
- Sherrington: hypnosis, i. 420
- Short: Raynaud's disease, i. 396
- Sihle, M.: blood-pressure, i. 302, ii. 167
- Simon: glycosuria, i. 195
- Simpson: acne rosacea, ii. 239
- Sinkler, Wharton: epilepsy, i. 337; lithaemia, ii. 59; migraine, ii. 369
- Smith, Eustace: gastric catarrh, i. 66, ii. 131; migraine, i. 212, 250
- Smith, E. E.: putrefaction, i. 361; urine (post-epileptic), ii. 55

- Smith, Percy: insanity, ii. 218
 Smith, Priestly: amblyopia, i. 398
 Solly: epilepsy, i. 216; migraine, i. 216
 Spender: osteo-arthritis, ii. 269, 270-272
 Spiegelburg: epilepsy, i. 236; phthisis, ii. 109; puerperal pyrexia, i. 199
 Spratling, William: epilepsy, i. 217, 223, ii. 289
 Squire, Balmanno: cutaneous disease, ii. 241
 Stadlin: menstruation, i. 137
 Stahl: haemorrhoids, ii. 83
 Starling, E. H.: blood-pressure, i. 334; asthmatic dyspnoea, i. 300
 Steele, Graham: angina, i. 407
 Steffen: pertussis, i. 340, 341
 Stelwagon, Dr.: urticaria, i. 446
 Stengel, Prof.: arterio-sclerosis, ii. 293, 297
 Stern, Heinrich: vaccination and gout, ii. 282
 Stewart, Andrew: haemoptysis, ii. 96
 Stewart, G. N.: blood-supply, i. 274; body temperature, i. 92; menstruation, i. 129; metabolism, i. 18, 19, 23, 91; nitrogen income, i. 131
 Stewart, James: arsenic, ii. 371; gout, ii. 369
 Stockvis: glycosuria, i. 356
 Stokes: venesection, i. 253
 Störck: asthma, i. 299
 Strasburger: faeces, i. 166
 Strumpfell: arterio-sclerosis, ii. 293; hydrops articulum, i. 399
 Suckling: arthritis, ii. 269, 270; migraine, i. 265, 425
 Sutherland: uric-acid crystals, ii. 321
 Sutton: insanity, ii. 215
 Svenson: body temperature, i. 92, 117, 118
 Sydenham: gout, ii. 4-6, 14, 61, 90, 261, 357; milk diet, ii. 148; purpose of disease, ii. 353
 Sykes, William: atypical affections, i. 401
 Symonds: headache and ice, i. 287
- THANE, G. Dancer: venous valves, i. 57
 Thayer, Prof.: arterio-sclerosis, ii. 291, 293
 Theilhaber: dysmenorrhoea, i. 371
 Thoma: arterio-sclerosis, ii. 291, 301; phlebo-sclerosis, ii. 311; renal cirrhosis, ii. 302, 328
 Thomas: asthma, i. 314; uric acid, ii. 42
 Thompson (of New York): epilepsy, ii. 132
 Thompson, Sir Henry: dyspepsia, i. 44; teeth, i. 37
- Thompson, W. E.: acne, ii. 251
 Thomson, J. A.: anabolism, i. 132
 Thorne, W. Bezly: cardiac degeneration, ii. 309; cutaneous veinlets, ii. 311; diet, ii. 367; melancholia, ii. 227; rheumatic fever, ii. 78; uric acid, ii. 59, 283
 Thornton: epilepsy, i. 342
 Tiegel: diet, i. 33
 Tilt: bronchitis, ii. 191; cancer, ii. 117; carbonic acid, i. 129; cutaneous disease, ii. 239, 241; diet, ii. 382; fat-formation, i. 237; gout, ii. 8-10, 12, 393; haemorrhoids, ii. 83; insanity, ii. 135, 215; menopause, i. 143, 144, 149, 234; menstruation, i. 142, 147, 369; neuralgia, i. 392; phthisis, ii. 108
 Tirard: renal cirrhosis, ii. 313, 315
 Tissot: epilepsy, i. 236; epistaxis, i. 252, 288; hemianopia, i. 293; migraine, i. 288
 Todd: renal cirrhosis, ii. 316
 Tomes: epilepsy, i. 428
 Treves, Sir Frederick: purpose of disease, ii. 353, 354
 Triper, M. M.: polyuria, ii. 175
 Trousseau: acne, ii. 239; angina pectoris, i. 192, 409, ii. 135; asthma, i. 217, 235, 305, 314; Bright's disease, ii. 315; coryza, ii. 188; convulsions, i. 252, 350; epilepsy, i. 333-335, 340, 343, 417; gall-stones, i. 83; gout, i. 201, ii. 10, 14, 210, 261, 262; haemorrhoids, i. 76, ii. 89; migraine, i. 242; menorrhagic fever, i. 146; neuralgia, i. 388; orthopnoea, i. 247; secretion of urine, ii. 176; vertigo, i. 400
 Tunnicliffe: blood-pressure, ii. 150
 Turner, A. Jefferis: case of, i. 448-455, 458; gastralgia, ii. 314; hepatic crises, i. 360; plumbism, i. 240; phthisis, ii. 108
 Tyson, James: uric acid, ii. 47
- UFFELMANN: fever, i. 198
 Ullrich: paralysis of insane, ii. 229
 Ultzmann: uric-acid crystals, ii. 321
 Umber: uric-acid excretion, ii. 51
- VALLEIX: neuralgia, i. 385, 405
 Van der Linden: migraine, i. 232
 Van Swieten: epilepsy, i. 248; gout, i. 202, ii. 6
 Van Valzah: periodic vomiting, ii. 131
 Velpeau: menstruation, i. 148
 Vergeby: angina pectoris, i. 216
 Vicaredi: gestation, i. 97
 Voisin: aura, i. 348; epilepsy, i. 190, 248, 361; haemorrhage, i. 344

- Voit : diet, i. 155 ; metabolism, i. 17, 19, 23 ; urea, i. 18
 Von Basch : manometer, ii. 297
 Von Jaksch : uric-acid, ii. 45, 46, 323
 v. Mering : sugar in blood, i. 196
 Von Noorden : glycosuria, i. 355, 356 ; gout, i. 201, ii. 28
 Von Rad, C. : angio-neurotic oedema, ii. 238

 WADE, Sir F. W. : pregnancy, ii. 66
 Walker, Geo. S. : insanity, ii. 215
 Wallace, J. Sim : teeth, i. 38
 Wallian, Samuel S. : asthma, i. 226 ; bronchitis, ii. 197 ; eczema, ii. 238 ; epilepsy, i. 226 ; migraine, i. 225 ; nasal catarrh, ii. 187 ; neuralgia, i. 392 ; neurasthenia, ii. 203
 Walshe : cancer, ii. 117
 Watson, Capt. T. E. : migraine, i. 244
 Watson, Chalmers : gout, ii. 17
 Watson, Forbes : urea, i. 19
 Watson, Sir Thomas : ague, ii. 174, 175 ; asthma, i. 247 ; skin in fever, ii. 245 ; phthisis, ii. 112
 Weber : hyperaemia in asthma, i. 297
 Weeks : epilepsy, i. 223
 Weintrand : uric-acid excretion, ii. 51
 West, Charles : asthma, i. 417 ; eczema, ii. 248 ; menstruation, i. 134, 142
 West, Samuel : albumen in urine, ii. 320 ; asthma, i. 240 ; gout, ii. 314
 Wherry, Geo. : cataract, ii. 208
 White, Hale : gastralgia, i. 380
 Whitehead, Walter : menstruation, i. 234 ; migraine, i. 243, 246 ; operation cited, ii. 192 ; seton treatment, i. 434

 Whittaker, James T. : asthma, ii. 371
 Whytt, Robert : paroxysmal neuroses, i. 326 ; secretion of urine, ii. 176
 Wiederhold : neurasthenia, ii. 202
 Wield : haemoptysis, ii. 97
 Wilks, Sir Samuel : vaso-dilation, i. 278
 Williams, Sir John : cancer, ii. 124
 Williamson : arterio-sclerosis and diabetes, ii. 294, 295 ; boils, ii. 247 ; diabetes, i. 256, 257 ; ii. 100, 102 ; dyspepsia, i. 68 ; glycosuria and phthisis, i. 195
 Wilson, Erasmus : cutaneous disease, ii. 250
 Wilson, Robert : gout, i. 202
 Winternitz : vaso-dilation, i. 90
 Wood, Horatio C. : epilepsy, i. 334, 342, 347 ; milk diet, ii. 148 ; sun-stroke, i. 99
 Woodforde, R. E. H. : acne vulgaris, ii. 247
 Woods-Hutchinson : gout, ii. 3 ; uric-acid, ii. 53, 54
 Wyman : hay-fever, i. 427
 Wynter, W. Essex : epistaxis, ii. 94 ; haematemesis, i. 380

 YEO, Burney : diet, i. 33, 155, 162 ; gout, ii. 2 ; gouty headache, ii. 284 ; rickets, i. 215

 ZIEGLER, Ernst : cell-protoplasm, i. 88 ; hyperaemia, ii. 74
 Zola, Emile : cited *re* secretion of urine, ii. 173

INDEX OF SUBJECTS

- ABSCISS**, climacteric, i. 143
 insanity and, ii. 217
Acarbonization. *See* Pathological,
 Physiological acarbonization
Accretion, carbonaceous, i. 24
 nitrogenous, i. 20
Acids in stomach, i. 42 *n*
Acne, amenorrhoea and, ii. 241
 combustion and, ii. 237
 diabetes and, ii. 246, 247
 diet and, ii. 144, 250-252
 epilepsy and, ii. 249
 fibricula and, ii. 243
 gout and, ii. 235, 245
 menopause and, ii. 242
 menstruation and, ii. 239
 paroxysmal neuroses and, i. 464
 phthisis and, ii. 244
 puberty and, ii. 256
 seton wearing and, ii. 244
 typhoid and, ii. 243
Acroparaesthesia, i. 401
Adenoids, arthritic children and, ii.
 280
 catarrhs and, ii. 189
Ague, brow, i. 293
 dietetic treatment of, ii. 77
 diuresis and, ii. 174
 double tertian, i. 293
Air, phthisis and, ii. 107
Albuminuria, arthritic children and, ii.
 280
 asthma and, ii. 319
 drugs and, ii. 370
 epilepsy and, ii. 320
 gout and, ii. 320, 323
 migraine and, ii. 319
 renal disease and, ii. 321
Alcohol, gout and, ii. 3
 hyperpyraemia and, i. 165
Amaurosis, lead-colic and, ii. 211
 plumbism and, i. 240
Amblyopia, i. 397
Amenorrhoea, i. 139-141
 acne and, ii. 241
 insanity and, ii. 215, 216
 phthisis and, ii. 108
Ametropia, i. 178
 migraine and, i. 447
Anabolic decarbonization, i. 102-127,
 158, 167, 179; ii. 337, 341
 correlation of katabolic, haemor-
 rhagic, and, i. 145-149
 deficient, i. 174-176
 divisions of, ii. 138
 menstruation and, ii. 82
 process of, a, i. 112, 113
Anabolism, i. 199, 200
 carbonaceous, i. 24
 glycosuria and, i. 194
 nitrogenous, i. 20
 pathological, i. 202-204; ii. 167
 pyrexia and, i. 199
Anaemia, blood-pressure and, ii. 153
 cerebral, i. 291
 convulsions and cerebral, ii. 164
 epilepsy and cerebral, i. 336, 343-
 348
 iron in, ii. 369
 uric acid and, ii. 46, 47
 venesection causing, ii. 364
Angina pectoris, i. 9, 192, 201, 316-329
 alterations of, i. 207
 arterial degeneration and, ii. 296
 cancer and, i. 258
 combustion and, i. 226
 coughing and, i. 322
 defaecation and, i. 322
 degeneration [cardiac] in, ii. 288
 diabetes and, i. 256
 diet and, i. 216, 263, 265-267
 diuresis and, i. 176
 drugs and, i. 321; ii. 370, 371
 epilepsy and, i. 409
 exercise and, i. 222, 260, 322-325
 fat-formation and, i. 237, 239
 flatulent distension of stomach and,
 i. 327
 gout and, i. 209; ii. 10, 281
 gradation of, ii. 134
 hypnotism and, i. 420
 illustrative cases, ii. 444-451
 malaria and, i. 327
 menstruation and, i. 234, 367

- Angina pectoris, neuralgia and, i. 392
 organic changes of heart and, ii. 299-301
 oxygen inhalation and, i. 226
 plumbism and, i. 241
 pyrexia and, i. 250, 325
 Raynaud's disease and, i. 395
 renal cirrhosis and, ii. 315
 rheumatoid arthritis and, ii. 271
 sex and, ii. 32
 symptoms, i. 319, 321
 syncope and, i. 326
 temperature and, i. 321, 322
- Anisometropia, epilepsy and, i. 443
- Anorexia, anaemia and, i. 141
 arthritic children and, ii. 280
 asthma and, i. 191, 192
 cyclic vomiting and, i. 202
 eye-strain and, i. 448
 food-restriction and, ii. 365, 366
 gastralgia and, i. 189, 191, 260
 liver and, i. 64
 menstruation and, i. 135, 235, 366
 migraine and, i. 187, 189, 191, 260
 plumbism and, i. 240
 recurrent, i. 66, 448
- Aortic atheroma, ii. 307, 308
- Aphasia, i. 397
- Apoplexy, heat, i. 99
- Arsenic, beneficial influence of, ii. 371
- Arterial degeneration, ii. 290-306
 angina pectoris and, ii. 296
 asthma and, ii. 294
 conservative view of, ii. 304-306
 gout and, ii. 294
 humoral factor, ii. 292-297
 kidney disease and, ii. 296
 malaria and, ii. 292
 mechanical factor, ii. 297-304
 migraine and, ii. 293, 294, 301
 premature physiological, ii. 306
 syphilis and, ii. 292
- Arterial disease. *See* Arterial degeneration
- Arterio-sclerosis, blood-pressure and, ii. 297
 causes discussed, ii. 290, 291
 drugs and, ii. 370
 glycosuria and, ii. 294, 295
 gout and, ii. 296
 neuralgia and, ii. 301
 obesity and, ii. 292, 293
 pathology epitomised, ii. 333
 plumbism and, ii. 296
 renal cirrhosis and, ii. 333-336
 sex and, ii. 295, 335
- Arthritis, i. 10 ; ii. 279
- Asphyxia, epilepsy from, i. 334, 335
- Asthma, i. 8, 9, 191, 192, 296-316
 albuminuria and, ii. 319
 alternations of, i. 207
 anorexia and, i. 191, 192
- Asthma, arterial disease and, ii. 294
 arthritic children and, ii. 279-281
 blood-pressure and, ii. 167
 bronchitis and, i. 301, 304 ; ii. 72-76, 193, 195
 catarrhs and, ii. 70
 chest enlargement in, i. 299
 colds and, i. 447
 combustion and, i. 226, 227, 230, 231
 concurrent affections of, ii. 141
 cutaneous disease and, ii. 248
 degeneration in, ii. 288
 diabetes and, ii. 103
 diarrhoea and, i. 254
 diet and, i. 213, 214, 263, 265-267
 diuresis and, ii. 56
 drugs in, i. 238, 305, 306, 308, 313 ; ii. 370, 371
 dry cupping in, i. 309
 dyspepsia and, i. 47
 emotion and, i. 311, 312
 epilepsy and, i. 406
 exercise and, i. 219-224, 260, 310
 expectoration in, i. 303
 fat-formation and, i. 237-240
 fistula [lymph] and, i. 254
 fumes of herbs in, i. 304
 gastralgia and, i. 377
 glycosuria and, i. 195
 gout and, i. 201, 209, 247, 248, 462 ; ii. 10, 281
 gradation of, ii. 133
 haemoptysis in, i. 315, 364
 haemorrhage and, i. 128, 253, 314, 315
 heredity and, i. 425, 427
 hypnotism and, i. 420
 illustrative cases, ii. 428-446
 insanity and, ii. 221, 222
 measles and, i. 251
 menstruation and, i. 232, 234, 367 ; ii. 84
 migraine and, i. 239
 nasal mucosa and, i. 437-441
 neuralgia and, i. 392
 oxygen inhalation in, i. 225
 periodicity, i. 259
 phthisis and, i. 247 ; ii. 112
 plumbism and, i. 240
 polyuria and, i. 302
 pregnancy and, i. 235, 236
 premonitory sensations, ii. 40
 pulse in, i. 298, 302
 purgatives in, i. 180
 pyrexia and, i. 5, 247, 251, 428
 râles in, i. 303
 reflex irritation and, i. 428, 429
 renal cirrhosis and, ii. 166, 167, 313, 314
 rheumatoid arthritis and, ii. 270

- Asthma, seton treatment of, i. 246
sex and, i. 432
temperature and, i. 216, 217, 304,
308, 309, 311, 423
uric-acid excretion and, ii. 41, 181
uro-lithiasis and, ii. 55
vapours in, i. 304, 306
whooping-cough and, i. 251
- Astigmatism, epilepsy and, i. 443
- Atheroma, ii. 298, 299, 304
aortic, ii. 307, 308
diabetes and, ii. 295
drugs and, ii. 370
mitral stenosis causing, ii. 297
sex and, ii. 335
- Australian aborigines, food of, i. 33
teeth of, i. 39
- BACKACHE**, dietetic treatment of, ii. 144
- Bile, emesis and flow of, ii. 365
glycogen in liver and, i. 361
secretion of, i. 51
- Bile-duct, blockage of, i. 63
- Biliousness, i. 8, 186
acute, i. 64
blood-pressure and, ii. 163
cancer and, i. 258
chronic, i. 69-73
diabetes and, i. 68, 254
diet and, i. 65, 163, 266, 267
eye-strain and, i. 448; ii. 33
glycosuria and, i. 68, 195
gout and, i. 201
haemorrhage and, i. 253
hepatic swelling and, i. 359
illustrative cases, ii. 400-407
liver in, i. 61, 186
menopause and, i. 143
menstruation and, i. 235, 366
migraine and, i. 188
periodicity, i. 259, 260
purgatives in, i. 180
pyrexia and, i. 62
recurrent, i. 65
seaside and, i. 462
subacute, i. 65
temperature and, i. 216
treatment, i. 62, 71
- Blindness, epilepsy and, i. 348
- Blood, alkalinity of, ii. 169
carbon contents of. *See* Carbon
contents of blood
carbonaceous accumulation in, i.
25
carbonization of, i. 50-53
fuel-supply of, i. 36-54
haemoglobin in, i. 162
lithic acid accumulations in, ii. 47
nitrogen in, i. 21
starvation and, i. 152-154
- Blood-pressure, arterio-sclerosis and,
ii. 297
asthma and, ii. 167
cancer and, ii. 167
causes of high, ii. 146
climate and, ii. 151-153
constipation and, ii. 162
convulsions and, ii. 163-166
diet and high, ii. 147-149
diseases conducive of high, ii. 153,
154, 157
drugs and, i. 354
epilepsy and, i. 333-343
exercise and, ii. 149-151
glycosuria and, i. 354, 355; ii. 161
gout and, ii. 158-160
haemorrhage and, i. 354; ii. 160
hygienic treatment of, ii. 150
insanity and, ii. 227-229
mechanism of persistent high, ii.
170-172
migraine and, ii. 145
negative factors in persistent high,
ii. 167, 168
neurasthenia and, ii. 203
obesity and, ii. 156
paroxysmal neuroses and, i. 464;
ii. 163-167
persistent high, ii. 145-172
plumbism and, ii. 162
pregnancy and, ii. 155, 156
purgation and, ii. 162
pyrexia and, ii. 157, 158
renal cirrhosis and, ii. 318, 326-333
symptoms of high, i. 365; ii. 149
temperature and, ii. 151-153
uricaemia and, ii. 169
urinary excretion and, ii. 172-185
- Body temperature, fluctuations of, i. 93-
96
menstruation and, i. 135
regulation of, i. 98
- Boils, diabetes and, ii. 246, 247
menopause and, ii. 242
typhoid and, ii. 243
- Brachycardia, illustrative case, ii. 451
- Brain, vicarious use of, ii. 351
- Brain workers, diet and, ii. 379
- Breast, cancer of, ii. 86, 117
- Bright's disease, Raynaud's disease and,
i. 396
- Bromides, influence of in epilepsy, ii.
373
- Bronchi, uratic deposits and, ii. 75
- Bronchitis, acute gouty, ii. 75
arthritic children and, ii. 280
asthma and, i. 247, 251, 301, 304;
ii. 72-76, 193-195
blood-pressure in chronic, ii. 154
broncho-pneumonia and, ii. 192
carbon contents of blood and, ii.
190

- Bronchitis, chronic, ii. 190-198
 combustion and, i. 172
 dengue and, ii. 192
 diabetes and, ii. 192
 drugs and, ii. 370, 371
 gout and, ii. 13, 192, 193
 haemorrhoids and, ii. 192
 illustrative cases, ii. 473-482
 insanity and chronic, ii. 222
 obesity and, ii. 191
 paroxysmal neuroses and, ii. 192
 pathological acarbonization and, ii. 192
 phthisis and, ii. 192
 physiological acarbonization and, ii. 191
 pregnancy and, ii. 191
 renal cirrhosis and, ii. 316
 special forms of chronic, ii. 197
 treatment, ii. 195-197
- Broncho-pneumonia, chronic bronchitis and, ii. 192
- Bronchorrhœa, illustrative case, ii. 483
- CANCER**, i. 203, 257; ii. 116-129
 blood-pressure and, ii. 167
 diet and, ii. 122
 fat-formation and, i. 112
 paroxysmal neuroses and, i. 258
 'tumour germ' theory, ii. 128
 vicarious menstruation and, ii. 86
- Carbohydrates, restriction of, ii. 339, 367, 378
- Carbon contents of blood, i. 25, 153; ii. 338
 bronchitis and, ii. 190
 combustion and, i. 100
 cutaneous disease and, ii. 238
 diet and, i. 166
 fluctuations in, i. 226; ii. 36, 37
 insanity and, ii. 211, 214
 liver distension and, i. 79-82
 neurasthenia and, ii. 201-203
 purgatives and, i. 180
 pyraemic variations, i. 151, 152
- Carbon income, i. 36-54; ii. 358
 adjustments to, i. 168
 excessive, i. 163
 regulation of, i. 54-85
 variations in, ii. 359
- Carbonaceous metabolism, i. 22-26
- Carbonic acid, menstruation and, i. 129
 work and, i. 23
- Carbuncles, diabetes and, ii. 246, 247
 insanity and, ii. 217
- Carcinoma. *See* Cancer
- Cardiac degeneration, ii. 306-310
- Carlsbad spa, liver disorders and, i. 71
- Cataract, sugar a cause of, ii. 208
- Catarrhs, ii. 64-72
 adenoids and, ii. 189
 causes of, ii. 64, 65
 chronic, ii. 187-198
 combustion and, ii. 66
 dietetic treatment, ii. 71
 exercise and, ii. 66
 eye-strain and, ii. 70
 fat-formation and, ii. 67
 glycosuria and, ii. 68
 gout and, ii. 188
 illustrative cases, ii. 471-473
 lithaemia and, ii. 68
 menstruation and, ii. 67
 paroxysmal neuroses and, ii. 69-71
 pregnancy and, ii. 67
 pyrexia and, ii. 68
 self-curative influence, ii. 70
- Celibacy, obesity and, i. 122
- Cephalalgia, oxygen inhalation and, i. 225
- Cerebral anaemia. *See* Anaemia
- Cerebral arteries, insanity and, ii. 230
- Cerebral inhibition, i. 231
- Chest, enlargement of, in asthma, i. 299
- Chilblains, arthritic children and, ii. 280
- Chinese, food of, i. 33
- Chlorosis, amenorrhœa and, i. 141
- Cholelithiasis, i. 204
- Chromidrosis, menstruation and, ii. 240
- Climacteric, i. 141-145
- Climate, ii. 368
 blood-pressure and, ii. 151-153
 combustion and, i. 91
- Colds, puberty and, i. 142
- Colic, arthritic children and, ii. 280
- Colic, lead, urinary secretion in, ii. 176
 vision and, ii. 210
- Combustion. *See* Katabolic decarbonization
- Constipation, arthritic children and, ii. 280
 blood-pressure and, ii. 162
 diabetes and, i. 75
 menopause and, i. 143
 plumbism and, i. 240
- Consumption. *See* Phthisis
- Convulsions, blood-pressure and, ii. 163-166
 haemorrhage and, i. 128
 measles and, i. 252
 rickets and, i. 419
 therapeutic treatment, ii. 164
 uricaemia and, ii. 164, 165
- Coryza, arthritic children and, ii. 279
 drugs and, ii. 370
 epilepsy and, ii. 188
 illustrative case, ii. 440
 immunity from, i. 427
 menstruation and, i. 367
- Croup, alternations of, i. 207

- Croup, catarrhal, i. 192**
 illustrative case, ii. 438
 pyrexia in, i. 192
- Cutaneous disease, ii. 234-257**
 combustion and, ii. 237
 fat-formation and, ii. 242
 glycosuria and, i. 195; ii. 246-248
 gout and, ii. 245, 246
 illustrative cases, ii. 493-500
 lactation and, ii. 242
 paroxysmal neuroses and, ii. 248-250
 pregnancy and, ii. 242
 pyrexia and, ii. 242-245
- DEBILITY, food withdrawal and, i. 153**
- Decarbonization. See Katabolic, Anabolic, Haemorrhagic**
- Defaecation, angina pectoris and, i. 322**
- Dengue, asthma and, i. 247, 251**
 chronic bronchitis and, ii. 192
 phthisis and, ii. 110
- Dental caries, i. 37-40, 47, 167, 169**
- Dermatitis, gout and, ii. 246**
- Diabetes, i. 196, 203; ii. 99-105**
 age and, ii. 100
 angina pectoris and, i. 256
 biliousness and, i. 68, 254
 chronic bronchitis and, ii. 192
 constipation and, i. 75
 cutaneous disease and, ii. 246-248
 diet and, ii. 99, 100
 dyspepsia and, i. 68, 109
 epilepsy and, i. 256, 257
 exercise and, ii. 99, 100
 gout and, ii. 9, 161
 insanity and, ii. 227
 liver and, i. 68
 mental shocks and, i. 177
 migraine and, i. 68, 254, 255
 obesity and, ii. 101
 pyrexia and, ii. 102
 rheumatoid arthritis and, ii. 271
 sex and, ii. 100
 statistics of, ii. 103
 temperature and, ii. 99, 100
 theory of, ii. 103-105
- Diarrhoea, i. 73-76, 194**
 asthma and, i. 254
 bilious, i. 73
 cancer and, i. 258
 diet and, i. 74
 haemorrhoids and, i. 77
 illustrative case, ii. 426
 menopause and, i. 75, 143
 menstruation and, i. 75, 135, 366
 mental emotion and, i. 177
 migraine and, i. 254
- Diatheses, i. 183**
- Diet, ague and, ii. 77**
 angina pectoris and, i. 215, 263, 265-267
- Diet, asthma and, i. 213, 214, 263, 265-267**
 average normal, i. 155
 biliousness and, i. 65, 163, 266, 267
 blood-pressure and, ii. 147-149
 boarding schools and, i. 161
 cancer and, ii. 122
 carbon contents of blood and, i. 166
 catarrhs and, ii. 71
 civilization and, i. 163
 customs, i. 30-33
 cutaneous disease and, ii. 250-254
 deductive investigation into, i. 27
 diabetes and, ii. 99, 100
 diarrhoea and, i. 74
 dyspepsia and, i. 67
 epilepsy and, i. 214, 215, 264-266
 excessive, i. 157
 gout and, i. 10, 46, 181; ii. 3, 18, 19, 283-285
 haemorrhoids and, i. 77
 harmonization of results of investigations into, i. 32
 heart disease and, ii. 310
 hemicrania and, i. 2
 hyperpyraemia and, i. 159
 idiosyncrasies in, i. 42
 inductive investigation into, i. 29
 insanity and, ii. 212-214
 leanness and, i. 109
 lithaemia and, ii. 59
 liver troubles and, i. 71
 menopause and, i. 144
 menstruation and, i. 147
 mental work and, i. 28, 29
 migraine and, i. 2, 10, 163, 180, 212, 262, 265-268, 284; ii. 41
 milk, ii. 148
 minor neuroses and, ii. 142
 muscular labour and, i. 28
 neuralgia and, i. 163, 393
 neurasthenia and, ii. 201, 204
 obesity and, i. 2, 109
 paroxysmal neuroses and, i. 211-216
 peristalsis and, i. 166
 phthisis and, ii. 107
 physiological, i. 27-35
 renal cirrhosis and, ii. 317
 rheumatoid arthritis and, ii. 264-267, 275
 salt-free, i. 268, 269
 science of, i. 29
 severe illness and, ii. 76
 uric acid and, ii. 47-49
 uricaemia and, i. 180
 uro-lithiasis and, ii. 58-60
 vision and, ii. 207, 208
 weight and, i. 126
- Digestion, alimentary canal and, i. 53**

- Digestion, gastric, i. 40-49
 intestinal, i. 49
 oral, i. 37-40
 saliva and, i. 37
 teeth and, i. 37
- Digestive organs, i. 36
- Diphtheria, Raynaud's disease and, i. 396
- Disease, acute, conceptions about, ii. 353
 carbonaceous food and, i. 34
 chronic, cause of, ii. 353
 gradation of, ii. 130-139
 hyperpyraemic theory, ii. 353
- Diuresis, ague and, ii. 174
 emotions and, ii. 173
 epilepsy and, ii. 181
 gout and, ii. 176
 menstruation and, i. 365; ii. 174, 179
 paroxysmal neuroses and, ii. 56, 175, 176
 plumbism and, ii. 176
 pyrexia and, ii. 174, 175
 renal cirrhosis and, ii. 301, 330-332
 temperature and, ii. 173, 178
 typhoid fever and, ii. 173, 175
- Diuretics, neurasthenia and, ii. 204
- Drugs, ii. 369-372
 albuminuria and, ii. 370
 angina pectoris and, i. 321; ii. 370, 371
 arterio-sclerosis and, ii. 370
 asthma and, i. 305, 306, 308, 313; ii. 370, 371
 atheroma and, ii. 370
 blood-pressure and, i. 354
 bronchitis and, ii. 195-197, 370, 371
 coryza and, ii. 370
 emphysema and, ii. 370
 epilepsy and, i. 336, 337, 343; ii. 371
 gout and, ii. 262, 370, 371
 hæmorrhage and, ii. 93-97
 hay-fever and, ii. 371
 insanity and, ii. 225
 menstruation and, i. 370
 migraine and, i. 285; ii. 370
 neuralgia and, i. 383; ii. 200
 rigor and, i. 295
 thirst and, ii. 332
- Dry-cupping, i. 309
- Dysidrosis, arthritic children and, ii. 280
- Dysmenorrhœa, i. 364, 365, 370-372
 arthritic diathesis and, ii. 280
 nasal mucosa and, i. 439
- Dyspepsia, anaemia and, i. 141
 arthritic children and, ii. 280
 asthma and, i. 47
 causes of, i. 43
- Dyspepsia, conservative influence of
 gastric, i. 44-48
 diabetes and, i. 68, 109
 diet and, i. 67
 emotion and, i. 177
 epilepsy and, i. 190
 exercise and, i. 67
 eye-strain and, i. 448; ii. 33
 gastric, i. 167, 169
 glycosuria and, i. 195
 gout and, i. 46; ii. 32
 gouty, ii. 15-18
 hepatic, i. 66
 illustrative cases, ii. 395-404
 induction of, i. 180
 intestinal, i. 167, 169
 menopause and, i. 143
 menstruation and, i. 235, 366
 migraine and, i. 47
 oral, i. 167, 169
 secondary effects of gastric, i. 48
 vertigo and, i. 399, 400
- Dysuria, urethral neuralgia and, i. 383, 384
- ECLAMPSIA, arthritic children and, ii. 280
 secretion of urine in, ii. 184
 vision and, ii. 210
- Eczema, arthritic children and, ii. 280
 asthma and, ii. 248, 249
 climate and, ii. 237
 diabetes and, ii. 103, 247
 diet and, ii. 250
 gonorrhœa and, ii. 243
 gout and, ii. 235, 236, 245, 246, 273
 lactation and, ii. 242
 menstruation and, ii. 239, 241
 oxygen inhalation and, ii. 238
 paroxysmal neuroses and, i. 464
 pregnancy and, ii. 242
 thyroid extract in, ii. 237
 typhoid and, ii. 243
- Emesis, ii. 365
- Emotion, asthma and, i. 311, 312
 diuresis and, ii. 173
 epilepsy and, i. 346
 menstruation and, i. 368
- Emphysema, blood-pressure and, ii. 154
 combustion and, i. 172
 drugs and, ii. 370
 renal cirrhosis and, ii. 316
 uric acid and, ii. 46
- Enteric, insanity and, ii. 218
- Entorrhagia, menopause and, i. 143
- Environment, i. 31; ii. 338, 340, 355, 356
- Enzymes, in cancer, ii. 127, 128
- Epilepsy, i. 8, 9, 330-352
 albuminuria and, ii. 320
 alternations of, i. 207
 angina pectoris and, i. 409

- Epilepsy, asphyxia and, i. 334, 335**
 asthma and, i. 406
 blindness and, i. 348
 blood-pressure and, i. 333-343;
 ii. 163
 catarrhs and, ii. 70
 cerebral anaemia and, i. 336, 343-348
 combustion and, i. 226, 231
 coryza and, ii. 188
 cutaneous disease and, ii. 249
 degeneration in, ii. 288
 diabetes and, i. 256, 257
 diet and, i. 214, 215, 264-266
 diuresis and, ii. 56, 181
 drugs and, i. 336, 337, 343; ii. 371
 dyspepsia and, i. 190
 emotion and, i. 346
 exercise and, i. 222-224, 260, 340
 eye-strain and, i. 443
 glycosuria and, i. 195, 355
 gout and, i. 201, 248, 250; ii. 10, 281
 gradation of, ii. 132, 133
 haemorrhage and, i. 254
 hemiplegia and, i. 349, 419, 420
 heredity in, i. 425, 426
 hypnotism and, i. 420
 idiocy and, i. 419
 illustrative cases, ii. 457-467
 insanity and, ii. 223-226
 major, i. 190, 191
 malarial, i. 350, 351
 manifestations of minor, ii. 141
 menstruation and, i. 233, 234
 migraine and, i. 406
 nasal mucosa and, i. 441, 442
 neuralgia and, i. 392
 oxygen inhalation in, i. 226
 periodicity, i. 259, 260
 perversions of sensation in, ii. 348
 plumbism and, i. 241, 341
 pregnancy and, i. 236
 premonitory sensations, ii. 40
 puberty and, i. 234
 pyrexia and, i. 188, 251, 434
 Raynaud's disease and, i. 395
 reflex irritation and, i. 428, 429
 renal cirrhosis and, ii. 314, 315
 rigor and, i. 350, 351
 seton treatment of, i. 246, 249
 sex and, ii. 32
 shivering and, i. 334
 temperature and, i. 216, 217, 340
 theory of, i. 331-333
 uric acid and, ii. 42, 181
 uro-lithiasis and, ii. 55
 venesection and, i. 338
 vertigo and, i. 399
 vomiting and, i. 338
- Epistaxis, arthritic children and, ii. 279**
 dependence upon, i. 193
- Epistaxis, menstruation and, i. 134;**
 ii. 83, 84, 86
 migraine and, i. 364, 462
 recurrent, ii. 86-88
 treatment, ii. 92, 94
 typhoid and, i. 199
- Equilibrium, nitrogenous, i. 16**
- Erysipelas, insanity and, ii. 217**
 migraine and, i. 243
 phthisis and, ii. 110
 Raynaud's disease and, i. 396
- Erysipelatoid affections, ii. 80, 81**
- Erythema, arthritic children and, ii. 280**
 menstruation and, ii. 240
- Erythromelalgia, i. 401, 402**
- Esquimaux, food of, i. 33**
- Excretion, carbonaceous, i. 22**
 nitrogenous, i. 17
- Exercise, i. 6; ii. 368**
 angina pectoris and, i. 222, 260, 322-325
 asthma and, i. 219-224, 260, 310
 blood-pressure and, ii. 149-151
 catarrhs and, ii. 66
 combustion and, i. 217; ii. 38
 diabetes and, ii. 99, 100
 dyspepsia and, i. 67
 epilepsy and, i. 222-224, 260, 340
 eye-strain and, i. 218
 gastralgia and, i. 223
 glycosuria and, i. 355
 gout and, ii. 5-7, 39
 menstruation and, i. 368
 migraine and, i. 218, 223, 285
 minor neuroses and, ii. 142
 neurasthenia and, ii. 202
 paroxysmal neuroses and, i. 217-225
 phthisis and, ii. 107
 rheumatoid arthritis and, ii. 264-267
 uric-acid excretion and, ii. 38, 45
 urinary water and, ii. 179
 uro-lithiasis and, ii. 54
 vision and, ii. 208
- Expectoration, asthma and, i. 303**
- Eye-strain, i. 178, 443-457**
 biliousness and, ii. 33
 catarrhs and, ii. 70
 dyspepsia and, ii. 33
 exercise and, i. 218
 migraine and, ii. 33
 morbid results of, ii. 33
see also Vision
- FÆCES, carbohydrates in, i. 51**
- Fat-formation, i. 24, 106-117, 237-240**
 alternations of, i. 168
 angina pectoris and, i. 237, 239
 asthma and, i. 237-240

- Fat-formation, cancer and, i. 112
 carbon equilibrium, i. 113-115
 catarrhs and, ii. 67
 combustion and, i. 117-119, 123
 cutaneous disease and, ii. 242
 decarbonizing influence of, i. 115-117
 deficiency of, i. 154, 174-176
 eye-strain and, i. 456
 functional factor of, i. 106-108
 insanity and, ii. 217
 menstruation and, i. 111, 149
 migraine and, i. 237, 239, 240
 minor neuroses and, ii. 142
 phthisis and, ii. 110
 pregnancy and, i. 111
 pyrexia and, i. 176
 rheumatoid arthritis and, ii. 267
 supply factor of, i. 108-112
- Fats, excess of, ii. 380
 liver and, i. 80
- Febricula, acne and, ii. 243
 illustrative case, ii. 427
- Febrile catarrh, asthma and, i. 247
 uro-lithiasis and, ii. 57
- Febrile gastritis, arthritic children and, ii. 280
- Fistula, asthma and, i. 254
- Food, excess of, an incubus, ii. 360
 restriction of, ii. 365, 366
see also Diet
- Food-supply, approximation of, ii. 338
- Fright, neuralgia and, i. 385
- GALL-STONES, liver and, i. 82-84
- Gastralgia, i. 8, 9, 189, 377-382
 alternations of, i. 207
 anorexia and, i. 189, 191, 260
 asthma and, i. 377
 blood-pressure and, ii. 163
 combustion and, i. 226
 exercise and, i. 223
 gout and, i. 201, 209; ii. 281
 haematemeses and, i. 364
 hypnotism in, i. 420
 illustrative cases, ii. 452-457
 malaria and, i. 378
 menstruation and, i. 234, 367, 377
 migraine and, i. 377
 neuralgia and, i. 377
 periodicity, i. 259
 plumbism and, i. 241
 renal cirrhosis and, ii. 314
 rheumatoid arthritis and, ii. 270
 sex and, ii. 32
 temperature and, i. 378
 urate deposits in, ii. 43
 uro-lithiasis and, ii. 55
 Weir-Mitchell treatment of, ii. 200
- Gastric atony, migraine and, i. 187
- Gastric catarrh, recurrent, i. 66
- Gastric juice, glycogen in liver and, i. 361
 secretion of, i. 177
- Gastritis, insanity and, ii. 219
- Gingivitis, i. 37
- Glycaemia, haemorrhage and, i. 355
- Glycogen, formation of, i. 60
- Glycosuria, i. 194; ii. 46
 anabolism and, i. 194
 arterio-sclerosis and, ii. 294, 295
 asthma and, i. 195
 biliousness and, i. 68, 195
 blood-pressure and, i. 354, 355;
 ii. 161
 catarrhs and, ii. 68
 cutaneous disease and, i. 195;
 ii. 246-248
 diabetes and, ii. 99-105
 dispersal of, i. 57
 dyspepsia and, i. 195
 epilepsy and, i. 195, 355
 exercise and, i. 355
 gout and, i. 195, 256; ii. 9
 haemorrhoids and, i. 77
 insanity and, ii. 227
 migraine and, i. 68, 195
 neuralgia and, i. 195
 obesity and, i. 121
 paroxysmal neuroses and, i. 254-257
 pregnancy and, i. 194
 pyrexia and, i. 355
 uro-lithiasis and, ii. 58
- Gonorrhoea, eczema and, ii. 243
 rheumatoid arthritis and, ii. 269
- Gout, i. 6, 8-10, 201, 202; ii. 258-287
 acute, ii. 1-24
 acute asthenic, ii. 259
 albuminuria and, ii. 320, 323
 alcohol and, ii. 3
 angina pectoris and, i. 209; ii. 281
 arterial disease and, ii. 294
 arterio-sclerosis and, ii. 296
 asthma and, i. 201, 209, 247, 248,
 462; ii. 281
 biliousness and, i. 201
 blood-pressure and, ii. 158-160
 cancer and, ii. 119
 catarrhs and, ii. 68, 188
 cause of, i. 44
 chronic articular, ii. 259-263
 chronic bronchitis and, ii. 192, 193
 cutaneous disease and, ii. 235-237,
 245, 246
 diabetes and, ii. 9, 103, 161
 diathesis, i. 183
 diet and, i. 46, 181; ii. 3, 18, 19,
 283-285
 drugs and, ii. 262, 370, 371
 dyspepsia and, i. 46; ii. 32
 epilepsy and, i. 201, 248, 250; ii. 281

- Gout, erysipelas and, ii. 81
 exercise and, ii. 5-7, 39
 factors in, ii. 27-34, 344
 gastralgia and, i. 201, 209 ; ii. 281
 glycosuria and, i. 195, 256 ; ii. 9
 gradation of, ii. 132, 133
 haemorrhage and, i. 193 ; ii. 7-9, 89
 hay-fever and, ii. 69
 headache and, ii. 31, 32
 heart disease and, ii. 307
 heart's action and, i. 403
 hemicrania and, ii. 281
 illustrative cases, ii. 467-470
 insanity and, ii. 220
 iron in, ii. 369
 laryngismus stridulus and, ii. 281
 mania and, i. 201, 202
 manifestations of, in children, ii. 279-281
 menopause and, ii. 8
 menorrhagia and, ii. 90
 menstruation and, ii. 30
 migraine and, i. 201, 208
 nationality of, ii. 32
 neuralgia and, i. 391 ; ii. 30, 281
 obesity and, ii. 7
 oxygen treatment, ii. 47, 283
 pancreatic duct and, ii. 17
 paroxysmal neuroses and, i. 464 ; ii. 10-12
 phthisis and, ii. 111, 112
 plumbism and, ii. 9, 43, 162
 premonitory sensations, ii. 40
 puberty and, ii. 8
 pyrexia and, i. 201 ; ii. 282
 Raynaud's disease and, i. 396
 renal cirrhosis and, ii. 314, 316
 self-curative effect of, ii. 12-15
 symptomatology of diathesis, ii. 278-281
 symptoms of suppressed, ii. 159
 theories of, ii. 22, 23
 treatment of, ii. 14, 18, 19
 ulcers and, ii. 12, 13
 uric acid and, ii. 19-24, 180, 181, 321
 uricaemia and, ii. 40
 urinary water and, ii. 179, 180
 uro-lithiasis and, ii. 61
 vertigo and, i. 399, 400
 visceral, ii. 12, 24-27
 vision and, ii. 210
- Gouty dyspepsia, ii. 15-18
 Gravel, diabetes and, ii. 103
- HAEMATEMESIS, i. 380-382 ; ii. 84, 86, 87
 gastralgia and, i. 364
 menopause and, i. 143
 menstruation and, i. 134
- Haematuria, ii. 90, 91
 menstruation and, ii. 83
- Haemoglobin in blood, i. 162
 deficiency of, i. 173
- Haemoptysis, asthma and, i. 315, 364
 menstruation and, i. 134 ; ii. 83, 84, 86
 over-eating and, ii. 88
 treatment, ii. 94-97
- Haemorrhage, i. 193, 194
 asthma and, i. 128, 253, 314, 315
 biliousness and, i. 253
 blood-pressure and, i. 354 ; ii. 160
 convulsions and, i. 128
 diabetes and, ii. 103
 drugs and, ii. 93-97
 epilepsy and, i. 254
 gastralgia and, i. 379
 glycaemia and, i. 355
 gout and, i. 193 ; ii. 7-9
 insanity and, ii. 226
 migraine and, i. 128, 173, 253, 288
 modes of, i. 128
 paroxysmal neuroses and, i. 252-254
 pyrexia and, i. 193
 recurrent, ii. 82-98
 rheumatoid arthritis and, ii. 268
 treatment of idiopathic, ii. 91-98
- Haemorrhagic decarbonization, i. 128-151, 158, 167, 179
 correlation of anabolic, katabolic, and, i. 145-149
 deficient, i. 176, 177
- Haemorrhoidal haemorrhage, recurrent, ii. 88
- Haemorrhoids, i. 76
 cancer and, ii. 120
 chronic bronchitis and, ii. 192
 diarrhoea and, i. 77
 menopause and, i. 143
 menstruation and, i. 366
 paroxysmal neuroses and, i. 464
- Hay-asthma, i. 422, 423
 insanity and, ii. 222
- Hay-fever, i. 422, 423, 436 ; ii. 66
 drugs and, ii. 371
 gout and, ii. 69
 menstruation and, ii. 67
 seton treatment of, i. 246
- Headache, anaemia and, i. 141
 blood-pressure and, ii. 154
 gout and, ii. 31, 32
 illustrative cases, ii. 417-426
 menopause and, i. 234
 plumbism and, i. 240
 puberty and, i. 142
 purgatives and, i. 180
 renal cirrhosis and, ii. 166
 ulcers and, i. 250
 see also Migraine
- Heart, angina paroxysms and, ii. 299-301
 enlargement of, ii. 306, 307

- Heart, gouty, ii. 308
 valvular affections, ii. 307-310
- Heart-beat, epilepsy and, i. 341-343
 migraine and, i. 287
- Heart disease, diet and, ii. 310
 gout and, ii. 307
 insanity and, ii. 230
 uric acid and, ii. 46
- Heat-production, i. 172
- Hemianaesthesia, i. 397
- Hemianopia, migraine and, i. 233; ii. 141
 paroxysmal neuroses and, ii. 209
 plumbism and, i. 240
- Hemicrania, gout and, ii. 281
 menopause and, i. 234
 treatment, i. 2
- Hemiplegia, cerebral haemorrhage and, ii. 305
 epilepsy and, i. 349, 419, 420
 radial artery and, ii. 305
- Hepatic cells, function of, i. 55, 57
- Hepatic crises, cases of, i. 360
- Hepatic glycogenesis, i. 59
- Herbs, fumes of, in asthma, i. 304
- Heredit, paroxysmal neuroses and, i. 425-427
- Herpes, gout and, ii. 235, 236
 menstruation and, ii. 240, 241
- Hindoos, teeth of, i. 38
- Hot baths, haemorrhage and, ii. 94
 rheumatoid arthritis and, ii. 265
- Human organization, struggle for existence of, ii. 354-356
- Hunger, causes promoting, i. 58
 alleviation of, i. 58
- Hydrops articulo-rum intermittens, i. 398
- Hyperglycaemia, i. 60, 195
- Hyperpyraemia, alcohol and, i. 165
 anabolic decarbonization, i. 174-176
 blood in starvation and, i. 152-154
 carbonaceous intake, i. 163-168
 climate and, ii. 387
 conclusions and concluding remarks on, ii. 358-362
 conservative principle involved in theory of, ii. 353-358
 degeneration, ii. 288-336
 demands of, ii. 352
 diatheses explained by, i. 183
 diet and, ii. 376-384
 exercise and, ii. 384-387
 food factor in, i. 158-168
 fresh air and, ii. 388
 functional factors in, i. 169-178
 haemorrhagic decarbonization, i. 176, 177
 hepatic regulation and, i. 170
 katabolic decarbonization, i. 170-174
- Hyperpyraemia, meaning of, i. 3
 mental strain, i. 177, 178
 nitrogenous intake, i. 159-163
 pathological acarbonization, ii. 99-139
 plumbism and, i. 172
 principles of treatment, i. 178-182
 probability of, i. 154-158
 psychical factors, i. 177, 178
 recapitulation, ii. 337-353
 recurrent, i. 206-408; ii. 1-98
 sleep and, ii. 384-387
 temperature and, ii. 387
 therapeutic measures, ii. 363-373
 treatment of, ii. 373-388
 unrelieved, i. 462; ii. 140-287
 variation in carbon contents of blood, i. 151, 152
- Hypnotism, tic-douloureux and, i. 420
 paroxysmal neuroses and, i. 420
- Hysteria, menstruation and, i. 235
 plumbism and, ii. 229
- IMPAIRMENT of function, ii. 348, 349
 of structure, ii. 348, 349
- India, food of natives of, i. 33
 fevers of, i. 99
- Indians, Crow, teeth of, i. 39
 S. American, food of, i. 33
- Indigestion. *See* Dyspepsia
- Individual, treatment of the, ii. 392, 393
- Infectious diseases, combustion and, i. 89
- Influenza, asthma and, i. 247, 251
 neuralgia and, i. 391
 Raynaud's disease and, i. 396
 rheumatoid arthritis and, ii. 269
- Insanity, ii. 211-234
 alternations of, i. 207
 asthma and, ii. 221, 222
 blood-pressure and, ii. 227-229
 carbon contents of blood and, ii. 211, 214
 causes of, ii. 233, 234
 chronic bronchitis and, ii. 222
 diabetes and, ii. 227
 diet and, ii. 212-214
 drugs and, ii. 225
 epilepsy and, ii. 223-226
 fat-formation and, ii. 217
 gout and, ii. 220
 gradation of, ii. 135
 haemorrhage and, ii. 226
 hay-asthma and, ii. 222
 lactation and, ii. 216
 menstruation and, i. 234; ii. 215, 216
 migraine and, i. 262; ii. 221
 morbid anatomy of, ii. 229-231
 plumbism and, ii. 229
 pregnancy and, ii. 216

- Insanity, pyrexia and, ii. 217, 233
thyroid extract in, ii. 372
- Insomnia, arthritic children and, ii. 280
- Intestinal juice, glycogen in liver and, i. 361
- Iron, in anaemia, ii. 369
- JAPANESE**, food of, i. 33
- Jaundice, fright and, i. 177
menopause and, i. 143
migraine and, i. 188, 189
- Java, food of natives of, i. 33
- KATABOLIC** decarbonization, i. 86-101, 151, 158, 167, 170-174, 178; ii. 337, 341
alternations of, i. 168
angina pectoris and, i. 226
asthma and, i. 226, 227, 230
bronchitis and, i. 172
catarrhs and, ii. 66
climate and, i. 91, 94; ii. 387
correlation of anabolic, haemorrhagic, and, i. 145-149
cutaneous disease and, ii. 237
divisions of increased, ii. 138
emphysema and, i. 172
epilepsy and, i. 226, 231
exercise and, ii. 38
fat-formation and, i. 117-119, 123
fluctuations in, i. 94-98; ii. 6-8, 36
gastralgia and, i. 226
gout and, ii. 6
inadequate, i. 100
infectious diseases and, i. 89
laryngismus and, i. 226
menstruation and, i. 96; ii. 82
migraine and, i. 227-230
obesity and, i. 92, 122, 176
oxygen supply and, i. 89
phthisis and, i. 172
physical exertion and, i. 217
proteids and, i. 24, 88
pyrexia and, i. 176
retardation of, i. 88, 89
secondary results of strained, i. 99
sleep and, ii. 387
thyroid gland and, i. 88
uric-acid excretion and, ii. 50, 54
uricaemia and, ii. 47
uro-lithiasis and, ii. 54
utero-gestation and, i. 96
variations in rate of, i. 87-94, 154; ii. 4-6
- Katabolism, carbonaceous, i. 22
nitrogenous, i. 17
- Keratosis pilaris, arthritic children and, ii. 280
- Kidney disease. *See* Renal degeneration
- Kidneys, intimal hyperplasia of arteries and, ii. 302, 304
radial artery an index to, ii. 303, 304
uric acid excreted from, ii. 178
water excretion from, ii. 178
- LACTATION**, i. 103
cutaneous disease and, ii. 242
insanity and, ii. 216
obesity and, i. 122
paroxysmal neuroses and, i. 236
rheumatoid arthritis and, ii. 266, 269
- Laryngismus stridulus, arthritic children and, ii. 279
combustion and, i. 226
gout and, ii. 281
- Lead-poisoning. *See* Plumbism
- Leanness, i. 6, 123-127
causes of, i. 123, 124
- Leprosy, oxygen inhalation and, ii. 238
- Leucocytosis (digestive), uric-acid excretion and, ii. 50-52
- Leukaemia, uric acid and, ii. 41
- Lichen, menopause and, ii. 242
- Lithaemia, i. 10, 76; ii. 214, 277-279, 315
amblyopia and, i. 397
diet and, ii. 59, 148
neuralgia and, i. 391
- Lithaemic nephritis, ii. 315
- Lithiasis, diabetes and, ii. 103
- Lithic acid. *See* Uric acid
- Liver, abscess of, menopause and, i. 143
anorexia and, i. 64
biliousness and, i. 61, 186
congestion of, i. 74
diabetes and, i. 68
disorders, Carlsbad spa and, i. 71
distension of. *See* Liver distension
eye-strain and, i. 456
fats and, i. 81
gall-stones and, i. 82-84
glycogen in, i. 50
glycogenic function of, i. 55, 154
hyperaemia of, i. 69
migraine and, i. 188, 359
nausea and, i. 64
pyrexia and, i. 72
rheumatoid arthritis and cancer of, ii. 271
uro-lithiasis and, ii. 61
vomiting and, i. 64
- Liver distension, acute, i. 63

- Liver distension, chronic, i. 69-73
glycogenic, i. 57-73, 82-84, 109, 152; ii. 347, 349, 351
recurrent, ii. 347
reduction of, i. 61
vaso-motor action and, i. 352-362
- Locke's fluid, i. 320
- Lungs, inflammation of, insanity and, ii. 217
- Lymphorrhoea, i. 194, 254
- MALARIA**, amblyopia and, i. 397
angina pectoris and, i. 327
arterial degeneration and, ii. 292
erythromelalgia and, i. 402
gastralgia and, i. 378
- Mania, acute, i. 193
erysipelas and, ii. 81
gout and, i. 201, 202
paroxysmal, i. 8
pyrexia in, i. 193
thyroid extract in acute, ii. 372
- Massage, blood-pressure and, ii. 150
- Mastication, digestion and, i. 40, 41
oral disease and, i. 37
- Measles, asthma and, i. 251
convulsions and, i. 252
epilepsy and, i. 251
- Medulla oblongata, a 'conning-tower,' ii. 359
- Megrim. *See* Headache, Migraine
- Melaena, menstruation and, ii. 86
- Melancholia, blood-pressure and, ii. 227, 228
thyroid extract in, ii. 372
treatment of acute passive, ii. 213
typical case, ii. 492
- 'Memory of the body,' ii. 346, 373
- Meningitis, i. 291
- Menopause, cutaneous disease and, ii. 241
diarrhoea and, i. 75
diet and, i. 144
gout and, ii. 8
haemorrhoidal haemorrhage and, ii. 83
headache and, i. 234
hemicrania and, i. 234
insanity and, ii. 215
lichen and, ii. 242
neuralgia and, i. 392
obesity and, i. 149
phenomena of, i. 143
temperature and, i. 146
- Menorrhagia, arthritic diathesis and, ii. 280
fat-formation and, i. 111
gout and, ii. 90
- Menorrhagic fever, i. 146
- Menstruation, i. 7, 179, 185, 193, 362-375
- Menstruation, alternations of, i. 168
angina pectoris and, i. 234, 367
anorexia and, i. 235, 366
asthma and, i. 232, 234, 367; ii. 84
bilio-sness and, i. 235, 366
catarrhs and, ii. 67
combustion and, i. 96
coryza and, i. 367
cutaneous disease and, ii. 239-242
decarbonizing process, i. 134
diarrhoea and, i. 75, 135, 366
diet and, i. 147
diuresis and, i. 365; ii. 174, 179
drugs and, i. 370
dyspepsia and, i. 235, 366
emotion and, i. 368
epilepsy and, i. 233, 234
epistaxis and, ii. 83, 84, 86
exercise and, i. 135, 368
fat-formation and, i. 111, 149
gastralgia and, i. 234, 367, 377
gout and, ii. 30
haematuria and, ii. 83
haemoptysis and, ii. 83, 84
haemorrhoids and, i. 366
hydrops articulo-rum and, i. 398
hysteria and, i. 235
inadequate, i. 154, 176
infantile, ii. 241
insanity and, i. 234; ii. 215, 216
meaning of, i. 128-137
migraine and, i. 232, 234, 367
nausea and, i. 135
neuralgia and, i. 235, 391
nitrogen excretion during, i. 130
oedema and, i. 366
ovulation and, i. 375
phenomena of, i. 133, 134
pyrexia and, i. 368, 372
Raynaud's disease and, i. 396
rheumatoid arthritis and, ii. 267, 268
symptoms of, i. 137-139, 365
temperature and, i. 135, 147, 368-370
tonsillitis and, ii. 190
urea output during, i. 131
uric-acid excretion and, ii. 37, 179
urinary water and, ii. 179
uro-lithiasis and, ii. 54
uterine changes in, i. 131
uterine theory of, ii. 85
vicarious, ii. 82-86
vision and, ii. 209
vomiting and, i. 135
- Mental aberration, seton treatment of, i. 246
- Mental anxiety, rheumatoid arthritis and, ii. 266
- Mercury, as an aperient, ii. 162

- Metabolism, i. 14-35; ii. 337
 acute rheumatism and, ii. 77
 carbonaceous, i. 22-26
 nitrogenous, i. 15-22
 physiological, i. 27-35
 plumbism and, i. 172
 retardation of, i. 172
 steam-engine analogy, i. 26, 27;
 ii. 337, 394
 temperature and, i. 91
- Micturition. *See* Diuresis
- Migraine, i. 8, 187-189, 277-296
 albuminuria and, ii. 319
 alternations of, i. 207
 ametropia and, i. 447
 anorexia in, i. 187, 189, 191, 260
 arterial disease and, ii. 293, 294,
 301
 arthritic children and, ii. 280
 asthma and, i. 8, 239
 biliousness and, i. 188
 blood-pressure and, ii. 145, 163
 cancer and, i. 258
 catarrhs and, ii. 69
 combustion and, i. 227-230
 cutaneous disease and, ii. 249
 degeneration in, ii. 288
 diabetes and, i. 68, 254, 255; ii. 103
 diarrhoea and, i. 254
 diet and, i. 163, 180, 212, 262, 265-
 268, 284; ii. 41
 diuresis in, ii. 56, 176, 182
 drugs in, i. 285; ii. 370
 dyspepsia and, i. 47
 epilepsy and, i. 8, 406
 epistaxis and, i. 364, 462
 erysipelas and, i. 243
 exercise and, i. 218, 223, 285
 eye-strain and, ii. 33
 fat-formation and, i. 237, 239, 240
 gastralgia and, i. 377
 gastric atony and, i. 187
 glycosuria and, i. 68, 195
 gout and, i. 201, 209; ii. 10
 gradation of, ii. 131, 132
 haemorrhage and, i. 128, 173, 253,
 288
 heart-beat and, i. 287
 hemianopia and, i. 233
 heredity in, i. 425, 426
 hypnotism and, i. 420
 illustrative cases, ii. 407-417
 insanity and, i. 262; ii. 221
 jaundice and, i. 188, 189
 lactation and, i. 237
 liver and, i. 188, 359
 mania and, i. 8
 menstruation and, i. 232, 234, 367
 nasal mucosa and, i. 442
 neuralgia and, i. 385, 392, 405;
 ii. 199
 oxygen inhalation and, i. 225
- Migraine, pathology of, i. 207
 periodicity, i. 259, 260
 perversions of sensation in, ii. 348
 phenomena of, ii. 141
 polyuria and, ii. 183
 pregnancy and, i. 8, 235
 premonitory sensations, ii. 40
 pseudo-, i. 209
 pyrexia and, i. 5, 188, 286, 294
 Raynaud's disease and, i. 395
 reflex irritation and, i. 428, 429
 renal cirrhosis and, ii. 313, 314
 rheumatoid arthritis and, ii. 269
 rigor and, i. 293-295
 seton treatment of, i. 243-245
 sex and, ii. 31
 temperature and, i. 216, 283, 284
 tonsillitis and, i. 243
 treatment, i. 2
 typhoid and, i. 242, 250
 uric-acid excretion and, ii. 39, 42,
 182
 uricaemia and, ii. 40, 41
 uro-lithiasis and, ii. 55
 vertigo and, i. 399
- Miliaria, arthritic children and, ii. 280
- Milk diet, ii. 148
- Mitral stenosis, atheroma in, ii. 297
 over-eating and, ii. 310
- Mitral valvulitis, ii. 308
- Mouth, digestive functions, i. 37
- Muscle glycogen, i. 104-106
 activity and, i. 104
 formation of, i. 154
 starvation and, i. 104
- Muscles, glycogenic function of, i. 105
- Myopia, ii. 208
- NASAL catarrh, oxygen treatment, ii. 188
- Nasal mucosa, i. 437-443
- Nausea, liver and, i. 64
 menstruation and, i. 135
- Nephritis, lithaemic, ii. 315
- Nerve-cell nutrition, insanity and, ii. 231
- Nervous manifestations, ii. 142
- Nettle-rash. *See* Urticaria
- Neuralgia, i. 382-394
 alternations of, i. 207
 angina pectoris and, i. 392
 arterio-sclerosis and, ii. 301
 asthma and, i. 392
 complications of, i. 386, 387
 diabetes and, ii. 103
 diet and, i. 163, 393
 diuresis and, i. 176
 drugs and, i. 383; ii. 200
 epilepsy and, i. 392
 erysipelas and, ii. 80
 facial, i. 383
 fright and, i. 385
 gastralgia and, i. 377

- Neuralgia, glycosuria and, i. 195
 gout and, i. 391; ii. 30, 281
 hypnotism and, i. 420
 influenza and, i. 391
 lithaemia and, i. 391
 malarial, i. 393, 394
 menopause and, i. 392
 menstruation and, i. 235, 391
 migraine and, i. 385, 392, 405; ii. 199
 plumbism and, i. 391
 puberty and, i. 391
 pyrexia and, i. 392
 Raynaud's disease and, i. 395
 rheumatoid arthritis and, ii. 270
 temperature and, i. 385
 urethral, i. 383, 384
- Neurasthenia, ii. 201-207
 blood-pressure and, i. 203
 carbon contents of blood in, ii. 201-203
 cause of, i. 163
 diet and, ii. 201, 204
 diuretics and, ii. 204
 exercise and, ii. 202
 oxygen inhalation and, ii. 203
 pathological acarbonization and, ii. 203
 Weir-Mitchell treatment of, ii. 204-207
- Neuroses, alternation of, i. 8
 puberty and, i. 142
- Night terrors, epilepsy and, ii. 141
- Nitrogen, in blood, i. 21
 deficient intake of, i. 159-163
 menstruation and excretion of, i. 130
 pregnancy and, i. 20
- Nitrogenous equilibrium, maintenance of, ii. 383
- Nitrogenous intake, ii. 339, 358
- Nitrogenous metabolism, i. 15-22
- Nutrition, results of perversion of, ii. 360
- OBESITY, i. 7, 120-123**
 arterio-sclerosis and, ii. 292, 293
 blood-pressure and, ii. 156
 bronchitis and, ii. 191
 causes of, i. 120
 celibacy and, i. 122
 combustion and, i. 92, 122, 176
 diabetes and, ii. 101, 103
 glycosuria and, i. 121
 gout and, ii. 7
 illustrative cases, ii. 467-470
 lactation and, i. 122
 menopause and, i. 149
 thyroid extract in, ii. 372
 treatment, i. 2
 utero-gestation and, i. 122
- Oculo-motor paralysis, rheumatoid arthritis and, ii. 272
- Oedema [angio-neurotic], affections alternating with, ii. 238
 arthritic children and acute, ii. 280
 diuresis and, i. 176
 gout and, ii. 246
 menstruation and, i. 366
 migraine and, ii. 249
 occurrence of, ii. 238
 rheumatoid arthritis and, ii. 272
- Oöphorectomy, double, cancer and, ii. 123, 127
- Oral sepsis, i. 40
- Orthopnoea, cardiac degeneration and, ii. 307
- Ovulation, menstruation and, i. 375
- Oxygen, causes of limited intake, i. 89
 combustion, and supply of, i. 89
- Oxygen inhalation, angina pectoris and, i. 226
 asthma and, i. 225
 bronchial affections and, ii. 188, 197
 cutaneous disease and, ii. 238
 epilepsy and, i. 226
 gout and, ii. 47, 283
 migraine and, i. 225
 neurasthenia and, ii. 203
- PANCREATIC duct, blockage of, i. 64
 gout and, ii. 17
- Pancreatic juice, glycogen in liver and, i. 361
- Paralysis, blood-pressure and, ii. 163
 recurrent, i. 397
- Paroxysmal neuroses, i. 187-193, 206-272; ii. 342-344, 347, 350
 alterations of, i. 207, 208
 chronic bronchitis, ii. 192
 diet and, i. 211-216
 fat-formation and, i. 237-240
 haemorrhage and, i. 252-254
 heredity and, i. 425-427
 'hybrid,' ii. 343
 hyperpyraemic theory of, i. 211-272
 lactation and, i. 236
 mechanism of, i. 273-277, 403-410
 memory of the body and, i. 459
 monthly fluctuation, i. 231, 232
 oxygen inhalation, i. 225, 226
 phthisis and, ii. 112
 physical exercise, i. 217-225
 plumbism and, i. 240, 241
 primary theory of, i. 207-209
 pyrexia and, i. 241-252
 secondary factors of, i. 415-457
 self-curative influence of, i. 258-26
 temperature and, i. 216, 217
 theories of, i. 206-211
 toxic theory, i. 209-211

- Paroxysmal neuroses, treatment, i. 436, 463-467
 uric-acid theory, i. 209-211
 utero-gestation and, i. 235, 236
 vision and, ii. 209
- Pathological acarbonization, i. 185-205 ;
 ii. 340-353
 adopted system of classification,
 ii. 137-139
 alternative systems of classification,
 ii. 136, 137
 chronic bronchitis and, ii. 192
 divisions of, ii. 138
 hyperpyraemia and, ii. 340
 neurasthenia and, ii. 203
 rheumatoid arthritis and, ii. 269-271
 substitutive, i. 461
- Pathological prepotency, i. 411-415 ;
 ii. 346, 360
 treatment of, ii. 372, 373
- Peristalsis, diet and, i. 166
- Pertussis, i. 340, 341
- Petit mal, i. 341, 345
- Phthisis, i. 200, 201 ; ii. 106-116
 acne and, ii. 244
 air and, ii. 107
 amenorrhoea and, ii. 108
 asthma and, i. 247
 blood-pressure and, ii. 154, 157
 cancer and, ii. 121
 chronic bronchitis and, ii. 192
 combustion and, i. 172
 diet and, ii. 107
 exercise and, ii. 107
 fat-formation and, ii. 110
 insanity and, ii. 217
 open-air treatment, ii. 388
 paroxysmal neuroses and, ii. 112
 pregnancy and, ii. 109
 pyrexia and, i. 200 ; ii. 110-112
 rheumatoid arthritis and, ii. 271
 temperature and, ii. 107
 treatment of, ii. 113-116
- Physiological acarbonization, i. 186 ; ii.
 338, 339
 chronic bronchitis and, ii. 191
 substitutive, i. 460
- Piles, i. 193
 menopause and, i. 143
 menstruation and, i. 134
- Pimples, fat-formation and, ii. 242
- Pityriasis, diabetes and, ii. 103
 gout and, ii. 235
- Pleurisy, uric acid and, ii. 46
- Pleurodynia, alternations of, i. 207
 hypnotism and, i. 420
- Plumbism, arterio-sclerosis and, ii. 296
 blood-pressure and, ii. 162
 epilepsy and, i. 341
 gout and, ii. 9, 43, 162
 hyperpyraemia and, i. 172
 insanity and, ii. 229
- Plumbism, kidney disease and, ii. 162
 metabolism and, i. 172
 neuralgia and, i. 391
 paroxysmal neuroses and, i. 240,
 241
 Raynaud's disease and, i. 396
 renal cirrhosis and, ii. 316
 uric-acid excretion and, ii. 43
 uricaemia and, ii. 43
 vision and, ii. 210
- Pneumonia, asthma and, i. 247
 Raynaud's disease and, i. 396
 uric acid and, ii. 45
- Polyuria, asthma and, i. 302 ; ii. 181
 eclampsia and, ii. 184
 mechanism of, ii. 173
 migraine and, ii. 183
 paroxysmal neuroses and, ii. 56
 renal cirrhosis and, ii. 330-332
- Portal circulation, i. 73-78
- Portal congestion, i. 69
- Portal vein, pressure on, i. 63
- Pregnancy, i. 8
 alternations of, i. 168
 asthma and, i. 235, 236
 blood-pressure and, ii. 155-156
 bronchitis and, ii. 191
 cancer and, ii. 119
 catarrhs and, ii. 67
 cutaneous disease and, ii. 242
 epilepsy and, i. 236
 fat-formation and, i. 111
 glycosuria and, i. 194
 health and, i. 166
 insanity and, ii. 216
 'menstrual rhythm' in, i. 434
 migraine and, i. 235
 nitrogen and, i. 20
 phthisis and, ii. 109
 pyrexia and, i. 199
 Raynaud's disease and, i. 396
- Presbyopia, ii. 207
- Prickly heat, i. 99
- Proteids, amount necessary, i. 16, 17
 anabolism and, i. 15
 bile-secretion and, i. 51, 52, 73
 combustion and, i. 24, 27, 88, 178,
 263 ; ii. 107
 divisions of, i. 17, 18, 164
 glycogen formation and, i. 60, 61
 in gout, ii. 3
 in high blood-pressure, ii. 148, 149
 in neurasthenia, i. 204
 mastication and, i. 41
 power of, i. 24
 restriction of, ii. 366, 367
- Prurigo, gout and, ii. 235, 236
 menopause and, ii. 242
- Pruritus, diabetes and, ii. 247
 diet and, ii. 253, 254
 gout and, ii. 235, 246
- Psoriasis, arthritic children and, ii. 280

- Psoriasis, asthma and, ii. 249**
 diet and, ii. 252, 253
 gout and, ii. 235, 246, 247
 headache and, ii. 249
 lactation and, ii. 242
 pregnancy and, ii. 242
 pyrexia and, ii. 242
 thyroid extract in, ii. 237, 372
- Puberty, i. 141-145**
 cutaneous disease and, ii. 241, 256
 epilepsy and, i. 234
 gout and, ii. 8
 neuralgia and, i. 391
- Puerperal mania, ii. 216**
- Pulmonary catarrh, uric acid and, ii. 46**
- Purgation, ii. 364**
 blood-pressure and, ii. 162
- Purgatives, blood contents and, i. 180**
- Pustules, diabetes and, ii. 246**
- Pyorrhoea alveolaris, i. 37-40, 47**
- Pyraemia, meaning, i. 4**
- Pyrexia, i. 196-202**
 anabolism and, i. 199
 angina and, i. 250, 325
 arterio-sclerosis and, ii. 290
 asthma and, i. 5, 423
 biliousness and, i. 62
 blood-pressure and, ii. 157, 158
 catarrhs and, ii. 68
 combustion and, i. 176
 croup and, i. 192
 cutaneous disease and, ii. 242-245
 diabetes and, ii. 102
 diuresis and, ii. 174, 175
 epilepsy and, i. 188, 434
 fat-formation and, i. 176
 glycosuria and, i. 355
 gout and, i. 201; ii. 282
 haemorrhage and, i. 193
 insanity and, ii. 217
 liver and, i. 61, 72
 mania and, i. 193
 menstruation and, i. 368, 372
 migraine and, i. 5, 188, 286, 294
 neuralgia and, i. 392
 paroxysmal neuroses and, i. 241-252; ii. 79
 phthisis and, i. 200; ii. 110-112
 pregnancy and, i. 199
 Raynaud's disease and, i. 396
 uric-acid excretion and, ii. 44-46, 56
 uricaemia and, ii. 44-46
 uro-lithiasis and, ii. 56
 vision and, ii. 210
 vomiting and, i. 202
- RALES, asthma and, i. 303**
- Raynaud's disease, i. 394-396**
 diuresis and, i. 176
 gradation of, ii. 135
 rheumatoid arthritis and, ii. 272
 treatment, i. 436
- Recurrent febricula, ii. 79, 80**
- Renal cirrhosis, age and, ii. 325**
 angina pectoris and, ii. 315
 arterio-sclerosis and, ii. 333-336
 asthma and, ii. 166, 167, 313, 314
 blood-pressure of, ii. 326-333
 bronchitis and, ii. 316
 diet and, ii. 317
 diuresis and, ii. 301, 330-332
 emphysema and, ii. 316
 epilepsy and, ii. 314, 315
 gastralgia and, ii. 314
 gout and, ii. 314, 316
 headache and, ii. 166
 hyperpyraemia and, i. 465
 illustrative cases, ii. 502-505
 mechanism of, ii. 318-320
 migraine and, ii. 313, 314
 pathology epitomised, ii. 333
 plumbism and, ii. 316
 polyuria of, ii. 330-332
 thirst in, ii. 331
 uric-acid excretion and, ii. 319-324
 urine and, ii. 329
- Renal degeneration, ii. 312-325**
 arterial degeneration and, ii. 296
 insanity and, ii. 231, 233
 plumbism and, ii. 162
 sex and, ii. 324, 335
 uricaemia and, ii. 322-325
- Rheumatic fever, asthma and, i. 247**
 uric acid and, ii. 45
- Rheumatism, acute, ii. 77, 78**
 diabetes and, ii. 103
 gout and, ii. 13
 insanity and acute, ii. 218
 rheumatoid arthritis and, ii. 269, 270
- Rheumatoid arthritis, ii. 263-277**
 angina pectoris and, ii. 271
 asthma and, ii. 270
 atypical joint cases, ii. 276
 cause of joint changes, ii. 273, 274
 cutaneous disease and, ii. 272, 273
 diabetes and, ii. 271
 diet and, ii. 264-267
 exercise and, ii. 264-267
 fat-formation and, ii. 267
 gastralgia and, ii. 270
 haemorrhage and, ii. 268
 illustrative cases, ii. 483-492
 lactation and, ii. 266, 269
 liver disease and, ii. 271
 menstruation and, ii. 267, 268
 mental anxiety and, ii. 266
 migraine and, i. 270
- QUADRIURATE theory, i. 11; ii. 23, 26**
- Queensland, dental caries in women of, i. 39**

- Rheumatoid arthritis, neuralgia and, ii. 270
 ocular palsies and, ii. 272
 pathological acarbonization and, ii. 269-271
 phthisis and, ii. 271
 pyrexia and, ii. 269
 Raynaud's disease and, ii. 272
 syncope [local] and, ii. 271, 273
 temperature and, ii. 264-267
 treatment, ii. 274-276
- Rhino-pharyngitis, arthritic children and, ii. 279
- Rickets, convulsions and, i. 419
- Rigor, drugs and, i. 295
 epilepsy and, i. 350, 351
 migraine and, i. 293-295
- Rosacea, paroxysmal neuroses and, i. 464
- Rut, i. 136
- SALISBURY** diet, i. 10, 61, 73; ii. 367
- Saliva, digestion and, i. 37
- Sarcoma, fat-formation and, i. 112
- Scabies, pyrexia and, ii. 242
- Scarlet fever, epilepsy and, i. 251
 insanity and, ii. 233
- Sclerodactylia, i. 401
- Scleroderma, thyroid extract in, ii. 372
- Seborrhoea, arthritic children and, ii. 280
- Secretion formation, i. 103
- Septicaemia, asthma and, i. 247
- Serumtherapy, cancer and, ii. 125
- Setons, i. 243-246; ii. 365
- Shivering, epilepsy and, i. 334
- Sinuses, menstruation and, i. 134
- Skin disease. *See* Cutaneous disease
- Skiping, in asthma, i. 310
- Sleep, hyperpyraemia and, ii. 384-387
- Somnambulism, epilepsy and, ii. 141
- Somniloquence, epilepsy and, ii. 141
- South Sea Islanders, food of, i. 33
- Starvation, blood in, i. 152-154
 uric-acid excretion during, ii. 53
- Steam-engine analogy, i. 26; ii. 337, 394
- Stomach, flatulent distension of, angina pectoris and, i. 327
- Structural degeneration, ii. 348
- Sudamina, arthritic children and, ii. 280
- Sugar-gluttony, i. 165
- Sunstroke, hyperpyrexial, i. 99
- Syncope, angina pectoris and, i. 326
 arthritic children and, ii. 279
 [local] rheumatoid arthritis and, ii. 271, 273
- Syphilis, arterial degeneration and, ii. 292
- TEETH**, digestion and, i. 37
- Temperature, angina pectoris and, i. 321, 322
 asthma and, i. 216, 217, 304, 308, 309, 311, 423
 biliousness and, i. 216
 blood-pressure and, ii. 151-153
 body: *see* Body temperature
 diabetes and, ii. 99, 100
 diuresis and, ii. 173, 178
 epilepsy and, i. 216, 340
 gastralgia and, i. 378
 menopause and, i. 146
 menstruation and, i. 147, 368-370
 metabolism and, i. 91, 94
 migraine and, i. 216, 283, 284
 neuralgia and, i. 385
 paroxysmal neuroses and, i. 216, 217
 phthisis and, ii. 107
 rheumatoid arthritis and, ii. 264-267
 vaso-constriction and, i. 417
- Thirst, drugs and, ii. 332
 renal cirrhosis and, ii. 331
- Thyroid extract, acute mania and, ii. 372
 cancer and, ii. 124, 127
 cutaneous disease and, ii. 237
 insanity and, ii. 372
 melancholia and, ii. 372
 obesity and, ii. 372
 psoriasis and, ii. 372
 rheumatoid arthritis and, ii. 274
 scleroderma and, ii. 372
- Thyroid gland, combustion and, i. 88
- Tic-douloureux, alternations of, i. 207
 hypnotism and, i. 420
- Tinnitus, migraine and, ii. 141
- Tonsillitis, arthritic children and, ii. 279
 gout and, ii. 13
 menstruation and, ii. 190
 migraine and, i. 243
 rheumatoid arthritis and, ii. 269
- Toothache, acute mania and, ii. 217
- Toxic hypothesis, i. 210
- Toxins, headache and, ii. 367
- Treatment, expectant, ii. 357
 symptomatic, ii. 357
- 'Tropical liver,' i. 69
- Tuberculosis. *See* Phthisis
- Typhoid, asthma and, i. 247
 cutaneous disease and, ii. 243
 diuresis and, ii. 173, 175
 epilepsy and, i. 251
 epistaxis and, i. 199
 migraine and, i. 242, 250
 phthisis and, ii. 110, 112
 rheumatoid arthritis and, ii. 269
 uric acid and, ii. 45

- ULCERS**, diabetes and, ii. 247
 gout and, ii. 12, 13, 236
 headache and, i. 250
 menstruation and, i. 134
- Uraemia**, venesection in, ii. 161
 vision and, ii. 210
- Urates**, gouty laryngitis and, ii. 74
- Urea**, i. 16, 18
 menstruation and output of, i. 131
 uric acid and, ii. 184, 185
- Urethritis**, gout and, ii. 68
- Uric acid**, factor in disease, ii. 61-63
 formative material of, ii. 28
 gout and, ii. 1
 liver and, i. 359
 retention of, ii. 36-61
 rôle of, in acute gout, ii. 19-24
- Uric-acid excretion**, ii. 36-61
 epilepsy and, ii. 181
 gout and, ii. 321
 renal cirrhosis and, ii. 319-324
 retarded, ii. 322-324
- Uricacidaemia**, hyperpyraemia and, i. 10
- Uricaemia**, blood-pressure and, ii. 163, 169
 combustion and, ii. 47
 convulsions and, ii. 164, 165
 diet and, i. 180
 factors in, ii. 27-29
 gout and, ii. 40
 migraine and, ii. 40
 plumbism and, ii. 43
 pyrexia and, ii. 44-46
 renal disease and, ii. 322-325
 treatment of, ii. 389-392
- Urinary water**, excretion of, ii. 172-185
- Urine**, blood-pressure and excretion of, ii. 172-185
 renal cirrhosis and, ii. 329
 urea excreted in, ii. 184, 185
 uric acid in, ii. 177-184
- Uro-lithiasis**, ii. 53-61, 322
 asthma and, ii. 55
 combustion and, ii. 54
 diet and, ii. 58-60
 epilepsy and, ii. 55
 exercise and, ii. 54
 factors in, ii. 60
 gastralgia and, ii. 55
 glycosuria and, ii. 58
 gout and, ii. 61
 liver and, ii. 61
 menstruation and, ii. 54
 migraine and, ii. 55
 pyrexia and, ii. 56
- Urticaria**, arthritic children and, ii. 280
 asthma and, ii. 248
 diabetes and, ii. 103
 eye-strain and, i. 446
 gout and, ii. 235, 246
 menopause and, ii. 242
- Urticaria**, menstruation and, ii. 239
 migraine and, ii. 249
 time of occurrence, ii. 238
- Uterine changes in menstruation**, i. 131
- Uterine theory of menstruation**, ii. 85
- Utero-gestation**, i. 103
 combustion and, i. 96
 mechanism [vascular] of, i. 373
 obesity and, i. 122
 paroxysmal neuroses and, i. 235, 236
- VALVES**, venous, i. 58
- Vapours**, in asthma, 304, i. 306
- Varicose veins**, ii. 311
- Vaso-constriction**, amblyopia and, i. 397
 angina pectoris and, i. 317-329, 404
 asthma and, i. 297-316, 404; ii. 73, 74
 epilepsy and, i. 331-352, 404; ii. 342
 gastralgia and, i. 404
 menstruation and, i. 362-375
 migraine and, i. 277-296, 404; ii. 342
 Raynaud's disease and, i. 394
 temperature and, i. 417
- Vaso-dilatation**, acute bronchitis and, ii. 73, 74
 angina pectoris and, i. 317-329
 arterial disease and, ii. 209-303
 asthma and, i. 299-316; ii. 73, 74, 141, 342
 epilepsy and, ii. 343
 menstruation and, i. 362-375
 migraine and, i. 278, 296; ii. 342
- Vegetarianism**, minor neuroses and, ii. 142
- Venesection**, ii. 364
 epilepsy and, i. 338
 insanity and, ii. 226
 uraemia and, ii. 161
 usage, i. 128, 193
 vision and, ii. 211
- Venous degeneration**, ii. 311, 312
 illustrative case, ii. 501
- Vertigo**, i. 399-401
 migraine and, ii. 141
- Vision**, diet and, ii. 207, 208
 disturbances of, ii. 207-211
 exercise and, ii. 208
 gout and, ii. 210
 menstruation and, ii. 209
 paroxysmal neuroses and, ii. 209
 plumbism and, ii. 210
 pyrexia and, ii. 210
 venesection and, ii. 211
see also Eye-strain
- Vomiting**, anorexia and, i. 202
 arthritic children and, ii. 280

- Vomiting, cyclic, i. 202
 epilepsy and, i. 338
 gastralgia and, i. 189
 gastric-juice secretion and, i. 177
 liver and, i. 64
 menopause and, i. 143
 menstruation and, i. 135
 plumbism and, i. 240
 pyrexia and, i. 202
- WATER, excretion of from kidneys, ii. 178
- Weight, diet and, i. 126
 skin condition and, ii. 242
- Weir-Mitchell treatment, of gastralgia,
 ii. 200
 of neurasthenia, ii. 204-207
- Wheals, vaso-dilation and, i. 301 and *n*
- Whooping-cough, asthma and, i. 251
- Womb, cancer of, ii. 117, 119
- Work, carbonic acid and, i. 23
 diet and, i. 28, 29
- XANTHIN group, uric-acid excretion and,
 ii. 51
- Xerodermia, arthritic children and, ii.
 280

END OF THE FIRST VOLUME.

BY THE SAME AUTHOR.

THE

COLD-BATH TREATMENT OF TYPHOID FEVER.

THE EXPERIENCE OF A CONSECUTIVE SERIES OF NINETEEN HUNDRED
AND TWO CASES TREATED AT THE BRISBANE HOSPITAL.

With Illustrations. 8s. 6d. net.

‘On the particular subject of which this volume treats it would be difficult to find what, without disparagement, may be termed a therapeutic experiment carried out on such a scale and under such rigid conditions as obtained in this instance. . . . It is impossible to read his experiences without being convinced of the efficacy of the treatment. . . . We have no doubt the publication of this book will lend an impetus to the more systematic adoption of the practice in our fever hospitals. . . . The book should be thoroughly and carefully perused by all who have the charge of fever patients.’—LANCET.

‘Of the treatment . . . Dr. Hare has made a most careful and conscientious study. . . . We gladly recommend Dr. Hare’s book, . . . not only for the detailed description it gives of the technique of the treatment, but also on account of the clear and unbiassed manner in which the whole question is put before the reader.’—BRITISH MEDICAL JOURNAL.

‘This is a very valuable handbook and ought to be welcomed in this country. . . . Dr. Hare’s long and varied personal experiences of the working and results of this treatment in the Brisbane Hospital entitle him to speak with authority upon his subject, and the present work—written in a particularly lucid manner—is the outcome of those experiences extending over upwards of 2,000 cases.’—THE PRACTITIONER.

‘The observations have been so exact that there is no difficulty in accepting the results. . . . Can only be described as a masterly exposition of the results of the treatment carefully applied to a large series (1902) of consecutive cases observed over a period of ten years in the Brisbane Hospital.’—GLASGOW MEDICAL RECORD.

‘Dr. Hare need make no apology to the profession for presenting them in this handsome volume with the results of his long experience in the cold-bath treatment of typhoid fever, with which his name, as well as that of Brand, is always associated. . . . The physician will find this an eminently practical book; in fact, no one should attempt to introduce this treatment in his hospital wards without a study of the methods and experiences of Dr. Hare as detailed in this volume. We would like to hear of a systematic attempt to treat a series of cases in Indian military hospitals in this way.’—INDIAN MEDICAL GAZETTE.

‘Dr. Hare’s position as resident medical officer of the Brisbane General Hospital, which was the first hospital of any size outside Germany and after Lyons to definitely adopt Brand’s system and carry it out systematically in all cases, afforded him peculiar opportunities for studying the practice and results of the treatment. The Brisbane Hospital, on account of immigration and other causes, has a large fever department, and consequently the author has been able to give in the work before us the results of his personal observation extending over some 2,000 cases of typhoid. . . . Without doubt Dr. Hare’s work will prove a valuable addition to the present knowledge of the therapeutics of typhoid fever.’—JOURNAL OF BALNEOLOGY AND CLIMATOLOGY.

LONDON: MACMILLAN & CO., LIMITED.

NEW YORK: THE MACMILLAN COMPANY.

A LIST OF WORKS ON
MEDICINE, SURGERY,
AND GENERAL SCIENCE,

PUBLISHED BY

LONGMANS, GREEN, & CO.,

39 PATERNOSTER ROW, LONDON, E.C.

91 AND 93 FIFTH AVENUE, NEW YORK, AND HORNBY ROAD, BOMBAY.

MESSRS. LONGMANS, GREEN, & CO.

Issue the undermentioned Catalogues and Lists of their Publications, any of which may be had post free on application.

- | | |
|---|--|
| 1. MONTHLY LIST OF NEW BOOKS AND NEW EDITIONS. | 7. EDUCATIONAL AND SCHOOL BOOKS. |
| 2. QUARTERLY LIST OF ANNOUNCEMENTS AND NEW BOOKS. | 8. BOOKS FOR ELEMENTARY SCHOOLS AND PUPIL TEACHERS. |
| 3. NOTES ON BOOKS; BEING AN ANALYSIS OF THE WORKS PUBLISHED BY LONGMANS, GREEN, & CO. (MARCH 15, JUNE 15, NOVEMBER 15.) | 9. THEOLOGICAL BOOKS. |
| 4. SELECT LIST OF BOOKS IN NATURAL AND PHYSICAL SCIENCE, MATHEMATICS AND TECHNOLOGY. | 10. THEOLOGICAL BOOKS (MAINLY ROMAN CATHOLIC). |
| 5. SELECT LIST OF BOOKS FOR SCIENCE AND TECHNICAL SCHOOLS. | 11. BOOKS IN GENERAL LITERATURE. |
| 6. MEDICAL AND SURGICAL BOOKS. | 12. A CLASSIFIED CATALOGUE (180 pp.) (GENERAL LITERATURE, SCIENCE, THEOLOGY, EDUCATION). |

ASHBY.—WORKS by HENRY ASHBY, M.D., Lond., F.R.C.P.,
*Physician to the General Hospital for Sick Children, Manchester; formerly
Demonstrator of Physiology, Liverpool School of Medicine.*

NOTES ON PHYSIOLOGY FOR THE USE OF STUDENTS
PREPARING FOR EXAMINATION. Seventh Edition,
thoroughly revised. With 148 Illustrations. 18mo, 5s.

HEALTH IN THE NURSERY. With 25 Illustrations. Crown 8vo,
3s. net.

ASHBY AND WRIGHT. THE DISEASES OF CHILDREN,
MEDICAL AND SURGICAL. By HENRY ASHBY, M.D.
Lond., F.R.C.P., Physician to the General Hospital for Sick Children,
Manchester; Lecturer and Examiner in Diseases of Children in the
Victoria University; and G. A. WRIGHT, B.A., M.B. Oxon., F.R.C.S.
Eng., Assistant Surgeon to the Manchester Royal Infirmary, and Surgeon
to the Children's Hospital; formerly Examiner in Surgery in the Univer-
sity of Oxford. Enlarged and Improved Edition. With 217 Illustrations.
8vo, 25s.

BAIN. A TEXT-BOOK OF MEDICAL PRACTICE FOR PRACTITIONERS AND STUDENTS. By Various Contributors. Edited by WILLIAM BAIN, M.D., M.R.C.P. With 75 Illustrations. Royal 8vo, 25s. net.

* * * Apart from the practical character of the book, the special features are that the anatomy, histology, and physiology of each organ or system precede the description of its diseases, and that the various sections are contributed by general physicians and specialists.

BENNETT.—*WORKS* by Sir WILLIAM H. BENNETT, K.C.V.O., F.R.C.S., Surgeon to St. George's Hospital; Member of the Board of Examiners, Royal College of Surgeons of England.

RECURRENT EFFUSION INTO THE KNEE-JOINT AFTER INJURY, WITH ESPECIAL REFERENCE TO INTERNAL DERANGEMENT, COMMONLY CALLED SLIPPED CARTILAGE: an Analysis of 750 Cases. A Clinical Lecture delivered at St. George's Hospital. With 13 Illustrations. 8vo, 3s. 6d.

CLINICAL LECTURES ON VARICOSE VEINS OF THE LOWER EXTREMITIES. With 3 Plates. 8vo, 6s.

ON VARICOCELE: A PRACTICAL TREATISE. With 4 Tables and a Diagram. 8vo, 5s.

CLINICAL LECTURES ON ABDOMINAL HERNIA: chiefly in relation to Treatment, including the Radical Cure. With 12 Diagrams in the Text. 8vo, 8s. 6d.

ON VARIX, ITS CAUSES AND TREATMENT, WITH ESPECIAL REFERENCE TO THROMBOSIS: an Address delivered at the Inaugural Meeting of the Nottingham Medico-Chirurgical Society, Session 1898-9. 8vo, 3s. 6d.

ON THE USE OF MASSAGE AND EARLY PASSIVE MOVEMENTS IN RECENT FRACTURES AND OTHER COMMON SURGICAL INJURIES: THE TREATMENT OF INTERNAL DERANGEMENTS OF THE KNEE-JOINT: THE MANAGEMENT OF STIFF JOINTS: Three Clinical Lectures delivered at St. George's Hospital. With 17 Illustrations. 8vo, 6s.

THE PRESENT POSITION OF THE TREATMENT OF SIMPLE FRACTURES OF THE LIMBS: an Address delivered in opening a Discussion at the Meeting of the British Medical Association held at Ipswich, August, 1900. To which is appended a Summary of the Opinions and Practice of about 300 Surgeons. 8vo, 2s. 6d.

BRODIE. THE ESSENTIALS OF EXPERIMENTAL PHYSIOLOGY. For the use of Students. By T. G. BRODIE, M.D., Lecturer on Physiology, St. Thomas's Hospital Medical School. With 2 Plates and 177 Illustrations in the Text. Crown 8vo, 6s. 6d.

CABOT. A GUIDE TO THE CLINICAL EXAMINATION OF THE BLOOD FOR DIAGNOSTIC PURPOSES. By RICHARD C. CABOT, M.D., Physician to Out-Patients, Massachusetts General Hospital. With 3 Coloured Plates and 28 Illus. in Text. 8vo, 16s.

CARR, PICK, DORAN, DUNCAN. THE PRACTITIONER'S

GUIDE. By J. WALTER CARR, M.D. Lond., F.R.C.P., Physician, Royal Free Hospital; Physician, Victoria Hospital for Children; Joint Lecturer on Medicine, London (Royal Free Hospital) School of Medicine for Women; T. PICKERING PICK, F.R.C.S., Consulting Surgeon, St. George's Hospital and Victoria Hospital for Children; ALLAN H. G. DORAN, F.R.C.S., Surgeon to the Samaritan Free Hospital; ANDREW DUNCAN, M.D., B.S. Lond., F.R.C.S., M.R.C.P., Physician, Branch Hospital Seamen's Hospital Society; Joint Lecturer on Tropical Medicine at London School of Tropical Medicine; Physician, Westminster Dispensary; Fellow of King's College, London. 8vo, 21s. net.

CHEYNE AND BURGHARD. A MANUAL OF SURGICAL

TREATMENT. By W. WATSON CHEYNE, C.B., M.B., F.R.C.S., F.R.S., Professor of Clinical Surgery in King's College, London; Surgeon to King's College Hospital, and the Children's Hospital, Paddington Green, etc.; and F. F. BURGHARD, M.D. and M.S. Lond., F.R.C.S., Teacher of Practical Surgery in King's College, London; Surgeon to King's College Hospital, and the Children's Hospital, Paddington Green, etc.

PART I. The treatment of General Surgical Diseases, including inflammation, suppuration, ulceration, gangrene, wounds and their complications, infective diseases and tumours; the administration of anæsthetics. With 66 Illustrations. Royal 8vo, 10s. 6d. [Ready.

PART II. The treatment of the Surgical Affections of the Tissues, including the skin and subcutaneous tissues, the nails, the lymphatic vessels and glands, the fasciæ, bursæ, muscles, tendons and tendon-sheaths, nerves, arteries and veins; deformities. With 141 Illustrations. Royal 8vo, 14s. [Ready.

PART III. The treatment of the Surgical Affections of the Bones. Amputations. With 100 Illustrations. Royal 8vo, 12s.

PART IV. The treatment of the Surgical Affections of the Joints (including excisions) and the spine. With 138 Illustrations. Royal 8vo, 14s.

PART V. The treatment of the Surgical Affections of the head, face, jaws, lips, larynx and trachea; and the Intrinsic Diseases of the nose, ear and larynx, by H. LAMBERT LACK, M.D. (Lond.), F.R.C.S., Surgeon to the Hospital for Diseases of the Throat, Golden Square, and to the Throat and Ear Department, the Children's Hospital, Paddington Green. With 145 Illustrations. Royal 8vo, 18s.

PART VI.—Section 1. The Surgical Affections of the tongue and floor of the mouth, the pharynx, neck, œsophagus, stomach and intestines. With 124 Illustrations. Royal 8vo, 18s.

Section 2. The Surgical Affections of the rectum, the liver, pancreas and spleen, and genito-urinary organs, the breast and the thorax. With 113 Illustrations. Royal 8vo, 21s.

COATS. A MANUAL OF PATHOLOGY. By JOSEPH COATS,

M.D., late Professor of Pathology in the University of Glasgow. Revised throughout and Edited by LEWIS R. SUTHERLAND, M.D., Professor of Pathology, University of St. Andrews. With 729 Illustrations and 2 Coloured Plates. 8vo, 28s. net.

COOKE.—*WORKS* by THOMAS COOKE, F.R.C.S. Eng., B.A., B.Sc., M.D. Paris, late Senior Assistant Surgeon to the Westminster Hospital.

TABLETS OF ANATOMY. Being a Synopsis of demonstrations given in the Westminster Hospital Medical School. Eleventh Edition in three Parts, thoroughly brought up to date, and with over 700 Illustrations from all the best sources, British and Foreign. Post 4to. Part I. The Bones, 7s. 6d. net; Part II. Limbs, Abdomen, Pelvis, 10s. 6d. net; Part III. Head and Neck, Thorax, Brain, 10s. 6d. net.

APHORISMS IN APPLIED ANATOMY AND OPERATIVE SURGERY. Including 100 Typical *vivá voce* Questions on Surface Marking, etc. Crown 8vo, 3s. 6d.

CURTIS. THE ESSENTIALS OF PRACTICAL BACTERIOLOGY: an Elementary Laboratory Work for Students and Practitioners. By H. J. CURTIS, B.S. and M.D. Lond., F.R.C.S., formerly Surgeon to the North-Eastern Hospital for Children; Assistant Surgeon, Royal Hospital for Children and Women, Waterloo Road; Surgical Registrar and Assistant to the Professor of Pathology, University College, London. With 133 Illustrations. 8vo, 9s.

DAKIN. A HANDBOOK OF MIDWIFERY. By WILLIAM RADFORD DAKIN, M.D., F.R.C.P., Obstetric Physician and Lecturer on Midwifery at St. George's Hospital, Examiner in Midwifery and Diseases of Women on the Conjoint Board of the Royal Colleges of Physicians and Surgeons in England, etc. With 394 Illustrations. Large crown 8vo, 18s.

DHINGRA. ELEMENTARY BACTERIOLOGY. By M. L. DHINGRA, M.D., C.M. Edin., Diplomate in State Medicine, University of Cambridge, etc. With Coloured Frontispiece and 26 Illustrations in the Text. Crown 8vo 3s. net.

DICKINSON.—*WORKS* by W. HOWSHIP DICKINSON, M.D. Cantab., F.R.C.P., Consulting Physician to St. George's Hospital; Consulting Physician to the Hospital for Sick Children, etc.

ON RENAL AND URINARY AFFECTIONS. Complete in Three Parts, 8vo, with 12 Plates, and 122 Woodcuts. £3 4s. 6d.

THE TONGUE AS AN INDICATION OF DISEASE; being the Lumleian Lectures delivered at the Royal College of Physicians in March, 1888. 8vo, 7s. 6d.

OCCASIONAL PAPERS ON MEDICAL SUBJECTS, 1855-1896. 8vo, 12s.

DOCKRELL. AN ATLAS OF DERMATOLOGY: showing the Appearances, Clinical and Microscopical, Normal and Abnormal, of Conditions of the Skin. 60 Coloured Plates and Descriptive Letterpress. By MORGAN DOCKRELL, M.A., M.D. (Dub. Univ.), Senior Physician and Chesterfield Lecturer on Dermatology to St. John's Hospital for Diseases of the Skin. Fcp. folio, 50s. net.

* * The plate showing the clinical appearance of each disease appears on the same page with that displaying the microscopical. The descriptive letterpress in each case is as brief as possible.

ERICHSEN. THE SCIENCE AND ART OF SURGERY: A TREATISE ON SURGICAL INJURIES, DISEASES AND OPERATIONS. By Sir JOHN ERIC ERICHSEN, Bart., F.R.S., LL.D. Edin., Hon. M.Ch. and F.R.C.S. Ireland. Tenth Edition. Revised by the late MARCUS BECK, M.S. and M.B. Lond., F.R.C.S., Surgeon to University College Hospital, and Professor of Surgery in University College, London; and by RAYMOND JOHNSON, M.B. and B.S. Lond., F.R.C.S., Assistant Surgeon to University College Hospital, etc. Illustrated by nearly 1,000 Engravings on Wood. 2 vols. Royal 8vo, 48s.

FOWLER AND GODLEE. THE DISEASES OF THE LUNGS. By JAMES KINGSTON FOWLER, M.A., M.D., F.R.C.P., Physician to the Middlesex Hospital and to the Hospital for Consumption and Diseases of the Chest, Brompton; late Examiner in Medicine at the University of Cambridge, and on the Conjoint Examining Board in England; and RICKMAN JOHN GODLEE, M.S., F.R.C.S., Honorary Surgeon-in-Ordinary to His Majesty, Fellow and Professor of Clinical Surgery, University College, London; Surgeon to University College Hospital and to the Hospital for Consumption and Diseases of the Chest, Brompton; Surgeon-in-Ordinary to His Majesty's Household. With 160 Illustrations. 8vo, 25s.

GARROD.—*WORKS* by Sir ALFRED BARING GARROD, M.D., F.R.S., etc.; Consulting Physician to King's College Hospital; late Vice-President of the Royal College of Physicians.

A TREATISE ON GOUT AND RHEUMATIC GOUT (RHEUMATOID ARTHRITIS). Third Edition, thoroughly Revised and Enlarged; with 6 Plates, comprising 21 figures (14 Coloured), and 27 Illustrations engraved on Wood. 8vo, 21s.

THE ESSENTIALS OF MATERIA MEDICA AND THERAPEUTICS. The Fourteenth Edition, Revised and Edited, under the Supervision of the Author, by NESTOR TIRARD, M.D. Lond., F.R.C.S., Professor of Materia Medica and Therapeutics in King's College, London, etc. Crown 8vo, 12s. 6d.

GOADBY. THE MYCOLOGY OF THE MOUTH: A TEXT-BOOK OF ORAL BACTERIA. By KENNETH W. GOADBY, L.D.S. Eng., D.P.H. Camb., L.R.C.P., M.R.C.S., Bacteriologist and Lecturer on Bacteriology, National Dental Hospital, etc. With 82 Illustrations. 8vo, 8s. 6d. net.

GOODSALL AND MILES. DISEASES OF THE ANUS AND RECTUM. By D. H. GOODSALL, F.R.C.S., Senior Surgeon Metropolitan Hospital, Senior Surgeon (late House Surgeon) St. Mark's Hospital; and W. ERNEST MILES, F.R.C.S., Assistant Surgeon to the Cancer Hospital, Surgeon (out-patients) to the Gordon Hospital, etc. (In Two Parts).

PART I.—Anatomy of the Ano-rectal Region—General Diagnosis—Abscess—Ano-rectal Fistula—Recto-urethral, Recto-vesical and Recto-vaginal Fistula—Sinus over the Sacro-coccygeal Articulation—Fissure—Hæmorrhoids (External and Internal). With 91 Illustrations. 8vo, 7s. 6d. net.

PART II.—(Nearly ready).

GRAY. ANATOMY, DESCRIPTIVE AND SURGICAL. By HENRY GRAY, F.R.S., late Lecturer on Anatomy at St. George's Hospital Medical School. The Fifteenth Edition Enlarged, edited by T. PICKERING PICK, F.R.C.S., Consulting Surgeon to St. George's Hospital, etc., and by ROBERT HOWDEN, M.A., M.B., C.M., Professor of Anatomy in the University of Durham, etc. With 772 Illustrations, a large proportion of which are Coloured, the Arteries being coloured red, the Veins blue, and the Nerves yellow. The attachments of the muscles to the bones, in the section on Osteology, are also shown in coloured outline. Royal 8vo, 32s. net.

HALLIBURTON.—*WORKS* by W. D. HALLIBURTON, M.D., F.R.S., F.R.C.P., Professor of Physiology in King's College, London.

A TEXT-BOOK OF CHEMICAL PHYSIOLOGY AND PATHOLOGY. With 104 Illustrations. 8vo, 28s.

THE ESSENTIALS OF CHEMICAL PHYSIOLOGY. For the Use of Students. With 83 Illustrations. 8vo, 4s. 6d. net.

HARE. A COMMON HUMORAL FACTOR OF DISEASE :

Being a deductive investigation into the primary causation, meaning, mechanism and rational treatment, preventive and curative, of the Paroxysmal Neurose (migraine, asthma, epilepsy, etc.), Gout, high blood-pressure, circulatory, renal and other degenerations. By FRANCIS EVERARD HARE, M.D., late Consulting Physician to the Brisbane General Hospital; Visiting Physician to the Diamantina Hospital for Chronic Diseases, Brisbane; Inspector-General of Hospitals for Queensland; Author of "The Cold-Bath Treatment of Typhoid Fever," and "The Mechanism of the Paroxysmal Neuroses". 2 vols. Medium 8vo.

HILLIER. THE PREVENTION OF CONSUMPTION. By ALFRED HILLIER, M.D., C.M., B.A., Secretary to the National Association for the Prevention of Consumption (London), Member of the Council of the International Association for the Prevention of Tuberculosis (Berlin), Visiting Physician to the London Open-Air Sanatorium. Revised by Professor R. KOCH. With 14 Illustrations. Crown 8vo, 5s. net.

INQUIRY (AN) INTO THE PHENOMENA ATTENDING DEATH BY DROWNING AND THE MEANS OF PROMOTING RESUSCITATION IN THE APPARENTLY DROWNED. Report of a Committee appointed by the Royal Medical and Chirurgical Society. With 2 Diagrams and 26 Folding-out Plates. 8vo, 5s. net.

LANG. THE METHODICAL EXAMINATION OF THE EYE. Being Part I. of a Guide to the Practice of Ophthalmology for Students and Practitioners. By WILLIAM LANG, F.R.C.S. Eng., Surgeon to the Royal London Ophthalmic Hospital, Moorfields, etc. With 15 Illustrations. Crown 8vo, 3s. 6d.

LUFF. TEXT-BOOK OF FORENSIC MEDICINE AND TOXICOLOGY. By ARTHUR P. LUFF, M.D., B.Sc. Lond., Physician in Charge of Out-Patients and Lecturer on Medical Jurisprudence and Toxicology in St. Mary's Hospital; Examiner in Forensic Medicine in the University of London; External Examiner in Forensic Medicine in the Victoria University; Official Analyst to the Home Office. With 13 full-page Plates (1 in colours) and 33 Illustrations in the Text. 2 vols., Crown 8vo, 24s.

NOTTER AND FIRTH. HYGIENE. By J. L. NOTTER, M.A., M.D., Professor of Hygiene in the Army Medical School, Netley; Colonel Royal Army Medical Corps; and R. H. FIRTH, F.R.C.S., late Assistant Professor of Hygiene in the Army Medical School, Netley; Major Royal Army Medical Corps. With 93 Illustrations. Crown 8vo, 3s. 6d.

PAGET. MEMOIRS AND LETTERS OF SIR JAMES PAGET, Bart., F.R.S., D.C.L., late Sergeant-Surgeon to Her late Majesty Queen Victoria. Edited by STEPHEN PAGET, F.R.C.S. With Portrait. 8vo, 6s. net.

SELECTED ESSAYS AND ADDRESSES BY SIR JAMES PAGET. Edited by STEPHEN PAGET, F.R.C.S. 8vo, 12s. 6d. net.

CONTENTS: Senile Scrofula (1867)—Cases that Bonesetters Cure (1867)—On Stammering with other Organs than those of Speech (1868)—What becomes of Medical Students (1869)—Sexual Hypochondriasis (1870)—On Dissection-wounds (1871)—Nervous Mimicry (1873)—On Disease of the Mammary Areola preceding Cancer of the Mammary Gland (1874)—On a Form of Chronic Inflammation of Bones (Osteitis Deformans) (1877)—Hunterian Oration (1877)—On some of the Sequels of Typhoid Fever (1879)—Anæsthetics: The History of a Discovery (1879)—Elementary Pathology (1880)—Theology and Science (1880)—Presidential Address at the Opening of the International Medical Congress (1881)—The Contrast of Temperance with Abstinence (1881)—Experiments on Animals (1881)—Some Rare and New Diseases (1882)—National Health and National Work (1884)—Periostritis following Strains (1891)—Spines Suspected of Deformity (1891)—Obscure Cases of Caries of the Spine (1891)—Errors in the Chronometry of Life (1891)—Use of the Will for Health (1891).

PHILLIPS. MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS: INORGANIC SUBSTANCES. By CHARLES D. F. PHILLIPS, M.D., LL.D., F.R.S. Edin., late Lecturer on Materia Medica and Therapeutics at the Westminster Hospital Medical School; late Examiner in the University of Edinburgh, etc. 8vo, 21s.

POOLE. COOKERY FOR THE DIABETIC. By W. H. and Mrs. POOLE. With Preface by Dr. PAVY. Fcap. 8vo, 2s. 6d.

POORE.—WORKS by GEORGE VIVIAN POORE, M.D., F.R.C.P.

THE EARTH IN RELATION TO THE PRESERVATION AND DESTRUCTION OF CONTAGIA: being the Milroy Lectures delivered at the Royal College of Physicians in 1899, together with other Papers on Sanitation. 13 Illustrations. Crown 8vo, 5s.

ESSAYS ON RURAL HYGIENE. With 12 Illustrations. Crown 8vo, 6s. 6d.

THE DWELLING HOUSE. With 36 Illustrations. Crown 8vo, 3s. 6d.

COLONIAL AND CAMP SANITATION. With 11 Illustrations. Crown 8vo, 2s. net.

PROBYN-WILLIAMS. A PRACTICAL GUIDE TO THE ADMINISTRATION OF ANÆSTHETICS. By R. J. PROBYN-WILLIAMS, M.D., Anæsthetist and Instructor in Anæsthetics at the London Hospital; Lecturer in Anæsthetics at the London Hospital Medical College, etc. With 34 Illustrations. Crown 8vo., 4s. 6d. net.

QUAIN. QUAIN'S DICTIONARY OF MEDICINE. By Various Writers. Edited by H. MONTAGUE MURRAY, M.D., F.R.C.P., Joint Lecturer on Medicine, Charing Cross Medical School, and Physician to Charing Cross Hospital, and to the Victoria Hospital for Children, Chelsea; Examiner in Medicine to the University of London. Assisted by JOHN HAROLD, M.B., B.Ch., B.A.O., Physician to St. John's and St. Elizabeth's Hospital, and Demonstrator of Medicine at Charing Cross Medical School, and W. CECIL BOSANQUET, M.A., M.D., F.R.C.P., Assistant Physician, Charing Cross Hospital, etc. Third and Cheaper Edition, largely Rewritten, and Revised throughout. With 21 Plates (14 in Colour) and numerous Illustrations in the Text. 8vo, 21s. net., buckram; 30s. net., half-morocco.

QUAIN. QUAIN'S (JONES) ELEMENTS OF ANATOMY. The Tenth Edition. Edited by EDWARD ALBERT SCHÄFER, F.R.S., Professor of Physiology in the University of Edinburgh; and GEORGE DANCER THANE, Professor of Anatomy in University College, London. In 3 vols.

* * The several parts of this work form COMPLETE TEXT-BOOKS OF THEIR RESPECTIVE SUBJECTS. They can be obtained separately as follows:—

VOL. I., PART I. EMBRYOLOGY. By E. A. SCHÄFER, F.R.S. With 200 Illustrations. Royal 8vo, 9s.

VOL. I., PART II. GENERAL ANATOMY OR HISTOLOGY. By E. A. SCHÄFER, F.R.S. With 491 Illustrations. Royal 8vo, 12s. 6d.

VOL. II., PART I. OSTEOLOGY — ARTHROLOGY. By G. D. THANE. With 224 Illustrations. Royal 8vo, 11s.

VOL. II., PART II. MYOLOGY — ANGEIOLOGY. By G. D. THANE. With 199 Illustrations. Royal 8vo, 16s.

VOL. III., PART I. THE SPINAL CORD AND BRAIN. By E. A. SCHÄFER, F.R.S. With 139 Illustrations. Royal 8vo, 12s. 6d.

VOL. III., PART II. THE NERVES. By G. D. THANE. With 102 Illustrations. Royal 8vo, 9s.

VOL. III., PART III. THE ORGANS OF THE SENSES. By E. A. SCHÄFER, F.R.S. With 178 Illustrations. Royal 8vo, 9s.

[Continued.]

QUAIN. QUAIN'S (JONES) ELEMENTS OF ANATOMY—*cont.*

VOL. III., PART IV. SPLANCHNOLOGY. By E. A. SCHÄFER, F.R.S., and JOHNSON SYMINGTON, M.D. With 337 Illustrations. Royal, 8vo, 16s.

APPENDIX. SUPERFICIAL AND SURGICAL ANATOMY. By Professor G. D. THANE and Professor R. J. GODLEE, M.S. With 29 Illustrations. Royal 8vo, 6s. 6d.

SCHÄFER.—WORKS by E. A. SCHÄFER, F.R.S. *Professor of Physiology in the University of Edinburgh.*

THE ESSENTIALS OF HISTOLOGY : Descriptive and Practical. For the Use of Students. With 463 Illustrations. 8vo, 9s. net.

DIRECTIONS FOR CLASS WORK IN PRACTICAL PHYSIOLOGY : Elementary Physiology of Muscle and Nerve and of the Vascular and Nervous Systems. With 48 Diagrams. 8vo, 3s. net.

SMALE AND COLYER. DISEASES AND INJURIES OF THE TEETH, including Pathology and Treatment. By MORTON SMALE, M.R.C.S., L.S.A., L.D.S., Dental Surgeon to St. Mary's Hospital, Consulting Dental Surgeon, Dental Hospital of London, etc.; and J. F. COLYER, L.R.C.P., M.R.C.S., L.D.S., Dental Surgeon to Charing Cross Hospital and to the Dental Hospital of London, Dean of the School, Dental Hospital of London. Second Edition Revised and Enlarged by J. F. COLYER. With 640 Illustrations. Large Crown 8vo, 21s. net.

SMITH (H. F.). THE HANDBOOK FOR MIDWIVES. By HENRY FLY SMITH, B.A., M.B. Oxon., M.R.C.S. Second Edition. With 41 Woodcuts. Crown 8vo, 5s.

STEVENSON. WOUNDS IN WAR : the Mechanism of their Production and their Treatment. By Surgeon-General W. F. STEVENSON, C.B. (Army Medical Staff), B.A., M.B., M.Ch. Dublin University; Professor of Military Surgery, Royal Army Medical College, London. With 127 Illustrations. 8vo, 15s. net.

TAPPEINER. INTRODUCTION TO CHEMICAL METHODS OF CLINICAL DIAGNOSIS. By Dr. H. TAPPEINER, Professor of Pharmacology and Principal of the Pharmacological Institute of the University of Munich. Translated from the Sixth German Edition, with an Appendix on Micro-Biological Methods of Diagnosis, by EDMOND J. MCWEENEY, M.A., M.D. Royal Univ. of Ireland, L.R.C.P.I., etc. With 22 Illustrations. Crown 8vo, 3s. 6d.

THORNTON. HUMAN PHYSIOLOGY. By JOHN THORNTON, M.A., Author of "Elementary Physiography," "Advanced Physiography," etc. With 267 Illustrations, some of which are Coloured. Crown 8vo, 6s.

WALLER.—*WORKS* by **AUGUSTUS D. WALLER, M.D.**, *Lecturer on Physiology at St. Mary's Hospital Medical School, London; late External Examiner at the Victorian University.*

AN INTRODUCTION TO HUMAN PHYSIOLOGY. Third Edition, Revised. With 314 Illustrations. 8vo, 18s.

LECTURES ON PHYSIOLOGY.

FIRST SERIES.—*On Animal Electricity.* 8vo, 5s. net.

Veterinary Medicine, etc.

FITZWYGRAM. **HORSES AND STABLES.** By Lieutenant-General Sir F. FITZWYGRAM, Bart. With 56 pages of Illustrations. 8vo, 3s. net.

STEEL.—*WORKS* by **JOHN HENRY STEEL, F.R.C.V.S., F.Z.S., A.V.D.**, *late Professor of Veterinary Science and Principal of Bombay Veterinary College.*

A TREATISE ON THE DISEASES OF THE DOG; being a Manual of Canine Pathology. Especially adapted for the use of Veterinary Practitioners and Students. With 88 Illustrations. 8vo, 10s. 6d.

A TREATISE ON THE DISEASES OF THE OX; being a Manual of Bovine Pathology. Especially adapted for the use of Veterinary Practitioners and Students. With 2 Plates and 117 Woodcuts. 8vo, 15s.

A TREATISE ON THE DISEASES OF THE SHEEP; being a Manual of Ovine Pathology for the use of Veterinary Practitioners and Students. With Coloured Plate and 99 Woodcuts. 8vo, 12s.

YOUATT.—*WORKS* by **WILLIAM YOUATT.**

THE HORSE. Revised and Enlarged by W. WATSON, M.R.C.V.S. With 52 Wood Engravings. 8vo, 7s. 6d.

THE DOG. Revised and Enlarged. With 33 Wood Engravings. 8vo, 6s.

General Scientific Works.

ARRHENIUS. A TEXT-BOOK OF ELECTRO-CHEMISTRY. By SVANTE ARRHENIUS, Professor of Physics at the University of Stockholm. Translated from the German Edition by JOHN McCRAE, Ph.D. With 58 Illustrations. 8vo, 9s. 6d. net.

BENNETT AND MURRAY. A HANDBOOK OF CRYPTO-GAMIC BOTANY. By A. W. BENNETT, M.A., B.Sc., F.L.S., and GEORGE R. MILNE MURRAY, F.L.S. With 378 Illustrations. 8vo, 16s.

BOSE. RESPONSE IN THE LIVING AND NON-LIVING. By JAGADIS CHUNDER BOSE, M.A., Cantab., D.Sc. Lond., Professor, Presidency College, Calcutta. With 117 Illustrations. 8vo, 10s. 6d.

* * * This volume describes experimental investigations on animal, vegetable, and inorganic substances regarding their response to stimulus. These researches show that the effects of fatigue, stimulants, depressants, and poisons are alike in the organic and inorganic, and demonstrate that the response phenomena in the "living" have been foreshadowed in the "non-living".

CHAPMAN. THE FORAMINIFERA: AN INTRODUCTION TO THE STUDY OF PROTOZOA. By FREDERICK CHAPMAN, A.L.S., F.R.M.S., formerly Assistant in the Geological Laboratory of the Royal College of Science; Palæontologist to the National Museum, Melbourne. With 14 Plates and 42 Illustrations in the Text. 8vo, 9s. net.

CROOKES. SELECT METHODS IN CHEMICAL ANALYSIS (chiefly inorganic). By Sir W. CROOKES, F.R.S., V.P.C.S. Editor of "The Chemical News". Third Edition, re-written and enlarged. Illustrated with 67 Woodcuts. 8vo, 21s. net.

DRUDE. THE THEORY OF OPTICS. By PAUL DRUDE, Professor of Physics at the University of Giessen. Translated from the German by C. RIBORG MANN and ROBERT A. MILLIKAN, Assistant Professors of Physics at the University of Chicago. With 110 Diagrams. 8vo, 15s. net.

FRANKLAND. MICRO-ORGANISMS IN WATER, THEIR SIGNIFICANCE, IDENTIFICATION AND REMOVAL. Together with an Account of the Bacteriological Methods Involved in their Investigation. Specially Designed for the Use of those connected with the Sanitary Aspects of Water Supply. By Professor PERCY FRANKLAND, Ph.D., B.Sc. Lond., F.R.S., Fellow of the Chemical Society; and Mrs. PERCY FRANKLAND, Joint Author of "Studies on Some New Micro-Organisms Obtained from Air". With 2 Plates and numerous Diagrams. 8vo, 16s. net.

FRANKLAND. BACTERIA IN DAILY LIFE. By Mrs. PERCY FRANKLAND, F.R.M.S. Crown 8vo, 5s. net.

HELMHOLTZ.—*WORKS* by **HERMANN L. F. HELMHOLTZ**,
M.D., late Professor of Physics in the University of Berlin.

ON THE SENSATIONS OF TONE AS A PHYSIOLOGICAL BASIS FOR THE THEORY OF MUSIC. Second English Edition; with numerous additional notes and a new Additional Appendix, bringing down information to 1885, and specially adapted to the use of Musical Students. By **ALEXANDER J. ELLIS**, B.A., F.R.S., F.S.A., etc., formerly Scholar of Trinity College, Cambridge. With 68 Figures engraved on Wood, and 42 Passages in Musical Notes. Royal 8vo, 28s.

POPULAR LECTURES ON SCIENTIFIC SUBJECTS. With 68 Woodcuts. 2 vols. Crown 8vo, 3s. 6d. each.

HERSCHEL. **OUTLINES OF ASTRONOMY.** By Sir **JOHN F. W. HERSCHEL**, Bart., K.H., etc., Member of the Institute of France. Twelfth Edition, with 9 Plates, and numerous Diagrams. 8vo, 12s.

HOFF. **THE ARRANGEMENT OF ATOMS IN SPACE.** By **J. H. VAN 'T HOFF**. Second, Revised and Enlarged Edition. With a Preface by **JOHANNES WISLICENUS**, Professor of Chemistry at the University of Leipzig; and an Appendix, "Stereochemistry among Inorganic Substances," by **ALFRED WERNER**, Professor of Chemistry at the University of Zürich. Translated and Edited by **ARNOLD EILOART**. Crown 8vo, 6s. 6d.

HUDSON AND GOSSE. **THE ROTIFERA OR "WHEEL ANIMALCULES"**. By **C. T. HUDSON**, LL.D., and **P. H. GOSSE**, F.R.S. With 30 Coloured and 4 Uncoloured Plates. In 6 Parts. 4to, price 10s. 6d. each; Supplement, 12s. 6d. Complete in Two Volumes, with Supplement, 4to, £4 4s.

* * * The Plates in the Supplement contain figures of almost all the Foreign Species, as well as of the British Species, that have been discovered since the original publication of Vols. I. and II.

JOUBERT. **ELEMENTARY TREATISE ON ELECTRICITY AND MAGNETISM.** By **G. CAREY FOSTER**, F.R.S., Fellow and Emeritus Professor of Physics in University College, London; and **ALFRED W. PORTER**, B.Sc., Fellow and Assistant Professor of Physics in University College, London. Founded on **JOUBERT'S "Traité Élémentaire d'Électricité"**. With 374 Illustrations and Diagrams. 8vo, 10s. 6d. net.

KLÖCKER. **FERMENTATION ORGANISMS.** A Laboratory Handbook. By **ALB. KLÖCKER**, Assistant in the Carlsberg Laboratory, Copenhagen. Translated from the German by **G. E. ALLAN**, B.Sc., Lecturer in the University of Birmingham, and **J. H. MILLAR**, F.I.C., formerly Lecturer in the British School of Malting and Brewing, and revised by the Author. With 146 Illustrations. 8vo, 12s. net.

LINDLEY AND MOORE. **THE TREASURY OF BOTANY, OR POPULAR DICTIONARY OF THE VEGETABLE KINGDOM**: with which is incorporated a Glossary of Botanical Terms. Edited by **J. LINDLEY**, M.D., F.R.S., and **T. MOORE**, F.L.S. With 20 Steel Plates and numerous Woodcuts. 2 Parts. Fcap. 8vo, 12s.

MACDOUGAL.—*WORKS* by **DANIEL TREMBLY MACDOUGAL**,
Ph.D., Director of the Laboratories of the New York Botanical Garden.

PRACTICAL TEXT-BOOK OF PLANT PHYSIOLOGY.
With 159 Illustrations. 8vo, 7s. 6d. net

ELEMENTARY PLANT PHYSIOLOGY. With 108 Illustrations.
Crown 8vo, 3s.

MELLOR. HIGHER MATHEMATICS FOR STUDENTS OF CHEMISTRY AND PHYSICS. With Special Reference to Practical Work. By J. W. MELLOR, D.Sc., late Senior Scholar, and 1851 Exhibition Scholar, New Zealand University; Honorary Research Fellow, the Owens College, Manchester. With 142 Diagrams. 8vo, 12s. 6d. net.

MENDELÉEFF. WORKS BY D. MENDELÉEFF.

THE PRINCIPLES OF CHEMISTRY. Translated from the Russian (Seventh Edition) by GEORGE KAMENSKY, A.R.S.M., of the Imperial Mint, St. Petersburg, and Edited by THOMAS H. POPE, B.Sc., F.I.C. With 110 Illustrations. 2 vols. 8vo, 32s. net

AN ATTEMPT TOWARDS A CHEMICAL CONCEPTION OF THE ETHER. Translated from the Russian by GEORGE KAMENSKY, A.R.S.M. 8vo, 2s. net.

MEYER. OUTLINES OF THEORETICAL CHEMISTRY. By LOTHAR MEYER, Professor of Chemistry in the University of Tübingen. Translated by Professors P. PHILLIPS BEDSON, D.Sc., and W. CARLETON WILLIAMS, B.Sc. 8vo, 9s.

MEYER. THE KINETIC THEORY OF GASES. Elementary Treatise with Mathematical Appendices. By Dr. OSKAR EMIL MEYER, Professor of Physics at the University of Breslau. Second Revised Edition. Translated by ROBERT E. BAYNES, M.A., Student of Christ Church, Oxford, and Dr. Lee's Reader in Physics. 8vo, 15s. net.

MORGAN. ANIMAL BIOLOGY. An Elementary Text-Book. By C. LLOYD MORGAN, F.R.S., Principal of University College, Bristol. With numerous Illustrations. Crown 8vo, 8s. 6d.

PLIMMER. THE CHEMICAL CHANGES AND PRODUCTS RESULTING FROM FERMENTATION. By R. H. ADERS PLIMMER, D.Sc. Lond. 8vo, 6s. net.

PROCTOR.—WORKS by RICHARD A. PROCTOR.

LIGHT SCIENCE FOR LEISURE HOURS; Familiar Essays on Scientific Subjects, Natural Phenomena, etc. Crown 8vo, 3s. 6d.

THE ORBS AROUND US; a Series of Essays on the Moon and Planets, Meteors and Comets. With Chart and Diagrams. Crown 8vo, 3s. 6d.

OTHER WORLDS THAN OURS; The Plurality of Worlds Studied under the Light of Recent Scientific Researches. With 14 Illustrations. Crown 8vo, 3s. 6d.

THE MOON; her Motions, Aspects, Scenery and Physical Condition. With Plates, Charts, Woodcuts and Lunar Photographs. Crown 8vo, 3s. 6d.

LARGER STAR ATLAS for the Library, in 12 Circular Maps, with Introduction and 2 Index Pages. Folio, 15s., or Maps only, 12s. 6d.

NEW STAR ATLAS for the Library, the School and the Observatory, in 12 Circular Maps (with 2 Index Plates). Crown 8vo, 5s.

OTHER SUNS THAN OURS: a Series of Essays on Suns—Old, Young and Dead. With other Science Gleanings, Two Essays on Whist, and Correspondence with Sir John Herschel. With 9 Star-Maps and Diagrams. Crown 8vo, 3s. 6d.

[Continued.]

PROCTOR.—WORKS by RICHARD A. PROCTOR—continued.

HALF - HOURS WITH THE TELESCOPE: a Popular Guide to the Use of the Telescope as a Means of Amusement and Instruction. With 7 Plates. Fcap. 8vo, 2s. 6d.

THE EXPANSE OF HEAVEN: Essays on the Wonders of the Firmament. Crown 8vo, 3s. 6d.

PLEASANT WAYS IN SCIENCE. Crown 8vo, 3s. 6d.

THE SOUTHERN SKIES: a Plain and Easy Guide to the Constellations of the Southern Hemisphere. Showing in 12 Maps the Position of the principal Star-Groups night after night throughout the year. With an Introduction and a separate Explanation of each Map. True for every Year. 4to, 5s.

MYTHS AND MARVELS OF ASTRONOMY. Crown 8vo, 3s. 6d.

HALF - HOURS WITH THE STARS: a Plain and Easy Guide to the Knowledge of the Constellations. Showing in 12 Maps the position of the principal Star-Groups night after night throughout the Year. With Introduction and a separate Explanation of each Map. True for every Year. 4to, 3s. net.

THE STARS IN THEIR SEASONS. An Easy Guide to a Knowledge of the Star Groups, in 12 large Maps. Imperial 8vo, 5s.

OUR PLACE AMONG INFINITIES: a Series of Essays contrasting our Little Abode in Space and Time with the Infinities around Us. Crown 8vo, 3s. 6d.

ROUGH WAYS MADE SMOOTH. Familiar Essays on Scientific Subjects. Crown 8vo, 3s. 6d.

NATURE STUDIES. By GRANT ALLEN, A. WILSON, T. FOSTER, E. CLODD and R. A. PROCTOR. Crown 8vo, 3s. 6d.

LEISURE READINGS. By E. CLODD, A. WILSON, T. FOSTER, A. C. RUNYARD and R. A. PROCTOR. Crown 8vo, 3s. 6d.

STRENGTH: How to get Strong and keep Strong, with Chapters on Rowing and Swimming, Fat, Age and the Waist. With 9 Illustrations. Crown 8vo, 2s.

REYNOLDS. EXPERIMENTAL CHEMISTRY for Junior Students.

By J. EMERSON REYNOLDS, M.D., F.R.S., Professor of Chemistry, Univ. of Dublin. Fcap. 8vo, with numerous Woodcuts.

PART I.—*Introductory*, 1s. 6d. PART III.—*Metals and Allied Bodies*, 3s. 6d.

PART II.—*Non-Metals*, 2s. 6d. PART IV.—*Chemistry of Carbon Compounds*, 4s.

ROMANES.—WORKS by GEORGE JOHN ROMANES, M.A., LL.D., F.R.S.

DARWIN, AND AFTER DARWIN: an Exposition on the Darwinian Theory, and a Discussion on Post-Darwinian Questions. Part I. **THE DARWINIAN THEORY.** With Portrait of Darwin and 125 Illustrations. Crown 8vo, 10s. 6d. Part II. **POST-DARWINIAN QUESTIONS: Heredity and Utility.** With Portrait of the Author and 5 Illustrations. Crown 8vo, 10s. 6d. Part III. **POST-DARWINIAN QUESTIONS: ISOLATION AND PHYSIOLOGICAL SELECTION.** Crown 8vo, 5s.

AN EXAMINATION OF WEISMANNISM. Crown 8vo, 6s.

ESSAYS. Edited by C. LLOYD MORGAN, F.R.S., Principal of University College, Bristol. Crown 8vo, 6s.

CONTENTS: Primitive Natural History—The Darwinian Theory of Instinct—Man and Brute—Mind in Men and Animals—Origin of Human Faculty—Mental Differences between Men and Women—What is the Object of Life?—Recreation—Hypnotism—Hydrophobia and the Muzzling Order.

SLINGO AND BROOKER. ELECTRICAL ENGINEERING FOR ELECTRIC-LIGHT ARTISANS AND STUDENTS. (Embracing those branches prescribed in the Syllabus issued by the City and Guilds Technical Institute.) By W. SLINGO and A. BROOKER. With 383 Illustrations. Crown 8vo, 12s.

SORAUER. A POPULAR TREATISE ON THE PHYSIOLOGY OF PLANTS. For the Use of Gardeners or for Students of Horticulture and of Agriculture. By Dr. PAUL SORAUER, Director of the Experimental Station at the Royal Pomological Institute in Proskau (Silesia). Translated by F. E. WEISS, B.Sc., F.L.S., Professor of Botany at the Owens College, Manchester. With 33 Illustrations. 8vo, 9s. net.

TEXT-BOOKS OF PHYSICAL CHEMISTRY.

Edited by Sir WILLIAM RAMSAY, K.C.B., F.R.S.

THE PHASE RULE AND ITS APPLICATIONS. By ALEX. FINDLAY, M.A., Ph.D., D.Sc., Lecturer and Demonstrator in Chemistry, University of Birmingham. With 118 Figures in the Text, together with an "Introduction to the Study of Physical Chemistry" by Sir WILLIAM RAMSAY, K.C.B., F.R.S., Editor of the Series. Crown 8vo, 5s.

* * Sir William Ramsay's "Introduction to Physical Chemistry" is also issued separately, price 1s.

ELECTRO-CHEMISTRY. PART I.—GENERAL THEORY. By R. A. LEHFELDT, D.Sc., Professor of Physics at the East London Technical College. Including a Chapter on the Relation of Chemical Constitution to Conductivity, by T. S. MOORE, B.A., B.Sc., Lecturer in the University of Birmingham. Crown 8vo, 5s.

CHEMICAL STATICS AND DYNAMICS, INCLUDING THE THEORIES OF CHEMICAL CHANGE, CATALYSIS, AND EXPLOSIONS. By J. W. MELLOR, D.Sc. (N.Z.), B.Sc. (Vict.). Crown 8vo, 7s. 6d.

THORPE. A DICTIONARY OF APPLIED CHEMISTRY. By T. E. THORPE, C.B., B.Sc. Vict., Ph.D., F.R.S., Treas. C.S., Director of Government Laboratories, London. Assisted by Eminent Contributors. To be published in 3 vols. 8vo. Vols. I. and II., £2 2s. each; Vol. III., £3 3s.

TILDEN. A SHORT HISTORY OF THE PROGRESS OF SCIENTIFIC CHEMISTRY IN OUR OWN TIMES. By WILLIAM A. TILDEN, D.Sc. Lond., D.Sc. Dub., F.R.S., Fellow of the University of London, Professor of Chemistry in the Royal College of Science, London. Crown 8vo, 5s. net.

TUBEUF. DISEASES OF PLANTS DUE TO CRYPTOGAMIC PARASITES. Translated from the German of Dr. CARL FREIHERR VON TUBEUF, of the University of Munich, by WILLIAM G. SMITH, B.Sc., Ph.D., Lecturer on Plant Physiology to the University of Edinburgh. With 330 Illustrations. Royal 8vo, 18s. net.

TYNDALL.—*WORKS* by JOHN TYNDALL, F.R.S., etc.

FRAGMENTS OF SCIENCE. 2 Vols. Crown 8vo, 16s.

NEW FRAGMENTS. Crown 8vo, 10s. 6d.

HEAT A MODE OF MOTION. Crown 8vo, 12s.

SOUND. With 204 Woodcuts. Crown 8vo, 10s. 6d.

RESEARCHES ON DIAMAGNETISM AND MAGNETIC-CRYSTALLIC ACTION, including the question of Diamagnetic Polarity. Crown 8vo, 12s.

ESSAYS ON THE FLOATING MATTER OF THE AIR in relation to Putrefaction and Infection. With 24 Woodcuts. Crown 8vo, 7s. 6d.

LECTURES ON LIGHT, delivered in America in 1872 and 1873. With 57 Diagrams. Crown 8vo, 5s.

LESSONS IN ELECTRICITY AT THE ROYAL INSTITUTION, 1875-76. With 58 Woodcuts. Crown 8vo, 2s. 6d.

NOTES OF A COURSE OF SEVEN LECTURES ON ELECTRICAL PHENOMENA AND THEORIES, delivered at the Royal Institution. Crown 8vo, 1s. 6d.

NOTES OF A COURSE OF NINE LECTURES ON LIGHT, delivered at the Royal Institution. Crown 8vo, 1s. 6d.

FARADAY AS A DISCOVERER. Crown 8vo, 3s. 6d.

THE GLACIERS OF THE ALPS: being a Narrative of Excursions and Ascents. An Account of the Origin and Phenomena of Glaciers and an Exposition of the Physical Principles to which they are related. With 61 Illustrations. Crown 8vo, 6s. 6d. net.

WATTS (H.). DICTIONARY OF CHEMISTRY. Revised and entirely Re-written by H. FORSTER MORLEY, M.A., D.Sc., Fellow of, and lately Assistant-Professor of Chemistry in, University College, London; and M. M. PATTISON MUIR, M.A., F.R.S.E., Fellow and Prælector in Chemistry of Gonville and Caius College, Cambridge. Assisted by Eminent Contributors. 4 vols. 8vo, £5 net.

WEBB. CELESTIAL OBJECTS FOR COMMON TELESCOPES. By the Rev. T. W. WEBB, M.A., F.R.A.S., late Vicar of Hardwick, Herefordshire. Fifth Edition, Revised and greatly Enlarged by the Rev. T. E. ESPIN, M.A., F.R.A.S. (Two Volumes.)

VOL. I. With Portrait and a Reminiscence of the Author, 2 Plates and numerous Illustrations. Crown 8vo, 6s.

VOL. II. With Illustrations and Map of Star Spectra. Crown 8vo, 6s. 6d.

WRIGHT. OPTICAL PROJECTION: A Treatise on the Use of the Lantern in Exhibition and Scientific Demonstration. By LEWIS WRIGHT, Author of "Light: a Course of Experimental Optics". With 232 Illustrations. Crown 8vo, 6s.

