THE GERM THEORY

APPLIED TO THE EXPLANATION

OF THE

PHENOMENA OF DISEASE

THE SPECIFIC FEVERS

BY

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TO

JOHN TYNDALL, D.C.L., LL.D., F.R.S.,

PROFESSOR OF NATURAL PHILOSOPHY IN THE ROYAL INSTITUTION OF GREAT BRITAIN,

This Volume is Dedicated;

NOT ONLY IN TOKEN OF THE AUTHOR'S ADMIRATION FOR HIS

BRILLIANT TALENTS AS A MAN OF SCIENCE;

BUT IN RECOGNITION OF THE LIGHT

WHICH HIS INVESTIGATIONS HAVE THROWN ON THE SUBJECT

DEALT WITH IN THESE PAGES;

AND

IN ACKNOWLEDGEMENT OF THE SERVICE WHICH HE HAS THEREBY

RENDERED TO THE SCIENCE OF MEDICINE.

PREFACE.

A SOUND pathology is the basis of all rational medicine: a eorreet knowledge of the mode of production of diseased processes, the surest means of finding out how these proeesses may be prevented and checked.

Bearing as The Germ Theory of Disease does, on the pathology of the most important ailments to whieh man is liable, the establishment, or the refutation of this theory, is a matter of importanee not only to medical seienee, but to mankind.

Hitherto, the question has been treated ehiefly as a biologieal one. More attention has been paid to the mode of origin, than to the mode of aetion, of the germs which were supposed to exist.

One object whieh I have in view is to rescue The Germ Theory of Disease from what I consider a false and misleading position, and to give to it its true and legitimate standing as a pathologieal question.

The subjeet discussed in the following pages, is not whether germs may originate *de novo;* but whether the propagation of germs in the system, is competent to produee the phenomena of disease. The former qucstion is part of the general doctrine of Heterogenesis: the latter constitutes the special question of The Germ Theory of Diseasc.

The diseases to the explanation of whose causation this theory is applieable, are so numerous and so varied, that their separate consideration would have prolonged my labours indefinitely.

Under these circumstances I have considered it advisable to deal, in this volume, only with the Specific Fevers.

I have chosen them, first, because they constitute the most important group of diseases to which man is liable; and second, because they are the maladies whose causation The Germ Theory is believed to be most competent to explain.

To this limitation of my subject, to the absence of all reference to surgical ailments, and to the fact that I wish to deal with The Germ Theory solely in its pathological aspects, is to be ascribed the absence of all reference to the investigations and writings of Lister, Billroth, and others, whose names are prominently and honourably associated with this question.

To each subject of discussion I have devoted a separate chapter.

In dealing with subjects so linked together as the phenomena of the specific fevers, this method has necessarily involved some repetition. But such a shortcoming is more than counterbalanced by the increased facility for stating each argument in full.

This plan, too, has better suited the manner in which the book was written—during odd hours snatched from the busy routine of practice.

Opinions and statements which differ so much from what is generally taught and held, as do those to which I have given expression, are likely to be keenly criticized.

That is no more than is desired.

One request only I would venture to make, and that is, that it should not be forgotten that I have purposely omitted all reference to forms of fever which are not regarded as due to the entrance into the system from without of a specific *materies morbi*.

With such forms of fever I hope to deal on a future occasion.

CONTENTS.

CHAPTER I.

THE GERM THEORY OF DISEASE.

The idea that many of the diseases to which man and the lower animals are subject, result from the presence in the system of minute organisms, is not a new one. But only of late years have the vague hypotheses to which this idea has from time to time given rise, assumed definite shape and form.

The introduction of the microscope, the discovery of the yeast plant, and the further discovery of the parasitic nature of many cutaneous diseases, revived this idea, and gave to it a foundation which was previously wanting. Instead of only vague hypothesis, there was now an argument founded on analogy. Gradually the views entertained became less hazy, and assumed more and more definite character, until the various hypotheses which had hitherto floated about, were welded into a definite theory—The Germ Theory of Disease.

This theory is, that many diseases are due to the presence and propagation in the system, of minute organisms having no part or share in its normal economy. This it is, and no more. It is essential to be clear on this point; for the opponents of the germ theory, and, to some extent, its advocates also, have introduced into the discussion of that theory, the question of the source and mode of origin of these organisms—a complication which has tended to hamper men's minds, and to divert attention from the real subject of discussion—THE COMPETENCE OF GERMS TO PRODUCE THE PHENOMENA OF DISEASE.

The explanation of this confusion is not difficult to find.

Side by side with the Germ Theory of Disease, there sprang into active existence the Evolution Theory of Life; and the discussions which of late years have taken place regarding the former, have been more or less influenced by the views held regarding the latter. The panspermist upholds the germ theory: the heterogenist regards it as retrograde and untenable; and *vice versa*, upholders of the germ theory are, as a rule, panspermists, and its opponents heterogenists. This mingling together of two distinct and separate theories, on two distinct and separate subjects, has introduced into the discussion of each, elements tending to increase the difficulty of a satisfactory solution of both.

It seems to us, that one may hold the evolution theory of life, and yet be a believer in the germ theory of disease —that one may attribute the phenomena of disease to the propagation in the system of minute organisms, without being bound down to the belief that these organisms can never originate *de novo*. That every germ must originate from a pre-existing germ may be true, but such a belief is no essential part of the germ theory of disease. This theory deals only with the competence of living organized particles to produce the phenomena of disease, and does not necessarily take cognisance of the question whether or not they may originate *de novo*. True it is, that one who is interested in the germ theory of disease, cannot fail to be interested also in the evolution theory of life. It is equally true, however, that if he would do justice to either, he must consider each separately and on its own merits.

It has been supposed, too, that a close analogy, if not identity, exists between the processes of fermentation and putrefaction, and the changes which take place in the system during the course of many of those diseases in which germs are believed to be propagated; and that the phenomena of the latter may

be illustrated and explained by what is observed during the former. In this way the opinions held regarding the germ theory of disease, have been more or less tinged by those entertained regarding the mode of production of fermentive and putrefactive changes. Too much has been made of this supposed analogy. To us it does not seem probable that any real analogy is likely to exist between the changes which take place in a decomposing organic fluid, and those which occur in a highly developed living being. Certain it is, notwithstanding the attention which has been bestowed on the subject, that our knowledge of the mode of production of fermentive and putrefactive changes, is not sufficiently precise to be used as a stand-point from which diseased processes may be studied.

For these reasons, we shall consider the germ theory in its application to the explanation of the phenomena of disease, without reference to the evolution theory of life, and uninfluenced by any theory of fermentation or putrefaction. We shall consider the question of the competence of living organized particles to produce the phenomena of disease, without entering on the question whether or not these particles ever originate *de novo*.

We shall, in short, study the germ theory from the pathological side, a mode of considering the question which has hitherto received little attention; but one which seems to us to be not less likely to lead to good results, than the generally adopted one of regarding the question from a biological point of view. The question is, indeed, essentially a pathological one; and, as such, is more likely to be profitably studied from the pathological, than from any other, side. What we purpose to do, is to take the phenomena of disease as they present themselves at the bedside of the patient, and in the post-mortem room, and see whether the germ theory is competent to explain the phenomena there observed.

The distinguishing characteristic of those maladies which are believed to result from the action of germs, is contagiousness. The diseases with which we shall chiefly have to deal in this inquiry are, therefore, those which are communicable from the sick to the healthy, epidemic and contagious diseases.

Before entering on the study of their phenomena, it will be well to see what is known regarding the poison which gives rise to them, and which is conveniently called the contagium.

CHAPTER II.

ON THE NATURE OF CONTAGION.

A CONTAGIUM is a morbific agent, which is propagated in, and given off from, the bodies of the sick, and is capable, when received into a susceptible healthy body, of producing in that body a disease similar to the one during whose course it was formed. For the production of such a result, some contagia require to be directly introduced into the system, while others are capable of producing their effects without such direct contact. For etiological purposes contagia may, therefore, be divided into two great classes, the *fixed* and the *vagrant*[1]—those whose direct introduction into the system is requisite to the production of disease, and those in which such direct application is not necessary, but in which the *materies morbi* may gain entrance into the system through the lungs or alimentary mucous surface. Diseases caused by the former never become epidemic: the propensity to become so is a distinguishing feature of those produced by the latter.

Maladies referable to the latter have ever occupied a prominent place among the ailments to which man is liable; and when regard is had, not only to their great fatality, but to their tendency to prevail in wide-spread epidemics, it is not matter of surprise that they should at all times have occupied a conspicuous place in the literature of the profession, and even in the history of the world.

[1] The word 'vagrant' is used to express that property to which the terms volatile and diffusible are usually applied. Neither of these words is sufficiently accurate. We shall presently see that contagion is not volatile in the popular sense of that term; and that it is not diffusible in the scientific sense of the word.

Notwithstanding the attention which has been bestowed on the subject, and the undoubted ability of many who have handled it, the nature of contagion is still, and probably more now than ever, a fruitful subject of speculation and diversity of opinion.

We shall not occupy space by considering all the various influences, natural and supernatural, astral, aerial, and telluric, organic and inorganic, mundane and extra-mundane, to which the occurrence of epidemics has been ascribed, but shall proceed at once to a practical consideration of the views at present held regarding the nature of contagion.

Our knowledge of the nature of contagion has been advanced in two ways; first, by the examination of fluids known to contain it; and secondly, by a consideration of the facts of infection.

These two modes of investigating the subject we shall consider separately.

The examination of fluids known to contain contagion.

Such fluids are either the blood and normal fluids of the body; or fluids formed during the course of the malady, which, though normal to the disease, are abnormal to the healthy body (the fluid of the vaccine vesicle or small-pox pustule).

When we bear in mind the enormous extent to which the poisons of infectious diseases are reproduced in the system, take into consideration the changes which undoubtedly take place in the blood during the course of such maladies, and have regard to the fact that the poison must exist in the blood, it is not unreasonable to suppose that examination of that fluid may throw light on the obscure cause of the changes which occur. Presenting itself thus, as a prominent field of observation, the blood of those suffering from infectious diseases has had much attention bestowed upon it; it must be confessed, however, with but little practical result.

The chemist tells us that he finds this or that constituent increased, or diminished; and the microscopist reports certain changes in the appearance and number of the corpuscular elements of the blood: but neither has explained to us how the changes which he reports are brought about; or has brought within his ken that particular substance which is known to exist, and which is, directly or indirectly, the cause of the reported changes.

In the case of only two diseases, relapsing fever, and splenic fever, have foreign organisms been detected in the blood: and the relation which these bear to the phenomena of the diseases during whose course they occur, is matter of diversity of opinion. According to one view, they are the cause of the symptoms which characterize these maladies: according to another, they are a mere pathological result of the changes which take place during their course. Their exact significance will be considered when the subject of relapsing fever is before us.

In the blood of other diseases some observers have detected what they supposed to be contagium particles: but the accuracy of these observations is doubtful; and the verdict of 'not proven' must still be pronounced with regard to the question of ocular demonstration of the existence of contagium particles in the blood.

Investigations into the physical characters of those fluids which are formed during the course of some contagious diseases, have been more fruitful in result.

Dr. Beale[2] was the first who pointed out the existence in clear and translucent vaccine lymph of minute particles. The existence of these he demonstrated by means of the microscope; and expressed the opinion that the activity of the fluid depended on the presence of these particles.

M. Chauveau[3] experimentally demonstrated that the vaccine

[2] Microscopical Journal, April 1864: and Report of Cattle Plague Commission.

[3] Comptes Rendus, 1868, lxviii; and 1871, lxxiii.

virus does consist of minute particles: and his observations have been verified by Dr. Burdon-Sanderson[4]. The fluids used by these observers in their investigations were those of the vaccine vesicle, and of the pustule of sheep-pox; but neither from chemical nor microscopic examination of these fluids was derived the information which their observations have afforded. They diluted the fluid derived from the vaccine vesicle and the pustule of sheep-pox with water, and found that the fluid thus diluted, if it acted at all, acted as potently as the undiluted; the difference between the activity of the pure, and that of the diluted lymph, manifesting itself solely in the relative number of successes and failures; the number of failures apparently bearing a direct relation to the extent of the dilution.

Again, by having recourse to the process of diffusion, in which a certain quantity of water is, as it were, superimposed upon the contagious fluid, it was found that, while such a comparatively indiffusible substance as albumen had been so thoroughly diffused as to be readily detected on the surface of the superimposed water, the infecting power of this superficial layer was, nevertheless, nil; the deeper portion had, however, lost none of its activity.

The conclusion which must inevitably be drawn from these observations is, that the contagia of cow-pox and sheep-pox, at least, are neither soluble nor diffusible, but consist of minute solid particles[5].

What has been proved for cow-pox and sheep-pox, may not unreasonably be accepted for all contagia, especially if we find it explain what in them cannot be explained on any other view of their nature; and this we find that it does. The recognition

[4] Twelfth Report of Medical Officer of Privy Council, 1869.

[5] The experiments of Chauveau and Sanderson have been recently repeated on vaccine lymph by Braidwood and Vacher, who confirm their accuracy in all points. (First contribution to the life-history of contagium, by P. M. Braidwood and F. Vacher.)

of the particulate nature of contagion, for instance, offers a ready explanation of a well known, and on any other view, inexplicable fact in the history of infectious diseases, viz. that of two persons situated in exactly the same circumstances, and exposed in exactly the same degree, to a given infectious disease, the one may be seized after a single exposure, while the other may be equally exposed for months without being attacked, and may even escape altogether. The contagium being particulate and indiffusible, and the minute particles of which it consists being irregularly scattered about in the atmosphere, it is evident that the inhalation of one or more of these particles, is purely a matter of chance—such chance bearing a direct relation to the number of particles which exist in a given cubic space.

The explanation of the varying extent to which those who are equally susceptible, and equally exposed, suffer from infectious diseases is the same as that which applies to the case of a regiment in action. If the contagium were as diffusible as the gases formed by the explosion of the powder, and if these gases were as destructive as the contagium, all those exposed to either would soon be placed *hors de combat:* but it is not the gases produced in the explosion which kill, it is the bullet which they impel. So with infectious diseases; it is not the breath of the patient which is deadly to those around, but the contagium particles which are given off with it: and just as some soldiers are killed in their first battle, while others go through many campaigns without receiving a scratch, so some persons are attacked by typhus, or scarlatina, after one or two exposures, while others may be exposed for months without suffering. The contagium which lays low the physician, is just as particulate as the bullet which kills the soldier: the former imparts to the contagious fluid, or to the breath of the patient suffering from infectious disease, the same quality which the bullet imparts to the rifle charge. But for the contagium

particles mingled with it, the breath of such a patient is as impotent for evil as a blank cartridge.

From an examination of fluids known to be contagious, then, it is found that contagium is particulate. This is a great step, which at once dispels many of the old and long-cherished views of its nature.

We have next to inquire into the nature of these particles.

The fact that chemistry has failed to detect their presence in fluids known to contain them, renders it probable that, so far as their ultimate chemical composition is concerned, they differ very little from the fluids in which they exist. Though no very cogent argument can be founded on this fact, it is certainly in favour of their being regarded as organic. For information on this point let us turn to the second means of investigation which we have indicated.

A consideration of the facts of infection.

The facts of infection are twofold: (*a*) those presented by the contagium within the body; and (*b*) those presented by it out of the body.

(*a*) The most noteworthy of those which it presents within the system, is its power of reproduction. A single contagium particle, or, at least, as minute a portion of infecting material as it is possible to introduce into the system, gives rise, in a susceptible individual, to a disease during whose course myriads of similar particles may be formed. This power of reproduction is a property by which contagium is distinguished from all ordinary morbific agents: it is a property, too, which is peculiar to organized structures, and which, therefore, points out contagium as being probably of similar nature. We know of no physical or chemical process at all identical with it; we know, indeed, of nothing in nature identical with it, except that power of producing their kind with which organisms are endowed.

But besides the fact that the poisons of contagious diseases are largely reproduced in the system during the course of the maladies to which they give rise, we have the additional fact that the poison thus formed is always true to its kind. The process by which it is formed is as regular, and as unvarying, as that by which an animal or a vegetable begets an offspring identical in nature with itself. As surely as an acorn produces only an oak, and a rose seed only a rose tree; and as surely as a dog produces only a puppy, and a cat only a kitten; so surely does typhus give rise only to typhus; measles only to measles; and every other contagious disease only to its own special poison and malady. There is not a single contagious disease during whose course the poison which gives rise to it is not largely formed; there is not one in which the poison thus formed ever varies in nature, or in the disease to which it gives rise.

This power of development, and this faculty of breeding true, were the first, and have ever been regarded as the chief arguments in favour of the germ theory of disease: and it is difficult to see how these properties of contagium can be accounted for on any other view of its nature.

It has, indeed, been supposed by some that the process by which the poisons of contagious diseases are reproduced, bears some analogy to that by which crystals are formed.

A crystal, say of sulphate of soda, is placed in a solution of that substance, and is found to grow in size from the deposition around it of what was previously in solution. By the introduction of a solid substance, say a bit of thread, into a saturated solution of any crystallizable substance the same result may be obtained; part of what was hitherto in solution becomes deposited in a crystalline form around the solid substance, and so long as this substance remains in the solution, and the solution contains the requisite quantity of crystallizable material, so long do the crystals continue to grow.

All that is quite true; but in that process there is no real analogy to the reproduction of the poison of contagious diseases. In the latter case the actual amount of the poison formed is increased many thousand times; while in the former the quantity of sulphate of soda, or whatever crystallizable substance we are dealing with, is not increased by one single grain. The crystals may grow in size, but their increase takes place at the expense of the strength of the solution; and at the end of the experiment we have exactly the same quantity of sulphate of soda that we had at the beginning. Contrast with this result the difference between the quantity of small-pox poison which is necessary to produce disease in an unvaccinated person, and the amount of poison which exists in the same person on the tenth day of the disease, when he is covered with eruption, and the emptiness of the analogy which is supposed to exist between the mode of growth of crystals, and of contagium, will at once be apparent. In the one case, we have to do with nothing but the passage of a soluble and crystallizable substance from a state of solution to a state of crystalline solidity: in the other, there is an enormous reproduction of a substance which, at the commencement of the process, existed only in infinitesimal quantity.

It has also been supposed that the process by which contagium is reproduced, is analogous to the action which takes place when the substance oxamide is, under favourable conditions, brought in contact with a solution of oxalic acid. The result of such contact is the decomposition of the oxamide into oxalic acid and ammonia, a change which continues without the addition of fresh acid so long as any oxamide remains. 'In this manner a very minute quantity of oxalic acid may be made to effect the decomposition of several hundred pounds of oxamide; and one grain of the acid to reproduce itself in unlimited quantity[6].'

[6] Chemistry in its application to Agriculture and Physiology, by Justus Liebig, M.D., F.R.S., etc., second edition, page 373, translated by Lyon Playfair.

The change produced in the oxamide by a small quantity of oxalic acid results in the formation of a large quantity of that acid; and the only limit to the continuance of this change is the quantity of the oxamide.

This large reproduction of oxalic acid during a process set agoing by its own presence in minute quantity, has been supposed to be analogous to the mode of formation of contagium; and to be sufficient to demonstrate that a substance capable of exciting a change in others may, during that change, be multiplied indefinitely, independently of the presence of germs[7].

As thus stated by the opponents of the germ theory the argument seems a most telling one. Taking the broad fact that oxalic acid is reproduced in large quantity during a chemical change induced by itself, we cannot fail, at first sight, to be struck by the analogy which seems to obtain between this process, and that which results in the formation of contagium during the course of the specific contagious diseases. On more minute examination, however, the analogy fails entirely. For what is oxamide? It is simply oxalate of ammonia, less two equivalents of water. When oxalate of ammonia is heated in a retort, oxamide is formed: when oxamide is boiled with a strong acid or alkali, oxalate of ammonia is produced. The decomposition of the one readily results in the formation of the other. The composition of oxalate of ammonia is $N H_4 O, C_2 O_3$[8]; that of oxamide is the same, minus two equivalents of water, or $N H_2 C_2 O_2$. The constituents of oxamide are thus the radical amide, $N H_2$, and $C_2 O_2$, which is the radical of oxalic acid; and the change which takes place during the decomposition of oxamide simply consists in the sharing between these two radicals of two equivalents of water: thus $-N H_2 C_2 O_2 + 2HO = N H_4 O, C_2 O_3$ or oxalate of am-

[7] Murchison in 'Transactions of Pathological Society of London,' for 1875.

[8] We have used the old formula because it is simpler and more generally understood than the new.

monia. But (and this is the point of our argument) the presence of oxalic acid is not necessary: *any* acid suffices to set agoing the changes by which oxamide is converted into oxalic acid and ammonia. If the acid used for this purpose be neutralized by the ammonia which is produced during the decomposition of the oxamide, a corresponding quantity of oxalic acid will be set free; this, in its turn, will act on the oxamide which remains, as any other acid would do; and thus the oxalic acid will continue to act so long as any oxamide remains.' It is to be specially observed, however, that a fresh portion of acid is constantly being liberated and brought to bear on the remaining portion of oxamide. It is, therefore, not strictly accurate to say that 'a small portion of oxalic acid will convert an infinite quantity of oxamide into oxalate of ammonia.' It seems to do so; but in reality it does not. A small portion of oxalic acid decomposes only a small portion of oxamide, just as any other acid would do; by this decomposition a little more acid is liberated; this, in its turn, exercises the same action on the oxamide; and so the process goes on, till all the oxamide is decomposed into oxalic acid and ammonia; but the original portion of acid has combined with the liberated ammonia, and ceased to exercise any decomposing influence on the oxamide, long before that substance has been completely transformed into oxalate of ammonia.

It is evident from all this that no real analogy exists between the process by which oxalic acid is formed during the decomposition of oxamide, and that by which contagium is reproduced during the process of disease. In the one case there is no fresh formation, no reproduction of the acid, but simply a slight changing of the constituent elements: in the other there is a large reproduction of a new material. Oxamide may be converted into oxalate of ammonia, and oxalate of ammonia into oxamide; but contagium exists only as contagium; is inconvertible into any other substance; and undergoes no change except (1) that which results in its reproduction, and (2) that which

results in its total destruction as contagium. With the failure of the analogy between the two processes, the argument founded thereon falls to the ground.

(*b*) The phenomena presented by contagium out of the body are also in keeping with the view which regards it as a living organism.

It has been proved by numerous observations that the poisons of many contagious diseases are capable of being preserved for a length of time without losing their infecting power. *Per se* this argument does not seem to us to carry so much weight as is usually attached to it: it is only of value in so far as it corroborates, and gives collateral support to, others. It is quite in keeping with the view which regards contagium as consisting of minute organisms, probably more in keeping with it than with any other: but it is not contradictory of the alternative view which regards the phenomena of the contagious diseases as the result of a physico-chemical process, rather than as the result of the propagation of an organism in the system; and which looks upon the poison which gives rise to this process, not as a living organism, but as a 'fragment of dead organic matter.'

But though, under certain circumstances, the poisons of contagious diseases may be preserved for a considerable time, there can be no doubt that this is the exception rather than the rule; and that, with free exposure to the atmosphere, the contagia of the most infectious diseases are soon destroyed. This ready destructibility of contagium has been adduced as an argument against the germ theory; it being supposed that its speedy destruction on free exposure to atmospheric air is inimical to the view which regards it as consisting of living organisms. To us it seems that this evidence rather points the other way; and that the fact that contagium readily undergoes destructive changes on exposure to the atmosphere, is a stronger argument in favour of the view which regards it as consisting of minute

organisms, than is the counter fact that, under certain conditions, its vitality is exceptionally prolonged. Its speedy destruction when freely exposed to the atmosphere, its occasionally prolonged vitality when not so exposed, and the large extent to which it is reproduced in the system during the course of the disease to which it gives rise, form a combination of facts which seems to us to tell more strongly in favour of the view which regards contagium as consisting of living organisms, than of that which looks on it as dead organic matter. Contagium only manifests its vital properties and its coincident disease-producing powers in the body of a susceptible person: separated from the conditions essential to its propagation it ceases to display the properties of a living organism, and becomes subject to those changes which are apt to take place in all protoplasm which is not in a state of vital activity. 'Of all perishable things protoplasm is the most perishable:' the protoplasm of contagium particles is no exception to this rule, and hence, when freely exposed to the air, is soon destroyed. Free exposure to the atmosphere is, indeed, the best of all disinfectants.

Contagium then, like all organized matter, is prone to undergo change when separated from the conditions essential to its continued vitality; and this very proneness becomes an argument, not against, but in favour of, the view which regards it as consisting of minute organisms. Placed in circumstances conducive to their continued vitality, these organisms speedily declare their presence: separated from these conditions, and placed in circumstances inimical to their propagation, they speedily die.

In considering the question of the destructibility of contagium, it is necessary we should also bear in mind that, in providing for the means of continuing a species, nature is almost wantonly lavish; and that, for every seed which in a state of nature comes to maturity, and develops into a full-grown organism, thousands perish. If every acorn produced an oak, and if every other seed were developed into its own kind, man would

have some difficulty in keeping under cultivation the extent of soil requisite to the production of the cereals which he requires for his daily food. If all the ova of every parasite came to maturity, few animals would be free from these pests. If every small-pox germ which came into existence developed and reproduced its kind in the same way as the parent from which it sprung, the civilised world would have been all but depopulated before the days of Jenner.

It is evident from all this that the destruction of germs is as much a law of nature as their development; that placed in circumstances favourable to such a result, they grow and reproduce their kind; that separated from such circumstances, they die. It is evident too, that throughout nature, those which perish far exceed in number those which flourish. The fact that contagium is subject to this law, indicates that it too is probably a living organism; and clearly shows that any argument founded on its ready destructibility on free exposure to the atmosphere, tells in favour of, rather than against, this view of its nature.

What we know regarding contagium is:—

1. That it is particulate.
2. That in chemical composition it probably closely resembles the fluids in which it exists.
3. That it is largely reproduced in the system during the course of the disease to which it gives rise.
4. That the poison thus reproduced is always identical in nature with that to which it owed its origin.
5. That it is readily destroyed when freely exposed to the atmosphere.
6. That, when not so exposed, it may be kept for a length of time without losing its infecting power.

Now, though one or two of these properties are such as may be explained on the view which regards contagium as consisting of dead organic matter; it seems to us that the view which best

explains the whole of them is that which looks upon it as a living germ, probably of albuminous composition; possessing the power of organic development; always reproducing its kind; capable, under favourable circumstances, of preserving its vitality for a considerable period; but speedily perishing when freely exposed to the atmosphere. Certainly, this view is the one which affords the simplest explanation of the phenomena with which we have to deal. To many its simplicity will be an argument in its favour.

Contagium, then, we find consists of minute particles whose known properties render it probable that they are organized. For further information regarding them we naturally turn to the microscope, as the means by which the nature of these minute particles is most likely to be demonstrated. At the outset of this part of our inquiry we are met by the difficulty of finding magnifying powers sufficient to bring them within our ken. The contagium particles are so exceedingly minute, that they cannot be individuated, and separately studied, by the powers which we can bring to bear upon them.

Organic forms of extreme minuteness have, indeed, under various names been described by different observers as occurring in contagious liquids. These organic forms have been supposed to bear some relation to the contagium, if not actually to constitute it. There is no direct proof, however, that a true contagium particle has ever been seen. Hallier, indeed, believes that the minute organisms which he has described under the name micrococci, and which he regards as minute unicellular fungi, are the contagium particles. Their identity of appearance, in different specific contagious fluids, he endeavours to explain by the supposition that, though exactly resembling one another, each is capable of being developed into a higher form in which the specific distinction is manifest, and from which again the mierococci or contagium particles may be produced. Though extremely suggestive and interesting, these views, in the absence

of more direct evidence to support them, cannot be accepted as true.

In the case of the cattle plague Dr. Beale[9] has seen, with the aid of very high powers, what he considers to be the living contagious matter; and in the fluids of the vaccine vesicle and small-pox pustule has found minute living forms, to the presence of which he ascribes the active properties of these fluids; but 'neither by its form, chemical composition, or other demonstrable properties, could the vaccine germ be distinguished from the small-pox germ, or the pus-germ from either.' He describes the 'minute contagious bioplast' as being 'less than $\frac{1}{100000}$th of an inch in diameter, and often so very clear and structureless, as to be scarcely distinguishable from the fluid in which it is suspended.' The germs which he describes and figures he does not, however, regard as foreign organisms, but as degraded or retrograde 'living matter, derived by direct descent from the living matter of man's organism.'

Dr. Sanderson[10] regards it as probable that 'contagium particles are spheroidal, transparent, of gelatinous consistence, of density nearly equal to that of the animal liquid in which they float, and that they are mainly, but perhaps not exclusively, composed of albumen.' Following Béchamp, he has described under the name of microzymes, the minute organic structures which occur in contagious fluids. In the spheroidal form, which in their earliest state they manifest, they do not exceed the $\frac{1}{20000}$th of an inch in diameter. With regard to their place in nature, Dr. Sanderson differs from Hallier, though this is a point to which he seems to attach no practical importance. 'Bacteria or microzymes,' he says, 'are placed by most naturalists in the animal kingdom, and have a position assigned to them next to the monads. Hallier, on the other hand, believing that

[9] Disease Germs: their real nature. 1870.

[10] Twelfth Report of Medical Officer of Privy Council, page 255.

they originate by the cleavage and multiplication of nuclei in the cells of fungi, and that they develop to the same forms from which they spring, regards them as plants. Their claim to be considered animals is founded partly on their motions, partly on the fact that their chemical reaction on air, when alive, resembles rather the respiration of animals than that which is associated with vegetation.' Further on he adds: 'Of the chemical composition of microzymes we know very little. It is assumed that the particles are albuminous, because they are readily stained with carmine, and browned by iodine; but of the matrix little can be said, except that it is probably also albuminous. Chemistry can as yet give no account of the difference between them. As regards their action on the liquids in which they live, the most important facts are: (1) that their growth is attended with absorption of oxygen and discharge of carbonic acid; (2) that they are remarkably independent of the chemical constitution of the medium, provided that they are supplied with oxygen; and (3) that they take nitrogen from almost any source which contains it, and use it for the building up of their own protoplasm.' Such are the chief characteristics of the minute organic forms to which it is probable that contagium is allied. The particular forms on which observation has hitherto been made were not contagium particles, but there is, Dr. Sanderson thinks, good reason to suppose that these are similar in nature, and obey like laws. 'All microzymes are not contagia, but all contagia may be microzymes.'

The minute organisms hitherto referred to as micrococci and microzymes, are now generally described under the generic term bacteria. The relation which these bear to diseased processes has, of late years, been the subject of much discussion. Some have seemed to think that they were the true *materies morbi*, the real contagium particles to which the occurrence of the diseases in connection with which they were found,

was to be attributed; that they were, in short, the ultimate cause for which pathologists had so long scarched in vain. The frequency with which they were found to exist in virulent and contagious fluids tended to corroborate this view, and for a time the idea was entertained by some that bacteria bore a causal relation to the phenomena of disease. Further research, has shown that there exist very cogent reasons for not assigning to all bacteria so important a place in pathology.

First, it has been found that bacteria may be introduced into the circulation of the lower animals without giving rise to any serious effects. Second, these bodies are found in great abundance on the mucous, and other surfaces in health, and in many fluids which are possessed of no morbific properties. Third, many fluids, known to be possessed of contagious properties, are most potent in the fresh state; their infecting power diminishing in intensity as bacteria are developed therein.

In accordance with his belief in the doctrine of spontaneous generation, Dr. Bastian[11] has advanced the opinion that bacteria may be developed *de novo* from the disintegrating elements of any dead or dying organism; he supports this opinion by numerous experiments and observations.

The accuracy of these observations is, however, called in question by most competent authority. As the result of numerous carefully conducted experiments, Professor Tyndall has been led to the conclusion that the doctrine of spontaneous generation is untenable, and that 'life has never been proved to arise independently of antecedent life.'

Much has yet to be learned regarding the nature and mode of origin of bacteria: but enough is known to enable us to say that all the bacteria which are seen in contagious fluids, and in diseased tissues, are not contagium particles: and this is the point which specially concerns us at present.

[11] Transactions of Pathological Society of London, 1875.

From the presence of bacteria in a given fluid we can postulate nothing as to its disease-producing properties. The fluid may be full of bacteria, and yet be incapable of causing disturbance: it may contain few, or none, of them, and yet a single drop introduced into the circulation may give rise to a most virulent disease.

The fact that contagious fluids are most potent in the fresh state, and that their virulence diminishes in intensity as bacteria increase therein, is looked upon by Dr. Bastian as fatal to the germ theory. Did this theory mean that bacteria are the germs which produce disease, and that all bacteria are alike in nature, there can be no question that the fact alluded to would be fatal to it. But such is not the case. The germ theory existed before the frequent presence of bacteria in contagious fluids had been demonstrated. The discovery of their common existence in such fluids, combined with the fact that contagium had been proved to be particulate and indiffusible, and the additional fact, that there was much evidence tending to show that these particles were organized, could not fail to strike pathologists, and lead them to look on these bacteria as having some connexion, possibly a causal one, with the phenomena of disease. Further researches, and especially those of Dr. Bastian, have, however, clearly shown that between the presence of bacteria, and the occurrence of diseased processes, there exists no necessary and constant relationship. It does not follow, however, that there may not exist an occasional and even causal relationship. All that has been proved is that there do exist bacteria which have no connexion with disease, causal or casual.

It is held by some most competent observers, and especially by Professor Cohn of Breslau, that the bacteria which are found in decomposing and putrid fluids are different from those observed in disease: if such be the case, it is evident that bacteria vary in nature, and that those found in not-

living matter may be different from those seen in living matter: the former have been shown to be void of disease-producing properties; but no such demonstration has been made regarding the latter. In some specific inflammatory affections, variola, diphtheria, erysipelas, the bowel lesion of typhoid fever, the skin lesion of sheep-pox, etc., the presence of organisms has been demonstrated. Though it has not been proved that the organisms observed bear a causal relationship to the diseased processes in connexion with which they are noted; it is very possible that such may ultimately be found to be the case; but it is also possible that they are secondary to the diseased processes—that they are, in short, pathological products.

The germ theory, therefore, stands just where it did before the frequent presence of bacteria in organic fluids (virulent and benign) had been demonstrated; and the words of Dr. Sanderson are as applicable now as they were six years ago—'all microzymes are not contagia, but all contagia may be microzymes.' It has been proved that all bacteria are not capable of producing disease. The question whether or not those seen in connexion with the specific inflammatory affections to which allusion has been made, are primary and causal, or secondary and consequent, will be fully considered when the local lesions of the eruptive fevers receive our attention.

But though Dr. Bastian's argument against the germ theory falls to the ground, the fact on which it was founded still remains; and we have to explain why it is that contagious fluids are most potent in the fresh state, and why it is that their infecting power diminishes in intensity as bacteria appear more abundantly therein.

One of the main facts in the natural history of bacteria which we have to bear in mind, is that they find the materials requisite to their growth in the disintegrating elements of

any organized substance or fluid. According to the germ theory, as we hold it, disease germs are other, and more minute, organisms than those which we see and describe as bacteria. Being organisms they of course tend, like organized matter in general, to undergo change. Now there is no reason why the protoplasm of contagium particles should not, like protoplasm in general, supply the materials required for the growth of the bacteria, or, as Dr. Bastian would say, undergo bacterial degeneration. Granting this (and we see no grounds on which, admitting the existence of germs, we can refuse to do so) it is evident that, whatever view we take of the mode of origin of the bacteria, we have in the occurrence of the changes which accompany their development, a sufficient and adequate explanation of the fact that the infecting power of contagious fluids diminishes in intensity as bacteria appear more abundantly therein: nay more, such a fact becomes, on this view of the matter, evidence not against, but in favour of, the germ theory; for though, independently of the presence of contagium particles, bacteria may be developed in organized fluids, the fact that the infecting power of fluids known to contain these particles, becomes less as bacteria are developed in them, affords strong evidence that some of the bacteria grow at the expense of the infecting material. If such be the case, it is evident that this infecting matter must be nitrogenous, and is probably albuminous. We have already seen that it has been proved in some cases to be particulate: we have also seen that there is good reason for believing it to be organized. The fact that its disintegrating elements serve to nourish bacteria, tends to corroborate this view of its nature, and becomes an additional argument in favour of the theory which regards contagium as consisting of minute living organisms. The bacteria which are observed in contagious fluids, are formed, in part at least, from the disintegrating elements of the organisms to which these fluids owe their specific properties. This is why the virulence of

such fluids diminishes in intensity as bacteria appear more abundantly in them; and thus it is that Dr. Bastian's main argument against the germ theory becomes an argument in its favour.

This argument against the germ theory, founded on the fact that the infecting power of contagious fluids is greater when they are fresh, than when they have begun to undergo change, is the same as that with which we have already dealt, founded on the ready destructibility of contagium on exposure to the atmosphere. The answer to it is likewise the same. All protoplasm is liable to undergo destructive change. The fact which was supposed to be inimical to the germ theory is found, on more careful examination, to tell in its favour.

The opponents of this theory may, and indeed do, advance the objection that they cannot see these organisms, and on this ground refuse to recognise their existence. But this is an objection which is very readily met; for the particulate nature of contagium has already been proved by the experiments of M. Chauveau and Dr. Sanderson, and yet the existence of the particles of which it consists has not been satisfactorily demonstrated by the microscope. We know that minute solid particles, possessed of infecting power, do exist; and the incompetence of the microscope to demonstrate their presence in a fluid known to contain them, cannot overturn the positive evidence of their existence gained in other ways: it simply declares the inadequacy of the microscope to decide as yet the vexed question of the nature of contagium. This seems to us a sufficient answer to the objection so persistently urged by the opponents of the germ theory—that if germs existed, they could surely be seen.

If any further answer were required we should find it in the beautiful experiments of Professor Tyndall, detailed in his 'Observations on the optical deportment of the atmosphere in

reference to the phenomena of putrefaction and infection' (Transactions of the Royal Society of London, Part i. 1876). By these experiments it has been shown that the passage of a beam of light through a liquid, or through air, may reveal the presence of minute particles which cannot be detected by the aid of the microscope. 'Though they are beyond the reach of the microscope, the existence of these particles, foreign to the atmosphere, but floating in it, is as certain as if they could be felt between the fingers, or seen by the naked eye.'

It is among the finest ultra-microscopic particles that, Dr. Tyndall shows, 'the matter potential, as regards the development of bacterial life, is to be sought.'

We have seen that contagium is particulate; that it possesses the properties of a living organism; but that it, nevertheless, eludes the microscope. With such experiments as Professor Tyndall's before us, we cannot fail to see that our inability to bring within the range of our vision the particles of which it consists, is no argument against the view which regards contagium as a germ—a living organized particle. As well might the astronomer say that there exist no stars but those which can be seen by the aid of the telescope, as the biologist say that there exist no organisms but those which can be seen by the aid of the microscope. To limit the possibilities of organized life by the range of our defective vision, no matter how aided, is at once to place limits on a creative power which we believe to be infinite, and to exalt to perfection a means of research which we know to be imperfect. A particle $\frac{1}{50000}$th of an inch in diameter is a thing which the eyes of few men can see. But are we, on that account, justified in saying that the creative power which brought into existence the universe with all its wonders and mysteries; which studded the infinity of space with innumerable worlds, among which our own is but as a drop in the ocean; which put in motion and regulated by fixed laws, the changes

which, during thousands and thousands of years, have taken place in and on the earth, and which gradually rendered this world a suitable habitation first for one race of animals, then for another, and finally for man himself; are we justified in limiting the creative capacity of such a power, by the capacity of one of the senses with which that power has seen fit to endow us?—a sense, too, which is less perfect in us than in some of the lower animals. Is man to step in and say to his Creator, 'Yes, you made both heaven and earth, and all that is therein; you fixed the stars in their proper place, and formed the laws by which they are kept there; you made the sun to shine by day, and the moon to shine by night; you established a correlation between the physical forces which act in the universe, a correlation which I am only now, thousands of years after my creation, beginning to understand; you formed the huge forests whose remains we now dig up as coal; you formed the huge mastodon and the tiniest protozoon; and, lastly, as the crowning act of all your creative power, you formed me—formed me in your own image, and gave me reasoning faculties wherewith I might study the wonders of your creation, and by means of which I might exercise dominion over the beasts of the field; and, above all, greatest of all the wonders of creation, you gave me a soul which cannot die, which will live on through all eternity, and which forms the link which binds me here on earth to you in heaven above. All this you have done; but I will tell you what you cannot do—you cannot make an organism which I cannot see: you cannot make, and endow with life, a particle of protoplasm less than $\frac{1}{5000}$th of an inch in diameter.' Absurd as it seems, this is really what the microscopic argument against the germ theory amounts to. It is simply a denial of the possibility of the existence of organized particles more minute than those which can be brought within range of our vision. It is at once an exaltation of our visual organs to a state of perfection to which they can never

attain; and a limitation of a power which we believe to be infinite.

But in the examination of contagious fluids there are observed exceedingly minute particles which, in our ignorance of their real nature, we describe vaguely and generally as granular matter. But what is granular matter? It is simply an aggregation of particles so minute, that we cannot define their shape or nature. But surely the fact that we are unable to describe them more accurately, is not to be accepted as proof that these particles wherever found are always the same, mere *débris*, possessed of no definite form, and serving no purpose in nature. Of the part which they play in the fluids in which they are observed we know nothing; we simply know that in fluids known to be contagious there do exist particles so minute that the highest powers of the microscope fail to do more than demonstrate their existence; and that, in some contagious fluids, the infecting material is inseparable from these particles. Though we are not warranted in saying positively that all, or even some, of these granules are contagium particles, the fact that such granules do exist in contagious fluids suffices at once to demonstrate the inadequacy of the microscope to determine the nature of the most minute particles which can be brought within range of our vision by its aid, and to expose the narrowness of the view which refuses to recognise the existence of organisms more minute than those to which, by its aid, we can assign definite shape and form.

It is, indeed, said that granular matter may be found anywhere, in boiled albuminous urine, for instance: this, no doubt, is the case, but it does not follow therefrom that all granular matter is alike in nature and in composition, or even in the ultimate form of the individual granules. The granular matter observed in contagious fluids is certainly not the same in nature as that seen in boiled albuminous urine: it has the same appearance under the microscope simply because the individual

particles of which each consists are alike in size; and because the necessarily limited range of our vision prevents us from defining the exact shape of particles so minute. But the fact that we cannot distinguish between them is not sufficient to warrant us in regarding them as identical in nature. Place under the microscope a white blood-corpuscle, a pus-cell, and a mucus corpuscle, and ask any one to say which is which, and he will find much difficulty in discriminating between them. Here we have much larger objects to deal with; but we do not allow their similarity in appearance, shape, and size, to blind us to the fact that they are essentially different in nature, and that each has a history and function of its own. Why then, when dealing with particles much more minute, so minute that they are with difficulty brought within range of our vision, should we attach to their external form an importance which we do not accord to those whose external configuration can be more readily defined? In the one case the shape is seen, and yet comparatively little importance is attached to it: in the other it cannot be defined, and yet its definition is looked upon as of the utmost importance. Surely this is not reasonable.

But how is the nature of different particles possessing the same external configuration to be determined? Place before a microscopist one of the cells to which reference has been made, and his first question is, 'Where did it come from?' On hearing whence you got it, he feels better able to come to a decision as to which it is, pus-cell, white blood-cell, or mucus corpuscle: to the source whence it came he attaches more importance than he does to its external configuration. Now when we come to deal with matter much more minute, why should the source whence it came be looked upon as of no importance, and its external configuration be regarded as all in all? If particles so much larger in size, and possessed of very distinct form, can with difficulty, or not at all, be distinguished from each other by the microscope, is it not reasonable to suppose

that bacteria, and the more minute granules with which we are now dealing, may differ much in nature without our being able to detect any difference in their external appearance?

The granular matter which is observed in vaccine lymph may not by the microscope be distinguished from that which is seen in boiled albuminous urine; but the introduction of the former into the system gives rise to very definite and unvarying symptoms, while the latter is impotent for evil. We know from this that these two forms of granular matter are as distinct as are the pus-cell and the mucus corpuscle; and our inability to distinguish between them by their external form does not, for a moment, invalidate the positive evidence which we have of the essential difference in their nature.

It may, indeed, be said that the granules seen in vaccine lymph are not the contagium particles: they may, or they may not be; we know that the contagium does consist of minute solid particles, and we know too that it is inseparable from those minute particles which we see as granular matter; and though it has not been demonstrated that these granules are the contagium particles, all the evidence is in favour of their being so regarded.

The time may come when we shall be able to distinguish between the different forms of granular matter observed in different fluids: meantime, we are forced to accept the fact that we cannot do so, and to acknowledge that differences do exist which the microscope is incompetent to explain, or even to indicate.

The microscope has done so much to advance our knowledge of biology, physiology, and pathology, that we are apt to be carried away by the very enormity of the advances thus made, and to look to an instrument, to which we owe so much, as the means of settling many problems and questions on which it has already thrown much light. We must bear in mind, however, that there is a point beyond which the microscope cannot carry

us, that our vision has bounds beyond which it cannot reach. But we are not warranted in regarding the limits of our imperfect vision as the bounds beyond which organized life is impossible. Neither, on the other hand, are we warranted in assuming the existence of organisms 'minute beyond the reach of all sense' without giving grounds for such a faith.

All that we know regarding contagium is, (1) that it consists of minute solid particles; (2) that these particles are probably organized; (3) that in chemical composition they so closely resemble the fluids in which they occur, that the chemist fails to detect even their presence; and (4) that they are so very minute that the highest powers of the microscope fail to give us definite information regarding their nature, or even their existence. Beyond this point the combined efforts of the biologist, the chemist, and the microscopist have failed to carry us.

But there is another mode of investigating the subject which has had but little attention bestowed on it, but which we believe to be capable of affording good results, and of leading to a more accurate knowledge of the true nature of contagium.

An organism, which is too minute for ocular examination, has its place in nature defined by its action on its environment.

Now, if contagium be organized; and if, as the advocates of the germ theory maintain, the organisms of which it consists are reproduced in enormous quantities within the body, it is not unreasonable to suppose that a careful consideration of the phenomena which manifest themselves during the period at which this reproduction is going on, may throw some light on the true nature of the cause which gives rise to them. In other words, a study of the action of the contagium on its environment, may not only advance our knowledge of the pathology of contagious and infectious diseases, but may throw much light on the nature of the contagium itself.

The balance of evidence being in favour of the view which regards contagium as consisting of minute organisms, we shall for the present assume that such is their real nature, and shall proceed to investigate the competence of such organisms to cause the phenomena of disease.

CHAPTER III.

ON THE MODE OF ACTION OF CONTAGION.

For the development of organisms certain external conditions are necessary: they will not grow in very low temperatures, and are destroyed by very high; they cannot thrive without water, and largely appropriate nitrogen in their growth. Assuming such to be the nature of contagium particles, we accord to them similar properties. In addition, they also possess other properties peculiar to them as contagia. We know, for instance, that the contagium of typhus, besides requiring for its development the conditions requisite to the propagation of organisms, has need of something more, which it finds in the human body; that the contagium of measles also requires its own peculiar element, which also is found in the human body, and is quite different from the element appropriated by the typhus contagium; and so on, with all the other contagia. Each contagious disease has its own peculiar contagium, requiring for its development some element which is appropriated by itself alone, and without which it cannot be reproduced. The nature of the element required, varies with the nature of the contagium particles, and presents to the chemist a wide and intensely interesting field of research. Before we can be said thoroughly to know and understand the natural history of contagia, we must be able to tell the exact circumstances under which each grows, and to indicate the peculiar elements which each appropriates to itself. We must be able to say

what condition peculiar to the human body favours the propagation of typhus, scarlatina, etc.; and what other condition common to man and some of the lower animals, favours the propagation of the poisons of rabies, glanders, and vaccinia. The day may come when we will be able to do this. Meantime, we may derive much information regarding the natural history and mode of action of contagia, from a careful study of the phenomena to which they give rise, and close observation of the circumstances under which they are propagated.

All poisons have a definite and specific action, no two producing exactly the same effects. This is as true of contagia as it is of ordinary medicinal agents. It is, indeed, very generally believed that there is considerable analogy between the mode of action of the morbid poisons which produce contagious diseases, and that of ordinary poisonous and medicinal agents; and that the period of incubation, the mode of action, and the mode of elimination of the former, may be illustrated by the more readily observed facts of the same processes in the latter.

Reasoning from analogy is often a most powerful weapon; and sometimes the only one available. But in this instance, we believe it to be altogether fallacious. We do not think that any fair or legitimate analogy can be drawn between the effects of either an inorganic or organic poison acting on this or that organ, and those of an organized substance which is reproduced to an enormous extent within the system, which requires for its reproduction the elements which are requisite to the well-being of its victim; and whose morbific action is intimately connected with its organic reproduction.

The arguments which have been brought forward in support of this supposed analogy may be briefly stated as follows:— It is believed regarding both ordinary poisons, and the morbid poisons to which we give the name of contagia;

1. That each has a definite and specific action.
2. That a certain time elapses after the reception of the poison into the system before morbid symptoms show themselves. (Period of latency or incubation).
3. That the severity of the symptoms varies with the dose of the poison.
4. That the effects are often modified by temperament, or constitutional peculiarity, on the part of the recipient.
5. That after a time the poison is eliminated from the system.

The first proposition—that each has a definite and specific action—is unquestionable; but indicates no necessary analogy in the mode of production of this action. Indeed, a very little consideration suffices to show that there is no real analogy. We find that in ordinary poisonous agencies, (*a*) a definite quantity is requisite to the production of certain results; (*b*) that the severity of the symptoms, and the extent of any local lesions to which the poison may give rise, bear a direct relation to the quantity received into the system; (*c*) that in the case of every one of this class of poisons, a small and varying quantity may be received into the system without giving rise to appreciable disturbance; and (*d*) that the quantity which exists in, and is eliminated from, the system, is never in excess of that which was received.

Contrast with this what is noted in connexion with the poisons of contagious diseases, and the essential difference between their mode of action and that of ordinary poisonous agencies will be apparent. In their case it is found (*a*) that the minutest possible dose suffices to produce most serious symptoms; (*b*) that the severity of the symptoms, and the extent of the local lesions, bear no relation to the amount of poison received into the system—the minutest possible dose producing the same results as a larger one; (*c*) that in none of the specific poisons can there be administered to a susceptible

subject, a dose small enough to be innocuous; and (*d*) that in the case of every one of them the quantity which exists in, and is given off from, the system, is always very greatly in excess of that which was received.

Of the second, third, and fourth points of supposed analogy to which reference has been made, we shall by and bye have to give an explanation which is applicable only to an organized substance. Regarding the fifth—the analogy which the fact of the elimination of the poison is supposed to imply—we would only now remark, that we do not think our knowledge of the mode of elimination of either the ordinary poisonous and medicinal agencies, or of contagia, is sufficiently accurate to permit of our regarding as a point of analogy the fact that they are eliminated, unless the other points alluded to can be maintained. It seems to us that any substance which may be taken into the system, may also be given off from it; the physical obstacles to the one process, being no greater than those presented to the other; and being only such as are inherent in the substance itself. If soluble, or if, being insoluble, it is sufficiently minute to pass through the absorbing and eliminating structures of the body, it will be readily both taken up, and given off, by these structures.

The means of investigation hitherto adopted have failed to give us any satisfactory idea as to the mode in which contagia produce the phenomena to which they are known to give rise. That these phenomena, somehow or other, bear an intimate relation to the organic development of the contagia, there can be no doubt. It shall be our endeavour to show that they are all the direct and necessary result of the propagation in the system of the millions of minute organisms which are formed during the course of the maladies in connexion with which they are noted. If such be the case, it is evidently vain to seek for analogies between the mode of action of contagia and that of ordinary organic and inorganic substances.

If this view of the nature of contagium be correct, and if it be the case that the action of contagia is intimately connected with their organic development, other and corroborative evidence of the accuracy of this view will be found in a careful consideration of the phenomena to which their propagation gives rise.

The most distinctive feature common to the diseases which are attributed to the propagation of germs in the system, is contagiousness. The best known and most important group of contagious diseases are the specific fevers. To the specific fevers, then, we shall for the present confine our attention. For the sake of accuracy and precision, we shall further limit ourselves to such of the specific fevers as occur in this country.

CHAPTER IV.

THE SPECIFIC FEVERS.

The speeifie fevers are divisible into two great groups—those whieh are eharaeterized by the possession of a loeal lesion, and those whieh possess no sueh eharaeteristie. The former may be conveniently referred to as the eruptive, the latter as the non-eruptive, speeifie fevers.

The types of the eruptive fevers are variola, varieella, measles, searlatina, typhus fever, typhoid fever, and eerebro-spinal fever.

The type of the non-eruptive is relapsing fever.

While the eruptive fevers and relapsing fever have many features in eommon, there also exist between them many important points of distinetion. So important are these points, that it will be eonvenient in our present inquiry to eonsider these two groups of the speeifie fevers separately. We shall eommenee with the most eommon and best known, the eruptive fevers.

CHAPTER V.

THE ERUPTIVE FEVERS.

The eruptive fevers are the type of infectious diseases. Each is believed to be due to the propagation in the system of a specific poison capable of producing in others a disease identical with that during whose course it was formed.

Each contagium has its own definite and specific action—its own disease, which it alone produces. Each, too, produces its symptoms in so regular a manner, that seeing a patient for the first time in the middle of any one of these fevers, the physician can not only tell the symptoms which have presented themselves in the past, but can prognosticate, with more or less certainty, the future course and duration of the malady.

Though each of the eruptive fevers has thus its own definite history and phenomena, the whole group have certain features in common. These features may be classed under the following heads :—

1. Each has a tolerably definite period of incubation.
2. Each has for its most prominent symptoms the existence of that aggregate of phenomena to which we apply the term fever.
3. Each possesses a characteristic local lesion.
4. Each has a pretty definite period of duration.
5. Each occurs, as a rule, but once in a lifetime.

The possession of so many features in common can only be due to similarity of causation.

It shall be our endeavour to show that the features to which reference has been made may be readily explained on the theory that contagium particles are minute organisms, requiring for their growth and propagation the same materials as organisms in general, but possessing other requirements and actions peculiar to them as contagia.

The existence of so many definite and distinct diseases proves that the poisons which give rise to them are specifically distinct. The possession by these diseases of so many features in common indicates that their poisons are generically allied.

That the poison of small-pox produces only small-pox, the poison of typhus only typhus, the poison of enteric fever only enteric fever, that of scarlatina only scarlatina, that of measles, measles and no other disease, sufficiently shows that there is a specific difference inherent in each contagium, and that each poison has its own definite and specific action. But that the poison of each of these diseases gives rise to symptoms which are common to all, those namely to which we apply the term fever, equally shows that these various specific poisons have certain actions in common.

For the explanation of the phenomena which are common to the eruptive fevers we look only to the organism: for the interpretation of those which constitute their specific differences we look beyond the organism to the disease germ.

The organic development, and specific action of contagia are, indeed, inseparably and essentially combined; they are so linked together that the one action cannot take place without or apart from the other. But in the consideration of the phenomena to which each contagium gives rise, it will be found convenient, and conducive to a clearer interpretation of these phenomena, to consider the generic results referable to the propagation of the organism, separately from the specific results peculiar to each germ.

We accept as proved the fact that during the course of

the eruptive fevers, the poisons which give rise to them are largely reproduced in the system. We find good grounds for believing that these poisons are minute organisms. Assuming such to be their nature, we accord to them the properties inseparable from organized life, and believe that they exercise a definite action on their environment.

The chief features of the action of an organism on its environment are the consumption of its nitrogen and of water. Now it is evident that the propagation in the system of millions of organisms having such wants, must lead to very serious disturbance; for nitrogen and water are the two substances which are most essential to the carrying on of the various actions and changes which result in the growth and repair of the tissues. Deprive the blood of these ingredients, and it ceases to be a nutritive fluid: reduce below a certain point the quantity of each, and the whole system suffers to a degree which corresponds to the extent of the reduction.

It is evident that we have in the propagation of millions of organisms in the system, a possible source of much evil. It remains for us to see whether such propagation is competent to produce the symptoms which are common to the eruptive fevers. These we shall consider separately, and in the order enumerated.

CHAPTER VI.

THE PERIOD OF INCUBATION.

This is the time which elapses between the reception of the poison into the system, and the first evidence of its action. The determination of the exact duration of this period is a matter of much interest and not a little importance. It is a subject, however, on which accurate data are not easily obtained. Such as exist serve to show that its duration varies in different diseases, and that each has a period of incubation of its own, which, though far from fixed and invariable, is sufficiently definite to form one of its characteristic features. The explanation of the variations observable in its duration will be given further on; meantime, we have to consider what constitutes the period of incubation, and what is taking place in the system during its continuance.

The period of incubation of infectious diseases, is by many supposed to be analogous to the period of latency of ordinary poisons. There is no real analogy, except that which is derived from the existence in each, of a certain interval between the reception of the poison, and the development of the symptoms of its action. The circumstances which lead to the existence of such a period, and the phenomena which correspond to, and are contemporaneous with, it in the two cases, are altogether different.

In ordinary poisonous and medicinal agents, as in contagia,

the period of latency varies in duration. It is much longer, for instance, in digitalis than in prussic acid, and in ergotin than in nitrite of amyl; but this varying duration is very readily explained by ordinary physical and physiological laws. The period of latency of ordinary poisons corresponds to the time which elapses between the reception of the poison, and its arrival in sufficient quantity at the particular organ on which it acts. Its duration varies with the volatility and diffusibility of the agent, and with the strength of the dose. The more volatile and diffusible the agent is, the more rapidly will it be received into the circulation, and the more rapidly, in consequence, will it produce its action. Prussic acid and nitrite of amyl are extremely volatile and diffusible; hence they are taken up with great rapidity; and act with corresponding celerity.

The larger the dose of an ordinary poisonous or medicinal agent, the more rapidly are its effects produced, and the shorter, consequently, is the period of latency. The explanation of this is easy. A certain quantity of a given agent, say a grain of opium, is taken into the system, and exercises a definite action on the brain; of course the whole of the opium does not at once go to the brain, but is probably pretty equally distributed through the circulation; it acts, however, only on the brain. Each fill of the left ventricle, during the period of latency, contains some of the opium, and at each beat of the heart a certain quantity of this will be sent to the brain, till, in the course of twenty or thirty minutes, sufficient has arrived to produce the effect for which it was administered. A smaller quantity, passed directly into the circulation of the brain, would produce a more decided and rapid action, because a sufficient quantity would thus at once reach the organ on which the opium acts. A dose of two grains taken in the ordinary manner would manifest its action more rapidly, as well as more decidedly, because, within a

given time, there would reach the brain twice as much as would reach it in the same time, when only one grain was taken.

The period of latency of ordinary poisonous and medicinal agencies is simply the time which each agent requires to arrive in sufficient quantity at the particular organ or organs on which its effects are manifested; and the duration of this period varies with the diffusibility of the agent, and the strength of the dose.

These are explanations which are quite inapplicable to the period of incubation of contagious and infectious diseases. The poisons which produce these diseases are particulate and indiffusible (we use the latter word in its scientific sense). Their varying periods of incubation cannot, therefore, be due to greater or less diffusibility of these poisons. Neither is the rapidity with which they act, nor the severity of the effects produced, materially affected by the dose of the poison: the full effects being produced by the smallest dose which can be administered.

What, then, is taking place in the system during the period of incubation of the eruptive fevers? The long duration of this period in these maladies, is alone sufficient to show that something more is requisite for its explanation than we find applicable in the case of ordinary poisons.

The first step in the production of any contagious disease is the reception of a contagium particle into the body. A full-grown organism is not necessary: a germ is all that is required; and one germ is as potent for evil as a dozen, if it only meet with the elements necessary to its growth and propagation. A single disease germ, then, is received into the system, and for twelve or fourteen days no apparent effect is produced. It must not be supposed, however, that the germ is dormant or inactive all this time. As soon as it is presented with the conditions necessary to

its growth it begins to develop; and in a short time is a full-grown organism. This in its turn produces other germs, and the constant repetition of this process by each germ as it is formed, leads, in a few days, to a considerable reproduction of these particles in the system. At first their number is so scanty, and the effect of their active development so slight, that the system does not feel it: still it goes on; and this is what is taking place during the period of incubation; this is indeed what constitutes that period; it corresponds to the time which elapses between the reception of the first disease germ, and the time when the development and propagation of the germs reach such a point, that the system can no longer tolerate their action. When their development has gone so far, the period of incubation ends, and the stage of invasion of the disease commences.

But, it may be asked, if such be the explanation of the period of incubation, how comes it to vary in different diseases, and in different cases of the same disease? and how is the *abrupt* onset of the stage of invasion to be accounted for? Nay, more, if the reproduction of these germs in the system by the appropriation of nitrogen and water be all that is requisite, how comes each to produce a distinct and separate disease? The answers to these questions will be given as we proceed.

It has already been indicated that the action of contagia is intimately connected with their organic growth, it has also been indicated that in their organic growth they consume the same materials which are required for the nutrition of the tissues. An organism which thus lives in, and at the expense of, another, is a parasite. For the development of parasites there is required something more than the bare materials requisite to organic growth. Each parasite has a special nidus in which it finds something which is requisite for its growth and propagation. Contagia, as parasites, conform to this

law, and require for their development something more than nitrogen and water. This something we shall, for convenience sake, refer to as the SECOND FACTOR—the contagium being the first. Without this second factor the contagium is not reproduced, and no result follows its reception into the system—the contagium being *per se* absolutely innocuous.

This subject will be no more fully entered into hereafter: meantime, we would only indicate the fact, that, for its reproduction the contagium is dependent on this second factor; and that on the extent to which this factor exists in the system, depends not only the severity of the individual attack, but also to some extent, the duration of the period of incubation.

It can readily be understood that germs will grow more rapidly in a system which contains much of this second factor, than in one which has only a scanty supply. In other words, the more abundantly the contagium particles are supplied with the material necessary for their increase, and the more readily they obtain it, the more rapid will that increase be, and the shorter, consequently, will be the period of incubation. As already mentioned, reliable data as to the exact duration of the period of incubation in different diseases are not easily obtained; but from a consideration of those data which do exist, it may be laid down as a rule, that cases in which that period is short, are more likely to be severe, than those in which it is prolonged; and this, simply because the same circumstances which tend to shorten the duration of the period of incubation give rise also to a more abundant reproduction of contagium particles, and a consequently severer attack of the disease.

The number of germs originally received into the system has also an important influence on the duration of this period. It is evident that a dozen centres from which their propagation might proceed, would cause a more rapid increase of the germs during the first few days following their reception,

than only one centre. Suppose a thousand contagium particles to be the number requisite to produce subjective disturbance of the economy; and suppose that each particle produces four others; it is evident that the requisite thousand will be sooner obtained if we start with a dozen germs, than if we start with only one. There is no reason to doubt that the number of germs originally taken into the system must vary in different cases; and there is every probability that the variations noted in the duration of the period of incubation in each of the eruptive fevers, are mainly attributable to this cause.

But, it may be said, if such be the explanation of the existence of the period of incubation; if it correspond to the time which elapses between the reception of the poison, and the time at which its propagation reaches a point which must give rise to disturbance of the economy; and if this propagation give rise to such a steady increase in the number of contagium particles, how is the *abrupt* onset of the stage of invasion to be explained? According to the view advanced as to the causation of the period of incubation, it might be supposed that the onset of decided symptoms of the action of the contagium ought not to be sudden, but should keep pace in its development with the steady and progressive increase of the disease germs to whose growth the symptoms are attributable.

To this objection there is a two-fold answer. In the first place, the occurrence of rigors, which are regarded as the first evidence of the action of the contagium, is often preceded by other symptoms, which are consequent on the development of the contagium, and which, therefore, form part of the subsequent illness: they are usually so slight as to attract no particular attention, and are commonly attributed to some passing derangement of the digestive organs. We have a very distinct recollection that the onset of the rigors which ushered in our own attack of typhus, was for several days preceded

by slight headache and diminished appetite, due, we thought, to gastric or biliary derangement, for which we took a simple alterative. Four years later we suffered from enteric fever, and on that occasion the first decided feeling of chilliness and *malaise* was for several days preceded by what, we thought, was rheumatism of the deltoid muscles. We have frequently noticed the same thing in others, and have been able by careful questioning to satisfy ourselves that the rigor or chilliness which marks the commencement of the stage of invasion, is often preceded for one, two, or more days by such trivial symptoms as were present in our own case[1].

The occurrence of rigors indicates the participation of the nervous system in the commencing disturbance, but does not necessarily imply an abrupt passage from a state of health to a state of disease. For obvious reasons, observations on the temperature during the period of incubation are wanting; but it is most likely that if such were had, they would indicate a higher than normal range before the stage of invasion. The observations of Zimmerman and Bärensprung have shown that this is sometimes the case in intermittent fever; and they, as well as Wunderlich, Michael and others, have also shown that, after the use of febrifuge remedies, paroxysms of such fever may occur without any subjective symptoms whatever, the sole indication of their existence being an elevation of temperature.

In most cases, however, the onset of the disease is abrupt: the patient seeming to come very rapidly under the influence of the poison; but not more rapidly than may be explained by the rapidity with which the contagium particles are reproduced in the system.

[1] The cases in which such minor symptoms precede the rigors are seldom very severe. To their occurrence, therefore, we have been in the habit of attaching some prognostic importance. A case which is abruptly ushered in by a decided rigor is more likely to be severe, than one in which the rigors are preceded by such slighter symptoms as we have indicated.

In the early days of the period of incubation these particles exist in comparatively small quantity. They very quickly increase, however; and during the last few days of that period must be very abundant. The more abundant they are, the more rapidly will the general mass of the contagium particles increase. Suppose that each produces four others, and that these, in their turn, give rise to as many more; it is evident that the number of germs will soon be so great that it cannot be quadrupled without causing almost an explosion of disease germs in the system. The advent of this inevitable result, terminates the period of incubation, and ushers in the stage of invasion.

From the commencement of this stage to the termination of the disease, the most prominent symptoms which present themselves are those which constitute THE FEBRILE STATE.

CHAPTER VII.

THE FEBRILE STATE.

Fever may be symptomatic or idiopathic—indicative of, and essentially connected with, some local lesion, which constitutes the disease from which the patient is suffering; or occurring independently of any local lesion capable of giving rise to such disturbance of the system.

The recognition of this distinction is of the utmost importance, not only in clinical study, but also in investigations into the causation of the febrile state. In the many attempts which have been made to account for the phenomena of this state, its existence has not been sufficiently borne in mind. To this circumstance, we believe, is attributable much of the present unsatisfactory state of our knowledge regarding the mode of production of the phenomena of fever. To try to explain or account for the phenomena of typhus or typhoid fever, by observations made on those suffering from pneumonia or pleurisy, or the reverse, is a mode of procedure which presupposes a knowledge of the mode of production of the phenomena of that disease to which we refer by way of illustration. But, in fact, we know no more in one case than in the other how the febrile symptoms are caused. We have no better knowledge of the causation of the high temperature, the quick pulse, the thirst, the wasting of the tissues, and the increased formation of urea, observed in pneumonia, than we have of the same symptoms in typhus fever. It may be that the mode of production of these symptoms is the same in both: their similarity would, indeed,

indicate some analogy in this respect. But to assume that such is the case, and to attempt to explain the phenomena of the one form of fever by similar phenomena observed in the other,—and that before we have any certain knowledge of the mode of production of the symptoms in either,—seems to us an unsatisfactory method of investigation.

Idiopathic and symptomatic fever have much in common: but there are also many points of distinction. These are of sufficient importance to render it probable that the separate study of the two forms of fever may lead to better results than have been got from their conjoint consideration.

Let us first get a thoroughly satisfactory explanation of the phenomena of one—be it idiopathic, or be it symptomatic—and we shall then be in a position to apply this knowledge (if it be so applicable) to the explanation of the phenomena of the other. But to blend the two forms of fever together, and study *en masse* the conditions thus presented for our consideration, is a method which can scarcely lead either to precision of detail, or to healthy inference.

Recognising this danger, and being anxious to avoid it, we shall for the present leave out of account the existence of symptomatic, and confine our attention entirely to idiopathic fever.

Idiopathic fever occurs in its most common and typical form in the eruptive fevers.

In endeavouring to explain the phenomena of this, and, indeed, of all forms of fever, the method usually adopted is to take these phenomena, and reason backwards from them to a possible cause. The results of this mode of investigation have not been satisfactory. We shall, therefore, adopt the opposite course. Having investigated the nature of the original cause of the febrile disturbance; we shall endeavour to find out whether this cause is capable of produeing the phenomena which present themselves for our consideration.

We have seen good reason to believe that the poisons which give rise to the eruptive fevers are minute organisms. The question which we have to consider is the competence of such organisms to produce the phenomena of idiopathic fever.

From the time of Hippocrates and Galen down to our own day, præternatural heat, *calor præter naturam*, has been regarded as the essence of the febrile state.

Regarding the cause of this increased temperature there have been advanced many different views. The most generally accepted at the present day is that of Virchow, which attributes it to increased tissue change, to an exaggeration of the same process which keeps up the normal temperature in health. 'Fever consists essentially in elevation of temperature, which must arise from an increased consumption of tissue, and appears to have its immediate cause in alterations of the nervous system.' The views of Virchow thus expressed have been ably supported and developed by the late Dr. Parkes, and are generally received by the profession as forming the most consistent and satisfactory theory of fever hitherto advanced; and so they do.

It seems to us, however, that even this theory is far from satisfactory; and that it serves to indicate, rather than to explain, the phenomena of the febrile state. So far as it goes, it may be correct enough; but it goes a very short way, and leaves untouched the questions which itself suggests, and whose solution must form the foundation of any thoroughly satisfactory theory as to the mode of production of the symptoms of fever,—Why is there increased consumption of tissue? and why should the nervous system exercise other than its usual and normal action?

The theory of Virchow, while offering a reasonable, and probably correct, explanation of the *calor præter naturam*, offers no explanation of what, according to this theory, is the cause of the increased heat, and, therefore, a prior step in the production of fever—increased tissue change. Virchow's definition, too,

totally ignores one characteristic of the febrile state which forms as constant and essential a feature of that condition as præternatural heat or increased tissue change, viz. increased consumption of water.

Parkes endeavours to account for this by supposing the existence in the blood of some substance which has an unusual attraction for water. Some such substance there evidently must be, otherwise there could not be an increased demand for, and consumption of, that fluid coincidently with a diminution in the quantity eliminated. But the hypothetical conjecture which he throws out that this substance may be some gelatinous compound which is formed in the rapid metamorphosis of the albuminous tissues, and which is ultimately converted into urea and uric acid, would, even if proved to be true, scarcely solve the difficulty; for the question would still remain—Why is this gelatinous compound formed in such enormous quantity, as it must be to cause so great a consumption of water? and what becomes of the urea and uric acid into which it is ultimately resolved?

So many points, indeed, are left unexplained, and so many difficulties unmoved by this theory, that, able and beautiful though it be, it seems to us to be far from satisfactory; and to be constantly requiring support from some hypothesis or conjecture, which finds the sole justification of its existence, in the necessity for such support.

A theory which needs such aid rests on no sure foundation. The most satisfactory part of it is that which ascribes the rise in temperature to increased tissue change. But rise in temperature is not the beginning: we must go farther back, and inquire—why is there increased tissue change?

A satisfactory answer to this question must be the key to the explanation of all the phenomena of idiopathic fever; and no explanation of the other phenomena can be regarded as complete or satisfactory, which leaves this question unanswered.

If the first step in the production of fever be increased tissue change, the first requisite to a satisfactory theory of fever is that it should account for this change. This the theory of Virchow fails to do.

In 1863 Traube advanced the hypothesis that the rise of temperature was due, not to increased production, but to increased retention of heat, consequent on contraction of the minute arteries. All observation is opposed to such a view. Liebermeister has demonstrated its inaccuracy; and defines fever as 'a symptom-group at the foundation of which is an elevation of the temperature of the body produced by a morbid general increase of metamorphosis.' Leyden completed the overthrow of Traube's hypothesis by demonstrating, by means of calorometric observations, that the febrile body gives off more heat than the non-febrile.

Senator[1] has revived in a modified form Traube's hypothesis. He believes that there are periodic diminutions of loss of heat, together with a constant though not great increase of heat production. The former he attributes to occasional contraction of the minute vessels resulting from the action of the fever-cause; the latter he attributes to increased oxidation; but he wisely abstains from giving a definition of fever. But this too is only removing the difficulty one step back. The questions still remain—What is the fever-cause? and how does it act?

It is a characteristic of the principal maladies in which idiopathic fever occurs, that they are communicable from the sick to the healthy—they are contagious or infectious, or both. In all such diseases the existence of a specific *materies morbi* introduced from without, is an assumption necessary to the explanation of the phenomena which they present, and especially of those which entitle them to be regarded as contagious.

[1] Untersuchungen über den fieberhaften Process und seine Behandlung. Berlin, 1873.

This foreign body introduced from without (conveniently called the contagium) must be the cause of the fever; before its introduction there is no fever; its reception into a susceptible system is followed by the phenomena of that condition.

But fever is not a distinct entity; it is a collection of different and various phenomena, all of which are abnormal, and all of which are developed subsequently to the reception of the contagium, and the co-existence of which in the body is conveniently characterized by the term 'fever.' That which gives rise to the fever must also be, either directly or indirectly, the cause of all the phenomena which go to constitute that condition. The contagium is the cause of the fever; the contagium must, therefore, be the cause of the individual phenomena which go to form the febrile state.

We have, therefore, to inquire how it is that the contagium gives rise to the præternatural heat, increased tissue waste, and other phenomena of that condition.

In investigating the action of ordinary poisonous and medicinal agents, we have to consider only their action on one or more organs, or on the system generally. In investigating that of contagia we have not only to consider this question, but we have also to bear in mind that we are dealing with an organized substance, which is largely reproduced within the system, and which appropriates in its development the same elements as the tissues of the body. We have further to consider whether the symptoms produced may not be due to the phenomena necessarily attendant on so large a reproduction of these organisms within the body, rather than to any specific action which they may have as poisons, on particular organs, or on the system at large. In other words, we must bear in mind that we are dealing with an organism, as well as with a poison; and must discriminate between the phenomena necessarily attendant on the growth of the former, and those attributable to the action of the latter.

Some idea of the extent to which these minute organisms are reproduced in the system may be gathered from a consideration of what is observed in a severe case of confluent small-pox. The introduction into the system of an almost infinitesimal quantity of the matter of a small-pox pustule, may be followed by an eruption so copious that scarcely a pin point can be placed on sound skin on any portion of the body. Each one of the enormous number of pustules which constitute this eruption, contains many times as much of the poison as was introduced into the system; and it is not too much to say, that the introduction of a single disease germ may be followed by a seizure, in which myriads of similar germs are reproduced.

Bearing this in mind; and taking into consideration the fact that these minute organisms appropriate in their growth elements requisite for the nutrition of the body in which they grow, we cannot fail to see that their propagation must be attended with serious disturbance of the system.

It shall be our endeavour to show that the characteristic features of the febrile state, are due to the growth of the contagium particles; and that the disturbance to which they give rise results from the appropriation by them of the essential constituents of the blood, rather than from any special action as poisons, which they possess.

The chief characteristics of such minute organisms as those to which contagium is believed to be allied, are:—

1. That they are mainly composed of albumen.
2. That they largely consume nitrogen.
3. That they largely consume water.
4. That they multiply by division.

The essential phenomena of the febrile state are:—

1. Increased waste of the nitrogenous tissues.
2. Increased consumption of water.
3. Increased rapidity of the circulation.
4. Præternatural heat.

This juxtaposition (*a*) of the chief characteristics of contagium, and (*b*) of the phenomena which accompany its propagation, alone suffices to suggest a probably causal relation between the two. The propagation in the system of millions of organisms which largely consume elements requisite for the nutrition and repair of all the tissues of the body, must be accompanied by serious disturbance. If nitrogen and water be the chief requisites for the growth of the contagium particles, it is evident that symptoms and changes referable to increased, but abnormal, consumption of these elements, will be among the chief characteristics of the disturbance, to which the propagation of the contagium gives rise. And if the view which has been advanced as to the mode of action of contagia be correct, its accuracy will be confirmed by a detailed consideration of the essential phenomena of the febrile state. These, therefore, we shall now consider.

CHAPTER VIII.

WASTING OF THE NITROGENOUS TISSUES.

All the tissues, nitrogenous and non-nitrogenous, waste during fever; but it is in the former that the loss of bulk is most marked. In spite of all that is done to support him, the fever patient rapidly emaciates, and wastes almost visibly before us. No matter how much nourishment he takes, it seems to serve no useful purpose in maintaining the bulk of the tissues, or in preventing their waste.

According to the generally accepted theory of Virchow, this emaciation and loss of weight are due to increased tissue metamorphosis—to an exaggeration of the normal disintegrative changes. To the same cause, according to this theory, are due the præternatural heat, and other essential phenomena of the febrile state. Increased tissue metamorphosis is, indeed, the foundation on which rests the whole superstructure of the modern views of the causation of fever. Let us see whether it offers a satisfactory explanation of the actual and great loss of weight which takes place during the course of fever.

That increased tissue disintegration, in the absence of increased tissue formation, would lead to loss of bulk there can be no doubt. The question that we have to consider is—Does such increased disintegration take place in the course of fever?

Actual and palpable loss of bulk would be one result of such increase; that we know takes place. Another result, and one by which the extent of the increased metamorphosis would be more accurately gauged, would be increased elimination of the

excretory products formed during the retrograde metamorphosis of the tissues. Does this take place?

The amount of urea eliminated in twenty-four hours is generally regarded as the best index to the extent to which the tissues are being consumed. Of course this does not represent the entire tissue change, but as it is believed to represent the result of the destruction of two-thirds of the nitrogenous tissues, it is believed also to afford a good indication of the extent of the disintegration of the tissues in general. The result arrived at can only be approximate, but as excessive waste of the nitrogenous tissues is a characteristic feature of fever, and as destruction of these tissues normally results in the formation of urea, it is evident that the approximation may be sufficiently close to guide us in our present inquiry. If there be increased metamorphosis of the nitrogenous tissues, there ought to be increased elimination of urea. Is such the case?

The subject is one which, within the last few years especially, has had considerable attention bestowed on it. The special object of those who have investigated it has been to determine whether or not there existed any definite relation between the amount of febrile heat, as indicated by the thermometer, and the extent of tissue change, as indicated by the excreta. Observations tend to show that there is no definite relation; for while some maintain that the quantity of urea is always increased in fever, others assert, on apparently sufficient and accurate data, that it is often diminished.

The fact is undoubted that increased elimination of urea, though a general, is not an invariable, accompaniment of the rapid loss of weight which takes place during fever. Even Dr. Parkes, whose name is intimately and honourably associated with this question, and who was the great champion in this country of Virchow's theory of fever, only said that the urea *may be* increased; and got over the difficulty which thus presented itself by supposing that the products of the increased tissue

metamorphosis were retained in the system. He therefore believed that the amount of urea eliminated is not an accurate index of the extent of the tissue metamorphosis. His conclusions are (*a*) that 'increase of temperature *may be* attended with increased elimination, and therefore presumably with increased tissue change;' and (*b*) 'that the products of metamorphosis as judged of by the excreta, *may be* diminished in febrile cases, in which the heat of the body is intense[1].'

The apparent discrepancy of these two conclusions he explains by supposing that more changes take place in the system than those which result in the formation of the substances which form the normal excreta, the metamorphosis of the blood or tissues not being carried so far as to produce 'those principles which can alone pass through the eliminating organs[1].'

Dr. Thudichum[2] gives expression to similar views when he says that 'it is impossible to tell the nature of the decomposition preceding the formation of the urea, and consequently to calculate the number of units of heat evolved:' he believes, however, (*a*) 'that in all diseases with raised temperature urea is increased; (*b*) that the process which produces the urea produces the fever; and (*c*) that the quantitative aberration is preceded by a qualitative one. But these three conclusions can by no means be reversed, nor are they absolute, though general, because (*d*) urea may be increased (to double the normal standard) while temperature is lowered. This is the case in diabetes. (*e*) Urea may be diminished in acute fever, if other products are discharged instead, the decomposition heats of which are the cause of the increased temperature observed, (leucine, tyroine, changed hematine.) (*f*) These decompositions precede the urea formed by the abnormal process, and their heats are, therefore, superadded to the heats which possibly may be, but are not necessarily, produced by the ultimate urea formation.'

[1] On Pyrexia, by E. A. Parkes, M.D. (Gulstonian Lectures for 1855).

[2] Eleventh Report of the Medical Officer of the Privy Council (1868), page 130.

What both Parkes and Thudichum have failed to do, is to tell us why the normal changes do not take place; why the tissue metamorphosis is only partial; why the ordinary excretory products are not formed; and why, if formed, they are not eliminated.

In the absence of such information their explanation of the difficulties which present themselves cannot be accepted as satisfactory.

Unruh's investigations led him to the conclusion that 'the rise of temperature theoretically due to increased consumption of nitrogen is not enough to account for the elevation of temperature in each case separately.'

Senator's observations on induced fever in dogs led him to the conclusion that increased urea elimination indicates increased activity of the processes by which it is formed in the body, and that such increased activity may be judged of by the rate of discharge.

Many other authors have written on the subject; but not much has been added to the able statement of Parkes; and little light has been thrown on the points which it leaves unsolved.

The facts with which we have to deal are:—

1. That there is rapid wasting of the nitrogenous tissues.
2. That this is generally accompanied by increased elimination of urea.
3. That in some cases in which the fever runs high, and the wasting of the tissues is marked, the amount of urea eliminated is below the normal standard.

Of the apparent contradiction involved in this third fact, there are three possible explanations. (*a*) It may be that the retrograde changes stop short of the formation of urea, and result only in the formation of products which cannot be freely eliminated by the kidneys. (*b*) It may be that urea is formed, but retained. (*c*) It may be that there is some other agency besides increased tissue disintegration, capable of causing rise of temperature, and wasting of the tissues.

The chief evidence in support of the first two hypotheses, is the fact on which each is based, that urea is eliminated in deficient quantity. (*a*) Against the view that this defective elimination of urea is due to incomplete disintegrative changes, there is one very strong argument. Such diminution is most marked in cases in which the fever runs high. The cases of fever in which the highest temperature is noted, are those in which there is partial or complete suppression of urine; and in which the amount of urea eliminated is much below the normal. If the increased body-heat be due to increased tissue change, the temperature ought not to be highest in those cases in which the retrogressive changes are incomplete, and stop short of the formation of urea. The more complete these changes the greater should be the heat produced.

(*b*) Adopting the view that urea is formed, but retained, we have to explain why it is that, with structurally sound kidneys, such retention is brought about. We have also to explain why, with so great retention of urea, so little of that substance is found in the blood and tissues after death.

We shall have to return to this subject by and bye: meantime we shall only repeat the conclusion to which Unruh arrived after careful observation and study 'that the rise of temperature theoretically due to increased consumption of nitrogen, is not enough to account for the elevation of temperature in each case separately:' and would add to this the rider, that the elimination of the products of retrograde tissue metamorphosis, theoretically due to increased tissue waste, is not enough to account for the loss of bulk which takes place in each case separately.

(*c*) Can it be that there is any other agency in operation besides increase of the normal changes? We shall presently see that there is at work an agency capable of explaining what Virchow's theory leaves unsolved.

The strong points of Virchow's theory are the proved and acknowledged facts, (*a*) that there is increased tissue meta-

morphosis, and (*b*) that such increase must give rise to many of the phenomena which characterize the febrile state. Its weakness consists (*a*) in its not offering a full and satisfactory explanation of the extent to which these phenomena occur, and of the varying degrees in which they exist; and (*b*) in its affording no adequate explanation of the occurrence of the increased tissue metamorphosis to which the febrile symptoms are said to be due.

On what then is based the hypothesis which has led to so general an adoption of the belief in increased tissue metamorphosis as the cause of the wasting and other phenomena of fever? It rests on the difficulty which is experienced in otherwise explaining them.

The influence of increased tissue metamorphosis has, indeed, been theoretically admitted without a thorough examination of the facts. Its competence to produce all the phenomena of the febrile state has not been demonstrated; and we shall presently show that many of these, and among others the phenomenon with which we are now dealing, may be more satisfactorily explained in a different manner. That increased tissue waste does occur is certain; but that it is not the sole cause of the phenomena of the febrile state is equally certain.

Besides increased disintegration, the only other cause capable of giving rise to loss of bulk in the tissues, is diminished nutrition. We have, therefore, to inquire whether there is at work in the system any agency capable of giving rise to defective nutrition. We think we shall be able to show that there is; and at the same time to show that the cause which produces this condition, gives rise also indirectly to the increased metamorphosis which forms the foundation of Virchow's theory.

The one cause to which, directly or indirectly, are to be ascribed all the phenomena of Idiopathic Fever, is the contagium. To this,

therefore, we turn for an explanation of the phenomena whose causation we are investigating.

The contagium is an organism. As such it largely appropriates nitrogen in its growth and propagation. The albuminous tissues and fluids are the only sources capable of supplying the quantity of nitrogen requisite for the enormous growth of contagium particles which takes place in the system during the course of idiopathic fever. Given such an organism, or rather millions of such organisms, growing and being propagated in the system, and it follows, that there must be serious interference with the changes which normally take place in the nitrogenous tissues. There is in the system no spare store of nitrogenous material, from which can be supplied the quantity of nitrogen requisite to the growth and propagation of the contagium: it must be taken from that which is destined for the nitrogenous tissues; it must, therefore, represent a loss to these tissues which is directly as the extent to which the contagium is reproduced.

This consumption of nitrogen by the contagium particles is the primary cause of the rapid wasting of the nitrogenous tissues which takes place during fever: increased disintegration playing only a secondary part in its production.

But nitrogen exists in various forms and combinations, liquid and solid, in the body; and we have now to consider at what point, or points, in its changing course through the system, it is most likely to be laid hold of by the contagium particles.

It will facilitate our inquiry into this subject, if we first consider the nature and seat of the changes which the nitrogen normally goes through, from the time of its entrance into, to that of its exit from, the body. Let us, therefore, trace the nitrogen in its course through the system, note the various changes which it undergoes, and the condition in which it exists after each change: we shall then be in a better position to say at what point it is most likely to be appropriated by the contagium.

Nitrogen is taken into the body with the food in the form of albumen, fibrine, or other nitrogenous compound. Passing into the circulation through the ordinary channels, it first appears in the system as it exists in the liquor sanguinis: in this form it is conveyed to the various organs and tissues, which, in the exercise of the powers with which they are endowed, take from the blood that which they require for their nutrition and repair. The greater part of the nitrogen of the albumen is taken up by the nitrogenous tissues properly so called, and is incorporated into their substance. The nitrogen now forms part of a solid organ. In this form it remains for a time: when it has served its purpose there, it again passes into the circulation, and is eliminated by the kidneys in the form of urea. It was long supposed that this was the form in which the nitrogen reappeared in the circulation; that the urea was formed in the muscles, and other nitrogenous tissues; and that increased muscular exercise, and excessive brain work, were followed by a corresponding increase in the amount of urea eliminated. This we now know is not the case.

The observations of Pettenkofer, Voit, Parkes, and others, have proved that the quantity of nitrogen which passes off by the kidneys, bears an almost fixed and definite relation to the quantity taken into the system with the food, and is little, if at all, influenced by any other agency. Let the quantity of nitrogen consumed be diminished, and there is a corresponding fall in the quantity eliminated; let it be increased, and there is a proportionate increase in the excretion. The explanation of this evident connexion between the entrance and elimination of nitrogen, was long believed to be that too much nitrogen was habitually consumed; that more was taken into the system than was necessary for its wants; and that what was superfluous, was oxidised in the blood, and eliminated by the kidneys, without having served any useful purpose.

Popular as it at one time was, this doctrine of 'luxus consumption' has been proved to be erroneous, and is now abandoned. Observation has shown that there is in every one a certain normal standard of consumption and elimination of nitrogen. If the amount consumed be brought below the normal, there is a corresponding fall in the quantity of urea eliminated; on increasing the consumption again, the elimination does not at once show a corresponding increase: part of the nitrogen is retained, in order to make good the loss resulting from the previously defective supply; and not till the equilibrium is restored, is the increased ingestion followed by increased elimination.

But if urea is not the result of the oxidation of the albuminous materials of the blood, and if it is not formed in the nitrogenous tissues, where is it produced? and how is the worn out nitrogenous material converted into it?

The observations and experiments of Cloetta, Meissner and Bullard, Stokvis, E. Cyon and others, have shown that urea is formed in the liver. Those of E. Cyon demonstrate experimentally its formation in that gland. He found from observations made on the blood of the portal and hepatic veins, that after passing through the liver, the blood contained more urea than it did before entering that organ: he found too that blood which was passed through the liver three or four times contained more urea than blood which was passed through only once.

Pathology affords evidence to the same effect. Frerichs and Murchison have shown that acute yellow atrophy of the liver, in which the cells of that organ are destroyed, is accompanied by an extraordinary diminution in the amount of urea eliminated, or even by its total disappearance from the urine.

Parkes likewise found a marked diminution in the urea eliminated in cases of hepatic abscess, in which there was much suppuration, and considerable destruction of the glandular substance; the decrease in urea elimination seeming to bear a direct relation to the extent of the hepatic destruction.

It is probable that other glands than the liver may have a share in the production of urea; and there is some evidence to show that the spleen has for one of its functions the formation of uric acid. On this subject, however, we shall not further enter, but shall content ourselves with the statement, that most of, if not all, the urea eliminated in health is formed in the liver and other glands. From what is it formed? from a nitrogenous substance of course.

Voit has distinguished between the fixed or organ albumen, which enters into the composition of the solid tissues, and which changes very slowly; and the circulating or store albumen, which is contained in the blood and fluids of organs, and very readily undergoes change. Of course, only the circulating albumen can enter the hepatic circulation; it must, therefore, be the source whence is derived the nitrogen of the urea.

But a still further distinction must be made. The circulating albumen must consist of two parts, a *constructive*, and a *retrogressive;* the former derived from the assimilated ingesta, and destined for the nutrition of the tissues; the latter derived from the retrograde metamorphosis of these tissues, and destined for excretion.

From which of these two sources, the only ones possible, does the liver get the materials from which it forms the urea? From the retrogressive, certainly. To suppose that the constructive store albumen is thus used, would be to fall back on the old and clumsy doctrine of luxus consumption, a doctrine which has been proved to be untenable.

The retrogressive store albumen is not only the most probable, but is also the only other possible source of the nitrogen of the urea.

The various stages through which the nitrogen passes whilst it is in the body may briefly, but for our present purpose with sufficient fulness, be stated as follows:—It is taken with the food as albumen, gluten, or other nitrogenous compound, and

passes by the ordinary channels of assimilation into the circulation, where it forms part of the constructive store albumen; passing in this form to the muscles, and other nitrogenous tissues, it is taken up by them, and incorporated into their structure, thus forming part of the fixed or organ albumen; in assuming this form it replaces some of the worn out albuminous tissue, which passes into the circulation as retrogressive store albumen, a form which the portion of nitrogen we have been tracing also assumes in time, and in which form it is conveyed to the liver, where it is converted into urea, and as such is eliminated by the kidneys.

The more nitrogen assimilated, the more goes to the system as constructive store albumen: the greater the quantity of this conveyed to the tissues, the more rapidly do they yield up the old and appropriate the new material: the more active these tissue changes, the greater the quantity of retrogressive store albumen conveyed to the urea-forming glands, and the more abundant, therefore, the excretion of urea. Such is the normal sequence of events; and such the detailed explanation of the demonstrated fact, that the quantity of urea eliminated in health, rises and falls with the increase and decrease of the nitrogen consumed.

The proper continuance in due force of the various actions which produce all these changes, depends *inter alia* on the supply of a proper quantity of nitrogen: that is the initial condition of their continuance. The nitrogen is eliminated in the form of urea; but before it assumes that form, it has to go through the other intermediate changes which have been indicated.

Having thus briefly considered the various changes through which the nitrogen normally passes, we may now enter on the consideration of the question of the source of the nitrogen consumed by the contagium particles.

In considering the source of the nitrogen of the urea, we

came to the conclusion (1) that it was not derived from the constructive store albumen, because such a supposition was equivalent to falling back on the doctrine of luxus consumption—a doctrine which has been proved to be erroneous: (2) that it was not derived from the fixed or organ albumen, because such albumen does not exist in sufficient quantity in the liver, the main seat of urea formation: and (3) that it was derived from the retrogressive store albumen, because that was not only the most probable, but also the only remaining possible source.

In considering the source of the nitrogen consumed by the contagium particles, we cannot make use of the same arguments; for we are considering a totally abnormal action, which is not limited to one organ, or set of organs, but takes place all over the body; and which really bears more analogy to that which results in the formation of tissue, than to that which results in its disintegration and excretion. The process by which the nitrogen, from whatever source derived, is converted into the protoplasm of the contagium particles, is not like that which results in the formation of urea, a retrogressive one: it is constructive, and is more analogous to the process by which the tissues are built up. The argument founded on the untenability of the doctrine of luxus consumption, which was found applicable in the case of urea, is consequently quite inapplicable to the contagium. The constructive store albumen, therefore, may be the source whence the contagium particles derive their nitrogen.

The second argument, that the fixed or organ albumen was not the source of the nitrogen of the urea, because it did not exist in the liver in sufficient quantity, is equally inapplicable to the contagium; for there is no reason to suppose that the formation of the contagium particles takes place chiefly in the urea-forming glands: the fixed or organ albumen, therefore, may be the source whence the contagium derives its nitrogen.

The third argument, that the nitrogen of the urea was derived

from the retrogressive store albumen, because that was, not only the most probable, but also the only remaining possible, source, is not applicable to the contagium; for we have just seen that there are other possible sources. There is no apparent reason, however, why it might not be got thence: the retrogressive store albumen, therefore, may be the source whence the contagium derives its nitrogen.

It is even possible that the urea itself may be the source whence it is derived.

It is thus apparent that any, or every, nitrogenous compound may yield up its nitrogen to the contagium. It remains for us to see which is the most probable source.

This is a more difficult subject of inquiry than the source of the nitrogen of the urea; for it cannot be elucidated in the same way by experimental inquiry and observation.

The subject may be approached, and a solution of the question attempted, in two ways:—first, by considering how an organism would most likely act when propagated in the system; and second, by considering how far the phenomena which follow the reception of the contagium into the system, and which constitute the 'fever,' may be regarded as directly or indirectly due to the consumption by the contagium particles of the nitrogen of (*a*) the constructive store albumen, (*b*) of the retrogressive store albumen, (*c*) of the organ albumen, or (*d*) of the urea.

First then, how would an organism be likely to act?

In considering this question we must bear in mind that we are dealing with the action of a foreign body introduced from without, which (so to speak) has only its own wants and requirements, and is not likely to be influenced by any consideration based on the well-being of the body; or to be swayed by any such influence as that which leads the cells of the liver to utilize the retrogressive store albumen, in preference to the constructive, in the formation of urea. The

action which results in the growth and propagation of the contagium, is a vital one; but it is an action independent of, and distinct from, any action or process which normally takes place in the body. The sole end of the contagium particle is to grow, and reproduce itself: for this purpose one of the essentials is nitrogen. From which of the four compounds in which it exists in the body, does the contagium take it? from the constructive store albumen, the retrogressive store albumen, the organ albumen, or the urea?

The circumstance most likely to affect its choice in favour of one or the other, is the facility with which the nitrogen is given up. The most fixed and stable of all the nitrogenous compounds, is the fixed or organ albumen; this is, therefore, the least likely source whence the contagium particles derive their nitrogen. The fact that increased waste of the albuminous tissues is one of the most prominent symptoms which accompany the development of the contagium in the system, might indeed lead to the inference that this increased waste was a direct result of the consumption of their nitrogen by the contagium particles; we shall presently see, however, that such an inference is not necessary, and that the consumption of the nitrogen of the less stable store albumen serves equally well to explain the increased waste of the organ albumen.

We may, therefore, conclude that the nitrogen which goes to build up the protoplasm of the contagium particles, is not directly derived from the organ albumen.

There remain as possible sources, the store albumen, and the urea. The claims of the latter we shall consider first.

It is difficult to see that the urea possesses any claim further than that which is common to all nitrogenous substances—the possession of nitrogen as one of its ingredients. It is a question whether, within the body, it is not as stable as the organ albumen; for although it has been supposed by some to be occasionally converted into carbonate of ammonia in the circulation, it is

far from proved, that such a change ever takes place prior to its elimination by the kidneys. Any argument founded on its stability within the body, rather goes against the idea that it is the source whence the contagium particles derive their nitrogen. There are still more cogent arguments, however, founded on the impossibility of explaining the phenomena which accompany the appropriation of the nitrogen by the contagium particle, by the mere denitrization of the urea.

On the supposition that the urea is the source of this nitrogen, how, for instance, can we explain the increased waste of the nitrogenous tissues?

But there is yet another cogent objection to this view. If the contagium particles appropriated the nitrogen of the urea, greatly diminished exertion of urea would be an invariable accompaniment of idiopathic fever; this we know is not the case. We, therefore, conclude that the urea is not the source whence the contagium particles derive their nitrogen.

The only other available source is the store albumen. This we have seen consists of two parts, a constructive, and a retrogressive. From one, or both of these, the nitrogen of the contagium particles must be derived. From which is it? or is it from both? So far as the readiness with which their nitrogen is yielded up is concerned, the two are probably very much alike; each is a transition compound, and, as such, possesses, as one of its most characteristic properties, a readiness to undergo change, and to part with its nitrogen; the one in the albuminous tissues, the other in the gland cells which form the urea. Any advantage which does exist, is on the side of the constructive store albumen; for while it is ever undergoing change, and constantly giving up its nitrogen to the albuminous tissues in all parts of the body, the retrogressive seems to yield up its nitrogen only in the glandular organs in which urea is formed.

Now, there is no reason to suppose that the growth of the

contagium takes place only in these glands, or that it gets its nitrogen in them only; indeed, there is not a little evidence to the contrary. In the course of our inquiry, we shall see good reason for believing that the contagium grows, and appropriates the materials necessary to its growth, in all parts of the body.

Is there any other agency likely to have an influence in determining the choice of the contagium, in favour of the constructive, or retrogressive store albumen? We think there is. The process by which the protoplasm of the contagium particles builds itself up is, as already indicated, quite an abnormal one—abnormal, that is, in the sense of being totally distinct from, and unconnected with, any process which usually takes place in the body. It may, however, have analogies with, and be capable of being illustrated and elucidated by, some of these processes. So far as the changes which normally take place in the nitrogenous compounds of the body are concerned, the main processes are the building up of the albuminous tissues from the constructive store albumen; and the formation of urea from the retrogressive. To which of these does the formation of the protoplasm of the contagium particles bear most analogy? To the former, certainly. Being, as organisms, mainly composed of albumen, it needs no elaborate argument to show that the process by which their protoplasm is formed, bears a much closer analogy to that by which the albuminous tissues are built up, than it does to that which results in the formation of urea. The formation of urea is a retrogressive step: urea is an excretory compound, and is the last form which the nitrogen assumes prior to its elimination. The formation of the albuminous tissues, and of the protoplasm of the contagium particles, are constructive steps: each results from the appropriation by living protoplasm of the elements requisite for its growth. The fluid which supplies each with these elements is the same; the material from which each is built up, is derived

from the blood; and it is but reasonable to suppose, that each should take from that fluid the same materials, and that the particular ingredient of that fluid from which the nitrogen is derived should be the same in both.

The great practical distinction between the constructive and the retrogressive store albumen, we have seen to be, that the former is destined to nourish the albuminous tissues, and that the latter, resulting as it does from the retrograde metamorphosis of these tissues, is destined only for excretion. If the retrogressive store albumen be unfit for the nutrition and building up of one tissue, it is probably unfit for the nutrition and building up of all; and if it cannot afford the materials necessary for the formation of the fixed albumen of a muscle, it is less likely than the constructive store albumen to supply that which is necessary for the formation of the protoplasm of the contagium particles. These considerations render it probable that the contagium particles derive their nitrogen from the *constructive* store albumen.

A consideration of the manner in which an organism would be likely to act, thus leads to the conclusion that it would take its nitrogen from the constructive store albumen in preference to any other source.

A consideration of the phenomena which accompany the propagation of the contagium in the system leads to the same conclusion.

The phenomenon at present under consideration is the wasting of the nitrogenous tissues. We have already seen the inadequacy of Virchow's theory to explain all the phenomena of the febrile state; and with reference to the special subject now under consideration, have seen that the evidence of the existence of increased disintegration is not sufficient fully to account for the loss of bulk which takes place during the course of fever.

Besides increased disintegration, the only other possible

cause of the emaciation which takes place is diminished nutrition. For an agency capable of giving rise to this we have been in search. Now, is not the consumption by the contagium particles of the constructive store albumen the very fact we have been looking for? We know that the constructive store albumen is destined for the nutrition and building up of the tissues, and that the consumption of its nitrogen in any other way must lead to defective nutrition, and consequent loss of bulk, in the tissues. The tissues which must suffer most from a deficient supply of nitrogen are, of course, the nitrogenous.

In the course of idiopathic fever we find on the one hand, (1) that millions of minute organisms are propagated in the system; (2) that these minute organisms largely appropriate nitrogen in their growth and propagation; and (3) that they take this nitrogen from the constructive store albumen: on the other hand we find (1) that there is rapid wasting of the nitrogenous tissues; (2) that the evidence of increased disintegration is insufficient to account for this waste; and (3) that there is at work an agency capable of giving rise to defective nutrition, an equally potent cause of loss of bulk in these tissues. We are, therefore, forced to conclude (1) that the wasting which takes place in the course of idiopathic fever, and which is most marked in the nitrogenous tissues, is in great part due to defective nutrition; and (2) that this defective nutrition results from the consumption by the contagium particles of the nitrogen of the constructive store albumen. The propagation of the contagium in the system is, therefore, the primary cause of the wasting of the nitrogenous tissues, which forms one of the most notable phenomena of idiopathic fever.

The nitrogenous tissues, then, waste not so much because of the increase in the normal retrograde metamorphosis, (though this agency is not inoperative) as because this waste is not compensated for by a due supply of fresh constructive material.

Blood continues to be supplied to, and to circulate through, the tissues; but it is blood charged with an organism which utilizes, for its own ends, the materials which ought to go to nourish and build up the frame.

Such being the case, it is evident that the propagation of the contagium in the system must be accompanied by emaciation and loss of weight, unless the nutrient materials are supplied in greatly increased quantity, so as to compensate in some degree for this increased demand. Are they so supplied? They are not; and it is impossible that they can be; for the same agency which deprives the nitrogenous tissues of their nutrient material, causes also a like deterioration of the blood which passes to all the organs of the body. Such deterioration of the blood supplied to the brain leads to impaired nutrition of that organ, and consequent impairment of that nervous influence which is requisite to the due performance of their functions by all the tissues and organs of the body. A similar deterioration of the blood which passes to the digestive organs leads to the imperfect performance by them of their peculiar functions; while the great consumption of water, which accompanies the development of the contagium particles leads to a marked diminution of the quantity of the secretions necessary for the digestion of the food. There are thus produced diminished appetite, impaired digestion, and defective assimilation, and all this while the blood which is in the body is being deprived of its nutrient properties by this organism, which pervades the whole system, penetrates every part to which blood flows, and everywhere seizes on the most essential constituents of the nourishing fluid, at the moment when they are about to be appropriated by the tissues.

A full supply of blood thus deteriorated, is no better than, and probably not so good as, a scanty supply of the ordinary fluid.

The emaciation which occurs in idiopathic fever has indeed many analogies, so far as its causation is concerned, with the

wasting which takes place when the supply of blood to a part is mechanically interrupted, or with that more general diminution in bulk which results from starvation. In starvation the necessary amount of nutrition is not taken into the system: in idiopathic fever, it may be taken, and in great part assimilated, but it is at all points deprived of its essential ingredients by the rapidly growing contagium particles. In either case the result is the same; it being immaterial, so far as the nutrition of the tissues is concerned, whether the nutrient ingredients of the blood are consumed after entering the circulation, or are cut off at the threshold of the system.

In fever, the wasting, due to the action of the contagium particles on the circulating fluid, is still further accelerated by the continuance of the normal retrograde tissue changes to an extent which does not obtain in starvation.

But the consumption of their nitrogen is not the only means by which the bulk of the tissues is diminished during the febrile process. At the same time that they consume nitrogen, the contagium particles also consume water, and that in large quantity. We shall presently see that to this action on their part are attributable many of the phenomena of fever. Meantime we would call attention to the fact, that water is as essential to the nutrition of the tissues as is nitrogen, and enters as largely into their composition. The propagation in the system, of an organism which largely consumes water, must, therefore, lead, not only to deranged nutrition, but also to diminished bulk of the tissues. The wasting of fever is probably due as much to the consumption, by the contagium, of the water which enters into the composition of the tissues, as it is due to the consumption, by the same agency, of the nitrogen destined for their nutrition.

In the fact that the loss of bulk which takes place in the body during the process of fever is largely due to the consumption of the water of the tissues, we have an adequate explanation of the fact that the evidence of increased tissue metamorphosis, as

judged of by the amount of exereta eliminated, is not enough to aeeount for the aetual loss of bulk whieh takes place in each ease separately.

The wasting which takes place during the course of the specifie fevers, we regard as due primarily and chiefly to the consumption by the contagium partieles of the nitrogen and water of the eonstructive store albumen; and only secondarily, and in a minor degree, to increased disintegration of the nitrogenous tissues.

Further and very valuable evidenee in support of this view, we have in the observations of Salkowski[2] on the elimination of potass and soda during fever. The result of his observations was to show first, that the quantity of potass eliminated on a febrile day, was three or four times, sometimes as mueh as seven times, greater than on a non-febrile day; and seeond, that the soda diseharge was redueed to a minimum during the febrile state, and rose again when the fever had eeased.

In fever potass is eliminated in increased quantity, while soda is retained. This shows, first, that the inereased discharge of exeretory produets, whieh takes plaee in fever, results from inereased disintegration of tissues rieh in potass; and seeond, that those rich in soda are retained in the system to a greater than normal extent.

The tissues rich in potass are the muscles and blood eorpuscles. The chief seat of soda, is the liquor sanguinis. Salkowski's observations, therefore, show, (*a*) that, during the febrile state there is inereased consumption of muscular tissue, and of blood corpuscles; and (*b*) that the liquor sanguinis is retained, and utilized, to a greater than normal extent.

This is exactly in aeeordance with the views whieh have been advanced as to the mode of production of the wasting of fever. We have seen that this is due chiefly to the consumption by the

[2] Virch. Arch., liii. Burdon-Sanderson in report of Medical Officer of Privy Council, New Series, No. vi.

contagium particles of materials destined for the building up of the tissues. The contagium particles consume the nitrogen and water of the constructive store albumen, i. e. of the liquor sanguinis, as these elements are in the act of passing from the condition of constructive, to that of fixed, or organ albumen. In thus consuming the nitrogen and water of the liquor sanguinis, the contagium must also take up the sodium salts which enter into its composition. The building up from this source, of the protoplasm of the contagium particles, must result in such retention of sodium salts as Salkowski has shown to occur in fever.

Increased formation of urea, implies increased disintegration of nitrogenous tissues. The tissue richest in nitrogen is muscle, which is also the chief seat of potassium salts. The increased formation of urea which occurs in fever we attribute chiefly to increased disintegration of muscular tissue. The muscles being the chief seat of potassium salts, it follows that such increased metamorphosis of their substance as occurs in fever must be accompanied by increased elimination of potass; that this does occur, has been demonstrated by the observations of Salkowski. His observations, therefore, strongly support the view which has been advanced, that the nitrogen required for the formation of the protoplasm of the contagium particles, is taken from the constructive store albumen; while that which goes to form urea, comes from the retrogressive.

But it may be said, if the wasting of fever be due mainly to the consumption by the contagium of the nitrogen of the constructive store albumen, and only in a minor degree to increased tissue metamorphosis, how comes there to be so commonly increased elimination of urea? and why, with similar wasting, is the amount of urea eliminated sometimes below the normal standard?

These questions are so important that we shall devote to each a special chapter.

CHAPTER IX.

INCREASED ELIMINATION OF UREA.

We have seen that urea is formed in the liver, and other glands, from the retrogressive store albumen. The quantity of urea thus formed must depend on the quantity of retrogressive albumen conveyed to these glands, and on their capacity to perform their functions aright.

An analogy has been drawn between the wasting which occurs in fever, and that which results from starvation. We must now indicate a very important contrast.

When the non-febrile body is deprived of nourishment, the pulse beats slowly, the whole vitality is low, and the amount of urea eliminated bears, within certain limits, a direct relation to the deprivation of nitrogenous food. The immediate cause of the diminished excretion of urea, is its diminished formation: this is due to decrease in those tissue changes, which normally result in the formation of retrogressive store albumen, and this decrease is a result of the defective supply of nutriment, which thus becomes the ultimate cause of the diminished excretion of urea. But the elimination of urea does not totally cease when the supply of food is cut off: it continues to be formed, though in greatly diminished quantity, after the supply of nutriment has ceased: even after three weeks' starvation urea has been found in the urine; plainly showing that the tissue changes still go on to some extent even when vitality is at its lowest. Indeed such must be the case: the vitality of the tissues ceases only with life itself; and so long as life lasts

some exerctory products must be formed, as the result of that tissue action, which the continuanee of life implies. Parkes[1] says, 'in all probability judging from the cases of death from starvation, the excretion of nitrogen by the urea would have continued at the rate of almost fifty grains daily until death.' It follows from all this that to a certain extent the tissues continue to undergo these retrograde changes which result in the formation of excretory products, after the normal assimilative changes have ceased to be possible. A necessary consequence of this is a gradual wasting of the tissues.

But in fever a disturbing element intervenes. In consequence of the propagation of the contagium there is an increased demand for, and consumption of, nitrogen; and we have now to consider whether or not this could lead to the production of the phenomenon under consideration—increased formation and elimination of urea.

The contagium in its growth appropriates the nitrogen of the constructive store albumen to an extent which is directly as the quantity of contagium reprodueed. (The circumstances which determine that we shall consider further on.) According to the ascertained faet that the quantity of nitrogen eliminated bears a definite relation to the amount assimilated, this aetion of the contagium in depriving the tissues of much of their nitrogenous material ought to be aecompanied by *diminished* excretion of nitrogen. How then account for the faet that, contemporaneously with this diminished supply of nitrogen to the tissues, there is an increased elimination of that substance in the form of urea?

The amount of urea formed depends on the amount of retrogressive store albumen conveyed to the urea-forming glands. If the propagation of the contagium is competent to produce an inereased circulation of retrogressive store albumen through

[1] Lancet, April 8, 1871.

these glands, it is competent to produce an increased formation of urea. That it does so we shall presently see.

The contagium particles pervade the whole system, and permeate all the tissues. Where do they appropriate the nitrogen of the constructive store albumen? Does the action which results in the formation of their protoplasm take place in the general circulation, or does it take place in the substance of the tissues? Do the contagium particles seize on the nitrogen of the constructive store albumen wherever they come in contact with it in the blood, or do they take it up in the same way and at the same time as the tissues, while it is circulating through their structure proper? It is possible that some of the constructive store albumen may be thus denitrized in the general circulation; but there is good reason to believe that by far the greater part of the nitrogen which is consumed by the contagium particles, is taken up by them in the minute structure of the tissues—that the protoplasm of the contagium particles, and that of the tissues themselves, is formed, and renewed, at the same time, and in the same place.

The changes which lead to the formation of tissue, from the constructive store albumen, and to the formation of retrogressive store albumen from the disintegrating tissues, take place in, and around, the capillaries. While passing through these minute vessels the blood movement is slowed, and the surface of blood exposed to the tissues is increased to the utmost extent; every facility is thus afforded to the tissues to take up from that fluid what they require. It is while the blood is passing through these minute vessels that its constructive store albumen goes to the tissues to become organ albumen, and that the organ albumen passes back into the circulation as retrogressive albumen. This, then, is the point at which the constructive store albumen normally and readily parts with its nitrogen; it is, therefore, the point at which the greatest facilities are afforded to the contagium particles to seize upon it. The constructive

store albumen is then in a transition state: its nitrogen is being liberated, in order that the demands of the tissues may be supplied, and the organ albumen built up. But the tissues are at all points permeated by minute organisms, whose wants are in the main identical with their own; and which, therefore, appropriate the nitrogen of the constructive store albumen at the moment at which it quits that form, and is about to be incorporated with the tissues as organ albumen.

The fact that such a change is taking place in the constructive albumen—that it is constantly and normally yielding up its nitrogen in the minute structure of the tissues—is a sufficient reason why the contagium particles should appropriate the nitrogen at that point, in preference to any other; and their doing so offers a ready explanation of the great and rapid wasting of the nitrogenous tissues during the course of idiopathic fever. It explains also the increased formation and elimination of urea, and that in the following manner.

Nutrition consists of two distinct processes, the taking up of new material, and the giving off of old. The action by which the tissues take up nitrogen from the constructive albumen, is simultaneous with that during which they part with their worn out nitrogen in the form of retrogressive albumen. Both actions take place in, and around, the capillaries, and are so contemporaneous that it is impossible to say, either that the old nitrogen of the organ albumen is deposed by the fresh nitrogen of the constructive, or that the latter steps in to fill up a gap created by the passage backwards into the circulation of the used up nitrogen of the organ albumen; in other words, the two actions are simultaneous, neither actually preceding the other, any more than the passage of one fluid through a membrane, precedes the passage of another which exists on the other side. While this simultaneous double action is going on, the contagium particles step in, and convert into their own protoplasm, so much as they require of the constructive albumen. So close, so to speak, is

the struggle between the tissues and the contagium particles for the possession of the constructive albumen, that the latter may seize upon it at the very moment at which it is about to be incorporated with the former, and consequently, not before some of the used up organ albumen has become retrogressive. The moment at which the constructive albumen is undergoing the change which results normally in the formation of organ albumen, is that at which its nitrogen is most readily taken up by the contagium particles. The simultaneous action by which the organ albumen is converted into retrogressive, is equally far advanced. The contagium particles step in to deprive the tissues of much of what they require for the formation of organ albumen; no such agency, however, intervenes to prevent the completion of the contemporaneous action which results in the formation of retrogressive albumen. This action, therefore, continues as usual.

It follows from all this that the retrogressive albumen, and, therefore, the urea, continues to be formed at the same rate, and in the same quantity, as would result from the continuance, and completion of the changes which normally result in the conversion of all the constructive albumen into organ albumen. In other words, the consumption by the contagium of the nitrogen of the constructive store albumen leads to the same retrograde tissue changes, as would normally result from its consumption by the tissues themselves. The increased consumption of constructive albumen, caused by the growth of the contagium, leads, therefore, to increased formation of retrogressive albumen, and of urea. There is reason to believe, then, that the quantity of nitrogen assimilated by the tissues, during the continuance of idiopathic fever, may be greatly diminished, without a corresponding diminution in the quantity eliminated from the system.

But another, and essential, phenomenon of fever intervenes to produce an actual increase. The continuance of the changes

which normally result in the formation and disintegration of the organ albumen depends, among other things, on the circulation through the tissues of a due supply of blood. The more active the circulation is, the more active also, *caeteris paribus*, will be the tissue changes. In health the heart beats at the rate of about seventy per minute, and, at each beat, sends onwards about the same quantity of blood, so that in twenty-four hours the heart has sent the fill of its left ventricle into the general circulation, and so through the body, 100800 times. But in fever there is increased rapidity of the cardiac action, and of the circulation through the tissues. Supposing the heart to beat at the rate of 120 per minute, the fill of its left ventricle would be sent through the body 172800 times in twenty-four hours. As there is no diminution, but rather an increase, in the amount of retrogressive albumen in the blood, it is evident that one result of the increased rapidity of its circulation must be the conveyance, in a given time, to the urea-forming glands, of a more than usual quantity of the ingredients from which they form that compound; and, of course, an increase in the quantity of urea formed.

The rapidity of the heart's action may, indeed, be greatly accelerated in health, as by muscular exercise, and by mental emotion, without producing increased formation of urea; but that is because the increased rapidity of the blood flow is not accompanied by a corresponding increase in the amount of retrogressive albumen formed. In the case of muscular exercise the increased frequency of the heart's action is due, partly to the pressure of the contracting muscles on the veins, and partly to their increased wants, consequent on the greater demands made upon them. It has been clearly proved that such increased action is not accompanied by increased metamorphosis; the muscles really increase in bulk; they conserve their energy and their nitrogen, and, while appropriating more, retain much of what they already have. The result of mental emotion is to

increase the frequency of the cardiac contractions, without causing any corresponding increase in the capillary circulation or in the tissue changes ; it is a mere nervous excitement, which does not necessarily lead to increase in the normal tissue changes.

The acceleration of the blood flow which takes place in fever is quite peculiar, and altogether different from anything that occurs in health. It is due to no increased demand on the part of the tissues, but to the propagation of the contagium in their minute structure. There is an increased demand for constructive albumen in the tissues, not because they themselves require more than is sent to them, but because they are everywhere pervaded by these minute organisms, whose wants and demands are, in the main, identical with their own, and cannot be separated from them. The consumption of the constructive albumen by the contagium particles, leads to an increased demand for nitrogen in the tissues, identical with that which would result from an increased demand on the part of the tissues themselves. It follows, that a larger supply of blood than usual is sent to the tissues thus pervaded by the contagium particles (and all the tissues of the body are so) ; it follows also, that, with the continuance of the changes which result in the formation of retrogressive albumen, there must be, with the heart beating at the rate of 120 per minute, and with a corresponding increase in the capillary circulation, more retrogressive albumen formed in a given time, than when it beats at the rate of only seventy per minute. The increase due to this cause is, not directly as the increase in the heart's rate of action ; allowance must be made for the lessened quantity of nourishment taken during fever ; but even with such allowance, there can be no doubt that there must be a considerable increase in the amount of retrogressive albumen circulating in the blood. Thus, then, we have, as a result of the propagation of the contagium particles in the tissues, both an increase in the quantity of retrogressive albumen formed, and an increase in the quantity of blood passing

through the urea-forming glands in a given time. The inevitable result is an increased formation of urea. With the conditions necessary to effective action of the kidneys, there is also an increased elimination of that substance.

According to this view of the matter, that is to say, according to the view which regards the propagation of the contagium as the primary agency in the production of the phenomena of the febrile state, and, among others, that which we are now considering, an increased elimination of urea ought to be one of the earliest indications of the existence of fever. The first act of the contagium is to be reproduced; the first result of such reproduction is increased consumption of nitrogen and of water; the first effect of such increased consumption is a hastening of the capillary blood flow, and of the tissue metamorphosis; the first evidence of such increased metamorphosis is increased elimination of excretory products. The derangement of the process of nutrition which gives rise to the increased excretion, is an essential part of the febrile state, and gives evidence of its existence at all stages of fever, the earlier, as well as the later. The febrile state is never found to exist prior to the occurrence of increased elimination of urea: but increased elimination of urea has been found to precede the pyrexia; an important fact, which was first demonstrated, in the case of intermittent fever, by Dr. Sydney Ringer [2].

At the period of defervescence, and even after the normal temperature has been regained, the amount of urea eliminated may be greater than it was at the height of the fever.

The theory which has been advanced as to the mode of production of the increased tissue change seems to us the only one which offers anything like an adequate explanation of the facts with which we have to deal. It shows why the evidence of

[2] Medico-Chirurgical Transactions, Vol. xlii.

deranged nutrition should precede the pyrexia; it shows why the febrile state should be accompanied by increased tissue metamorphosis; it shows (as we shall see when considering the phenomena of the crisis) why the process of defervescence should be accompanied by an increase in the urea elimination; and it explains the whole of these phenomena, by simply referring them to the propagation in the system of a poison which we know is being largely reproduced in it at the time of their occurrence, and whose reception into the system we regard as necessary to the development of the disease during whose course these phenomena occur. There is wanting not one link in the chain of evidence which points to the propagation of an organism in the system, as the ultimate cause of the increased formation of urea, which precedes, accompanies, and follows, the pyrexia of the specific fevers.

We have now to meet the question—Why, under such circumstances, is the amount of urea eliminated sometimes below the normal standard? Why does the agency which causes an increased elimination of urea in one case, give rise, in another, to exactly the opposite result?

CHAPTER X.

DECREASED ELIMINATION OF UREA.

The diminished excretion of urea, which is noted in some cases of fever, was attributed by Dr. Parkes, not to diminished formation of excretory products, but to the retention of these products in the blood: and he suggested such retention as a cause of many of the phenomena which occur in the course of a febrile attack; and especially of the local inflammatory complications which are occasionally found in cases in which there is decreased elimination of excreta. The copious discharge of products so retained he looked upon as explanatory of the phenomena observed at the crisis.

Decreased elimination of urea must be due (1) to decreased formation of retrogressive store albumen, (2) to defective action of the urea-forming glands, (3) to defective action of the kidneys, or (4) to a combination of two or all of these agencies.

Let us consider separately each of these possible causes of defective elimination of nitrogen.

Decreased formation of retrogressive albumen. We have seen that increased formation of urea during fever, is a consequence of the continuance of, or rather of an increase in, the normal retrograde tissue changes, and the coincident occurrence of increased rapidity of the circulation through the tissues and urea-forming glands. Such being the usual effect of the propagation of the contagium in the system, is there any possibility of its producing an opposite result? It seems

unlikely that one and the samc eause should be capable of produeing two direetly opposite effects. A eareful study of the subject, however, would seem to indicate that such a result is not impossible.

Thc eontagium particles in their growth appropriate the nitrogen of the constructive store albumen: this they do for two reasons, first, beeause it is necessarily an unstable, and everchanging compound, and, therefore, very readily parts with its nitrogen; and second, because it supplies the nitrogen in the form best adapted for the building up of their protoplasm. The extent to whieh the construetive albumcn is thus eonsumed, and the consequent deprivation of the tissues, obviously depends on the quantity of eontagium reproduced in the system; the greater its reproduction, the greater will be the eonsumption of eonstructive albumen, and the wasting of the tissues. But if it be true that the consumption of eonstruetivc albumen is directly as the extent to which the contagium partieles are reproduced, it is, on the other hand, equally true that the propagation and growth of these particles depends *inter alia* on a due supply of nitrogen. Obtaining this as they do from the constructive albumen, it would seem to follow that the propagation of the eontagium depcnds on a due supply of that substanee, and should be more active when there is a good, than when there is only a scanty, supply. But we know from clinical experience that the most severe eases of fever, those in which there is the largest reproduetion of the eontagium, are also those in which nourishmcnt, the only possible source of eonstruetive albumen, is with most difficulty got into the stomaeh; and is most imperfectly digested and assimilated after it is swallowed. The constructive albumen, as a souree of nitrogenous supply, is therefore most likely to be defieient in those cases in whieh most is required.

Supposing it to fail, is there any other souree from whieh, under sueh eircumstances, the eontagium partieles eould get the

nitrogen requisite to their growth? There are three possible—the organ albumen, the retrogressive albumen, and the urea.

We have already seen that one of the two reasons why the contagium particles take their nitrogen from the constructive albumen in preference to these other possible sources, is that it is an unstable compound, which normally and very readily parts with its nitrogen: we have seen too, that the moment at which its nitrogen is in the transition state, when it is passing from the constructive to the organ albumen, and cannot really be regarded as belonging to either, is the time at which it is seized upon by the contagium. This is a reason which excludes the more stable organ albumen and urea, from being regarded as probable sources of nitrogen supply to the contagium particles; but does not exclude the retrogressive albumen: it too is an unstable compound, which normally and readily undergoes change. If then, either from excessive reproduction of the contagium, or from diminished formation of constructive albumen, the supply of nitrogen from that source were to prove insufficient for the wants of the contagium particles, it is possible that they might supplement the deficiency by consuming part of the nitrogen of the retrogressive albumen. Nitrogen they must have: it presents itself most conveniently to them in the constructive albumen, whence by preference they take it: that source failing, they might fall back on the next most accessible, and take it from the retrogressive. The result of such denitrization of the retrogressive albumen, would be a diminution of the quantity conveyed to the urea-forming glands, and a consequent decreased formation of urea. In this way decreased formation of retrogressive albumen might be the cause of the decreased elimination of urea.

It may, indeed, be said that the consumption of the whole of the constructive albumen would not only put a stop to the formation of organ albumen, but would also indirectly cause a cessation of those changes which result in the formation

of the retrogressive. But we have already seen that retrograde changes may continue to some extent, after constructive have ceased to be possible; and that, in cases of starvation, urea may be excreted at the rate of fifty grains a day, after the deprivation of food has continued for two or three weeks; the continuance of the blood flow through the tissues, seeming necessarily to result in some change therein. Whether or not constructive changes are possible, retrograde changes seem always to take place to some extent. If such be the case in starvation, the same thing must obtain to even a greater extent in fever; for the increased rapidity of the blood flow, which is a prominent characteristic of that state, must necessarily lead to a corresponding increase in those changes which accompany the circulation of that fluid through the tissues.

But yet another objection may be advanced against the view that the contagium particles may consume the nitrogen of the retrogressive albumen, after that of the constructive is insufficient to meet their demands. If the whole of the constructive albumen be thus consumed, and if the increased rapidity of the circulation causes increased metamorphosis of the tissues, what is to become of these tissues? If all the organs of the body are thus deprived of the materials necessary for their nutrition, and continued vitality, and are at the same time the seat of a greater than normal waste, how is life to be sustained? If the brain, heart, liver, kidneys, muscles, nerves, and all the organs and tissues of the body, be deprived of what is necessary for their nutrition; and if, at the same time, these organs and tissues disintegrate at a more than usually rapid rate, it is evident that the cause which produces this state of affairs, cannot long continue in operation without causing death. Unquestionably that is the case: but then, is not death a frequent result of fever? True: but recovery in cases in which there has been defective elimination of urea is also frequent—too frequent, we think, to permit

of our regarding the ageney now under eonsideration, as the sole eause of the oeeurrenee of such defeetive elimination: for there ean be no question that the eonsumption by the eontagium for any length of time, of the whole of the nitrogen of the eonstruetive store albumen, and the eontinued formation of the retrogressive, are incompatible with the eontinued vitality of the most important organs of the body, and espeeially of the brain. Sueh rapid and eomplete deprivation of nutrient material would inevitably give rise to most alarming nervous symptoms, eonvulsions, coma, or fatal typhoid depression. Though sueh symptoms are most apt to oeeur in eases in whieh there is partial or total suppression of urine, it is equally the ease that a eonsiderable defieieney in the amount of urea excreted often oeeurs, and persists for a time, without the development of sueh alarming symptoms.

But there is a still stronger argument against this view of the eausation of the deereased elimination of nitrogen. In eases whieh prove fatal, and in whieh there has been defeetive elimination of urea, that substanee has been found in exeess in the blood and other fluids, elearly showing that, though not eliminated by the kidneys, the urea was, nevertheless, formed. This faet alone suffiees to show that the retrogressive albumen is eonveyed to the urea-forming glands, that it is not denitrized by the eontagium partieles, and that diminished formation of retrogressive albumen is not the eause of the diminished exeretion of urea.

Defective action of urea-forming glands. When oeeasion requires, these glands are eapable of doing mueh more than their normal amount of work. That during the eontinuanee of the febrile state, this eapaeity is not materially interfered with, is proved by the faet that urea is generally exereted in more than normal quantity. This renders it probable that the cause of the lessened exertion of that substanee, whieh

is frequently noted, is not to be found in incapacity of the glands in which it is formed. And this probability is elevated almost to a certainty by the fact just noted, that, in cases in which its excretion is defective, urea exists in the blood in more than normal quantity. The same fact which proved that the diminished excretion of nitrogen is not due to diminished formation of retrogressive albumen, shows also, that it is not solely due to defective action of urea-forming glands. We say not *solely* due to this, because it is quite possible, that, even in cases in which these glands are forming more than the normal quantity of urea, their capacity may be so overtaxed that some of the retrogressive albumen conveyed to them may be incompletely metamorphosed. We shall presently see good reason for believing that the main cause of the defective excretion of nitrogen, is the consumption by the contagium particles, of the water which is requisite to enable the kidneys to perform their excretory function. This is an agency which must also operate on all the organs of the body. The kidneys suffer most, because of their peculiar function. But it is not unlikely that the liver too may feel its effects; and that defective nutrition of its glandular substance, and deficient supply of water, may lead to imperfect performance of the functions of that, and other urea-forming glands.

There is, in the presence in the blood of a more than normal quantity of urea, positive evidence of the formation of that substance. But, with the passage to the urea-forming glands, of a more than normal quantity of retrogressive albumen, it is evident that we may have, at one and the same time, increased formation of urea, and imperfect metamorphosis—increased formation of urea, because the urea-forming glands are capable of forming more than the normal quantity of that substance, and imperfect metamorphosis, because they may have sent to them more retrogressive albumen than they are capable of converting into urea. They may have sent to them four times the normal

quantity of retrograde material: but they may be capable (in consequence of defective nutrition, and deficient supply of water,) of converting into urea only three fourths of this: the remaining fourth being changed into leucine, or some intermediate compound. Under such circumstances there would be increased formation, and, with normally acting kidneys, increased elimination of urea, and yet, imperfect metamorphosis of part of the retrogressive albumen. But though such imperfect metamorphosis of part of the albuminous tissue is possible, it could not give rise to a *less than normal* excretion of urea; and there is sufficient evidence to show that it is not the agency which leads to decreased elimination of that substance. Defective action of urea-forming glands is, therefore, not the cause of the decreased elimination of urea.

Defective action of the kidneys. That the structurally sound kidney is capable of eliminating a much larger quantity of urea than is habitually excreted in health, is proved by the fact that in fever, and other ailments, the normal quantity is often greatly exceeded; and by the additional fact, that when one kidney is by any means lost, the remaining one does as much work as was previously done by two. That there is a limit to the excreting power of the kidneys there can be no doubt: it is, therefore, possible that there might be produced more urea than the kidneys are competent to eliminate, and that uræmia might thus result, solely from excessive formation of urea—the amount eliminated, though above the normal standard, being still inadequate to counterbalance the excessive formation. This, however, would not constitute defective action of the kidneys, and would not give rise to the phenomenon which we are now considering, decreased elimination of urea.

What we have to deal with, is a condition in which there is decreased elimination of urea, without evidence of decreased formation; and what we have to consider is, whether or not

this decreased climination results from defeetive aetion of the kidneys.

Cases of fever aecompanied by decreased climination of urea, may be divided into two classes,—those in which the kidneys were diseased prior to the occurrence of the febrile attack; and those in which they were healthy at the time of its onset.

That a febrile attack occurring in one who is the subject of renal disease, should be more or less modified by the previously existing ailment; and that the symptoms of the kidney disease should, in their turn, be intensified by the grafting on to them of those refcrable to the febrile attaek, is no more than one would expect. We know that without the prior existence of any renal complieation, bad cases of fever are apt to present fcatures which bear a very close resemblance to those presented by advaneed cases of renal disease. It is not, therefore, to be wondered at that fever occurring in one who is the subject of renal disease, should present, in an unusually marked manner, thosc symptoms which are apt to occur in each of thcse ailments from which he is suffering; and which, in both, have been attributed to the same cause, defective elimination of excretory products. Thc existence of renal diseasc in those suffering from fevcr, only increases the risk of defective climination of excretory products, and of the oceurrence of so-called uræmic symptoms. We need not, therefore, enter into a dctailed analysis of such cases, but may at once proceed to the consideration of those in which there is decreased elimination of urea, but in which the kidneys are healthy at the onset of the fcbrile attack; premising only, that everything said regarding the mode of production of the renal symptoms in them, is doubly applicable to those in which there was previous disease of the kidneys.

Finding the evidence of defective renal action, and thc oc-currence of serious nervous symptoms, constantly co-exist, thc latter have naturally been looked upon as the consequenee of the former: the head-symptoms are supposed to bc of uræmic

origin, and (what concerns us at present) the decreased elimination of urea, and its consequent retention in the blood, are attributed to morbid change in, and defective action of, the kidneys.

But how are the morbid changes in the kidneys produced? We know that in such cases the kidneys are perfectly healthy at the commencement of the febrile attack; that in those which recover, the urinary secretion again, as a rule, becomes normal; and that in those which prove fatal, the morbid appearances presented by the kidneys are recent. We know, in short, that the renal disorder is secondary to the fever, and results, either directly or indirectly, from the action of the fever poison. That it is not due to any *direct* action on the kidneys of the poison which gives rise to the febrile symptoms, is rendered certain by the fact that such disorder occurs in only a small number of the total cases of fever: that it is due to some *indirect* action of the poison, is proved by the fact that it manifests itself subsequently to the onset of the febrile state, and that, in cases which recover, it disappears after defervescence.

Again, the fact that the symptoms of renal disorder occur in only a small number of cases, shows that those in which they do occur must be in some way peculiar, and that the direct cause of the renal complication is not to be found in any *necessary* condition of the febrile state.

Let us then analyze these cases, and try to find out wherein their peculiarity consists.

The first thing to be noted regarding them is, that they are all severe—the febrile symptoms running high from an early period: even before the appearance of any renal complication, there is great thirst, rapid pulse, high temperature, and specially prominent nervous symptoms. As the fever advances, the symptoms become more marked; delirium is constant, often violent, and not unfrequently, culminates in convulsions, coma, and death; at the same time the urine is scanty and high-coloured, is frequently albuminous, often contains casts of the

renal tubes, with excess of renal epithelium, and at times is tinged with blood. In fatal cases, the kidneys give evidence of irritation, or even of inflammation; they are increased in size, and more or less gorged with blood: their tubes are loaded with epithelium, occasionally mingled with blood—the evidence of renal disorder being recent.

Besides the occurrence of renal disturbance, and defective elimination of urea, the chief peculiarity of the cases now under consideration, is the height to which the fever runs. Cases in which the temperature is high at an early period of the attack, are those in which we are likely to have albuminuria, and bad head symptoms[1]. But it is to be particularly noted, that all the febrile symptoms are thus marked, before there is evidence of renal disturbance, and that the early occurrence of a high temperature only leads us to be on the outlook for such a complication. Now, what peculiarity do these cases present, prior to the occurrence of evidence of renal disorder, and maybe even before there is diminished excretion of urea? And what is there in them that should lead to such a complication? Nothing apparently, beyond an unusually smart attack of fever. Well, what does this imply? It means that the various actions, the existence of which in the body the febrile state implies, are taking place in a more than usually marked manner: it means that there is a very large propagation of contagium particles, a greater than usual consumption of nitrogen and water, a greatly increased formation of retrogressive albumen, a more than ordinary increase in the rapidity of the circulation through the tissues, and an unusually large formation of urea. To one feature in these cases we would draw special, and prominent attention,—the greatly diminished excretion of water.

It has already been noted, that the contagium particles, in

[1] See Paper by Author on the Thermometry of Typhus, in Edinburgh Medical Journal, Vol. i, 1869.

their growth and propagation, largely eonsume water as well as nitrogen. The important part whieh the eonsumption of water plays in the produetion of many of the phenomena of the febrile state, we shall by and bye see. Meantime, we would draw attention to the part whieh it plays in the produetion of the phenomenon now under eonsideration, defeetive elimination of urea.

We never find diminished exeretion of urea in fever, with a normal quantity of urine. Defeetive exeretion of water is, indeed, even more charaeteristie of the eases whieh we are now eonsidering, than is defeetive elimination of urea. In their early stages, the quantity of urea eliminated may be, and generally is, in excess of the normal; but the quantity of urine is always more or less seanty. But one interpretation ean be put on this: the kidneys are quite eompetent to perform their function; they exerete a larger than normal quantity of urea, beeause a larger than normal quantity is sent to them: they exerete an abnormally small quantity of water, beeause they cannot get more. But, let the eause whieh gives rise to both these eonditions (the propagation of the eontagium) pass a eertain limit; let urea be formed, and sent to the kidneys in sueh large quantity, that the eliminating eapacity of the glands is taxed to a greater than normal extent; and let the quantity of water plaeed at their disposal, be at the same time so defieient, that they ean get very little to exerete, and retention of urine must result—not beeause the kidneys are affeeted, not beeause they are ineompetent to exerete urea, but beeause the eonditions requisite to its exeretion are not to be had. The diminished exeretion of urea, then, is due not to diminished formation of that substanee, not to any struetural ehange in the substanee of the kidneys, but to the absenee of the quantity of water which is essential to the due performanee of their function by these glands. It is thus an indireet result of the propagation of the eontagium.

What must be the effect of all this on the kidneys themselves? And how are we to explain the albuminuria, and other evidence of disorder, which they so frequently present, in conjunction with the diminished excretion of urea?

The circumstances with which we have to deal are, (1) that there is a great and increasing excess of urea in the blood, and (2) that the quantity of water necessary to its elimination by the kidneys is not to be had. Now, it is evident, that this unusual quantity of urea cannot circulate, and continue to circulate, through the kidneys, with no possibility of elimination, without seriously irritating these glands. The action of urea on the nervous system is still a matter of discussion; but of its action on the kidneys there is no doubt; it is decidedly stimulant to these organs, as is manifested by its normal action on them, and by the fact that its injection into the circulation gives rise to diuresis. It is obvious that if this stimulation be excessive, irritation and even inflammation may result; it is equally obvious that this stimulation must be excessive, and that there must, therefore, be considerable renal irritation in those cases of fever in which excessive propagation of the contagium leads at once to excessive formation of urea and increased consumption of water. The defective elimination of urea, therefore, is not secondary to the morbid changes which take place in the kidneys; but these changes, and the evidences of renal mischief which, as a consequence of them, are noted in the urine during the patient's lifetime, are the result of the uræmia, and the consequent presence in the kidneys of an excessive quantity of their natural stimulant, which, for reasons already given, they are unable to eliminate. The ultimate cause of both the uræmia and the renal symptoms, is the excessive propagation of the contagium.

The appearances presented by the kidneys bear out this view. Referring to typhus fever, Murchison says, 'If death occur before the fourteenth day the organs are usually hyperæmic and

hypertrophied, while the tubes are gorged with granular epithelium and sometimes contain blood. Occasionally they present the appearances of acute nephritis, as intensely developed as in any case of scarlatina' (Murchison, 2nd ed. p. 265). The urine secreted by such a kidney must be albuminous, and contain tube casts, and sometimes blood. The appearances thus described by Murchison are exactly those which would be produced by the circulation through the kidneys of something which would be stimulant, or irritant, according as it existed in greater or less quantity. Is not urea the substance which, if unduly retained in the circulation, would be most likely to produce such an action? Is it not the case that urea is unduly retained, and does circulate in undue quantity through the kidneys in cases in which the renal symptoms are marked? And is it not the case, that we do not know of the existence in the blood of any other agency capable of producing such an action on the kidneys? And, finally, is not this view of the pathology of the renal changes occurring in the course of idiopathic fever, the necessary and logical inference to be drawn from such an exposition of the facts as has been given?

When the quantity of contagium produced in the system is not too great, the amount of urea formed is not above that which the kidneys are capable of excreting. There is increased formation of urea, but there is also increased elimination. When, however, the propagation of the contagium passes a certain limit, there is produced, as a consequence of the greatly increased rapidity of the capillary blood flow, not more urea than the kidneys could excrete, if they could get the necessary quantity of water, but more than they are capable of eliminating with the small quantity of water which is at their disposal. It is thus that the uræmia is produced; and it is the continued circulation through, and presence in, the kidneys, of an excess of their normal stimulant, which gives rise to irritation, and, maybe, even to inflammation of these organs, and leads to the symp-

toms, and morbid appearances, presented by the urine and kidneys of many of those cases of fever in which there is defective excretion of urea. The kidney affection, therefore, is secondary to the uræmia.

That the increased *formation* of urea which takes place during the febrile state, results in stimulation of the kidneys, is evidenced by the fact that there is generally increased *elimination* of that substance; this could not be, without increased action of the kidneys. That there is not at the same time an increased elimination of water is due to the fact that, for reasons already given, an increased, or even the normal, quantity of water, is not to be had. Were the requisite quantity of water available, there can be no doubt, that an increased flow of urine would be as characteristic a phenomenon of the febrile state, as is an elevated temperature, or a quick pulse. When considering the phenomena of the crisis, we shall see that these are mainly the result of the comparatively sudden cessation of the demand for water, consequent on the almost abrupt cessation of the propagation of the contagium.

A careful consideration, then, of the phenomena presented by those cases of fever in which there is decreased elimination of urea; and a minute study of the circumstances which precede and lead up to this, have led us to the conclusion, that the defective elimination of urea does not result from decreased formation of that substance; that it is due, not to decreased formation of retrogressive albumen, not to defective action of the urea-forming glands, but to defective excretion by the kidneys; this, in its turn, results, not from morbid change in these glands, and not from want of excreting power in them, but from the absence of the quantity of water which is necessary to enable them to form urine, and to eliminate the urea which is circulating through them. The defective supply of water results from its excessive consumption by the contagium particles. The ultimate cause of the defective excretion of urea, and of

all the phenomena resulting therefrom, is, therefore, excessive reproduction of contagium particles—the same agency which, occurring in a minor degree, we have seen to be also the ultimate cause of the increased elimination of urea common in fever.

The connexion between the febrile state and the elimination of urea may be briefly stated thus. The febrile state is always accompanied by increased formation of urea, and by increased consumption of water, the two chief ingredients of the urine. So long as the quantity of water at the disposal of the kidneys is sufficient for the purpose, there is increased elimination of urea. In severe cases, in which there is a large propagation of contagium particles, the balance is apt to be disturbed; there is, in them, a very great consumption of water, and a coincidently great increase in the amount of urea formed. The kidneys are thus placed in the position of the Israelites of old, when they were ordered to make bricks without straw; they have more than enough urea, but scarcely any water with which to form urine. If this abnormal state of affairs be not excessive, or do not continue too long, the difficulty may be tided over, with no more than an anxious and smart attack of fever, accompanied by very scanty excretion of urine, but not by any very marked renal complication. If the disturbance be excessive, however, and manifest itself at a comparatively early period of the attack, renal symptoms are inevitable; albumen appears in the urine, then casts of the renal tubes are detected, and even blood may appear; there is greater or less retention of urine, greatly diminished excretion of urea, and very prominent nervous symptoms; the patient either lapses into a state of coma, in which he dies; or makes the narrowest of escapes.

Between the mild attack, in which neither the increased elimination of urea nor the decreased elimination of water, is at any time marked; and the severe one, in which there is, at last, complete suppression of urine, there are all shades and degrees.

CHAPTER XI.

INCREASED CONSUMPTION OF WATER.

THIRST is one of the most prominent of the subjective phenomena of the febrile state. To allay this, there is consumed a much larger than usual quantity of water. So great is the demand for water that the most copious draught has only a transient effect: barely has it had time to get into the system, when another draught is called for. In this way the quantity consumed during a febrile attack of two or three weeks' duration, is enormous.

Coincidently with such increased consumption, there is decreased elimination. Hence the phenomenon with which we are now dealing, is usually referred to as excessive *retention* of water. It is obvious, however, that the enormous quantity of water taken into the system during the course of a febrile attack, cannot be retained as water: it is equally certain that it is not eliminated; for while the patient may be almost constantly drinking, his skin is hot, dry and unperspiring; his bowels are constipated; and his urine scanty. The demand for water, and the concentration of the urine, are both greatest when the fever runs high—so that we have in each of these symptoms a good index of the amount of febrile disturbance. But if the water be neither eliminated nor retained, what becomes of it?

The only attempt at a feasible explanation is the hypothesis of Parkes, who suggests that, during the metamorphosis of the albuminous tissues, there may be formed a gelatinous compound intermediate between them and urea, and possessing, in virtue of its gelatinous nature, a great attraction for water. This

hypothesis is quite in keeping with his former one, that the tissue metamorphosis is imperfect in fever; but it also lands us in the same difficulty, by suggesting, without answering, the question—why should such imperfection exist?

The competence of any gelatinous compound to produce so great a consumption of water as takes place in fever is extremely doubtful. It is evident, however, that there is at work in the system some agency competent to produce such a result. The water consumed is not retained in the system as water; it is not eliminated: it must, therefore, be somehow used up and utilized. The normal ingredients and tissues of the body require no such large supply, and are incapable of utilizing it: the only abnormal agent of whose presence we are aware, is the contagium. We have, therefore, to inquire whether the propagation of the contagium in the system calls for an increase of the water supply. We shall find that it does.

In virtue of the properties common to them, and all organisms, contagium particles require water for their growth and propagation. So long as their rate of reproduction is slight, a slight increase in the quantity of fluid taken into the system suffices to meet this demand. But if it be excessive, the system cannot with impunity supply the requisite amount. The demands of the contagium particles lead to the consumption of much of the fluid which the system requires for the supply of its own wants; the consequent deprivation of the system results in unusual thirst, the degree of thirst bearing a direct relation to the extent to which the contagium is produced. The large quantity of water taken to quench this, is consumed by the contagium particles, almost as soon as it is received into the system; and so long as they continue to grow, and to be propagated, does the demand for water last. The consumption of the water by the contagium no doubt takes place in the substance of the tissues, in the same place and at the same time as the nitrogen of the constructive albumen is appropriated by them.

In this consumption of water by the contagium particles we have a ready explanation of some of the usual symptoms of fever. The thirst, the loss of appetite, the dry skin, the parched tongue, the constipated bowels, and the scanty urine, are all due to one cause, the consumption by the contagium particles of the water which is requisite to enable the stomach, the skin, the tongue, the bowels, the kidneys, and all the organs of the body, to perform their due and proper functions. Notwithstanding the enormous quantity of water consumed, all the tissues and organs are deprived of that fluid by the still more enormous quantity of contagium particles which are formed, which pervade all parts of the body, and which everywhere consume the water of their environment.

The consumption of water is, of course, greatest in severe cases of fever, in which there is produced the largest amount of contagium particles; and it has already been pointed out, that the wasting which occurs in all cases of fever, and the decreased elimination of urea, which is noted in bad cases, result, the one from the consumption by the contagium of the water which so largely enters into the composition of the body, and the other from the absence of the water which is necessary to enable the kidneys to form urine. The consumption of water by the contagium particles thus gives rise, not only to some of the most common and constant phenomena of fever, thirst, dry skin, constipated bowels, scanty urine, and diminished bulk of the tissues; but, when excessive, causes also one of its most formidable symptoms, suppression of urine.

CHAPTER XII.

INCREASED FREQUENCY OF THE CIRCULATION.

The special purposes attained by the circulation of the blood through the tissues are (*a*) the supply of the materials requisite to their nutrition; and (*b*) the removal of the waste materials formed during their disintegration. The more active these processes, the more rapid the circulation. The motor powers which keep up the blood flow, are the heart and the arteries; the latter by their alternate contraction and dilatation, aiding and regulating the movement set going by the former.

When, from any cause, the process of nutrition is excited in an organ, there is an increased flow of blood to it. It is primarily through the action of the vasomotor nerves on the minute arteries of the excited organ, that the increased blood flow is brought about. If the excitement, and consequent increase of blood sent to the organ, be slight, no general disturbance is produced: but if they are great, the central organ of the circulation will participate in the disturbance, and the system generally will feel the effects of it. Supposing such excitement to exist all over the body at the same time, there would necessarily result an increased rapidity of the general circulation. This is what occurs in idiopathic fever.

We have already seen that it is in the tissues themselves that the contagium particles appropriate the materials necessary to their growth. They lay hold of the nitrogen and of the water of the constructive store albumen at the moment at

which they are on the point of being taken up by the tissues, and incorporated into their structure to form organ albumen. So far as the demand for the chief nutritive ingredients of the blood, nitrogen and water, is concerned, there is no difference between that created by the tissues, and that to which the contagium particles give rise. The propagation of the contagium in the tissues, therefore, causes an increase in the demand for blood in all the tissues of the body, identical with that which would result from a similarly increased demand resulting from excitement of the normal process of nutrition. Excitement of the normal process of nutrition means an increased demand on the part of the excited tissue, for nutrient material. The propagation of the contagium particles in these tissues, implies an increased demand for, and consumption of, exactly the same material. The propagation of the contagium in the tissues, therefore, gives rise to exactly the same hastening of the blood flow as would result from a corresponding general excitation of the normal process of nutrition; and so long as this propagation continues, does the increased rapidity of the blood flow resulting therefrom last.

It is thus that the increased frequency of the cardiac action in fever is produced. The greatly increased demand for blood in the tissues, consequent on the superaddition to their normal wants, of those referable to the growth of the contagium particles, leads to a greatly increased rapidity of the blood flow through the tissues. Such a general hastening of the blood-current in the minute vessels, must lead to increased flow through the veins, and necessarily to increased frequency of the cardiac action. The ultimate cause of this, is the propagation of the contagium in the tissues. In accordance with this view, we find that (*caeteris paribus*) the cardiac action is most rapid in those cases in which marked prominence of all the symptoms, indicates a large propagation of contagium particles.

The continued propagation of the contagium more than

counterbalances the increased flow of blood through the tissues. Notwithstanding the increased quantity of blood sent to them, there is not received nutrient material enough for their ordinary wants. They all suffer from the deprivation of nitrogen and water, which results from the growth of the contagium particles in their minute structure. Being thus deprived of the material necessary to their nutrition, and the due performance of their functions, the mode in which these functions are performed is necessarily imperfect. To every organ of the body this is applicable; and among others to the heart. The muscular substance of that organ suffers from malnutrition to an extent which is directly as the quantity of contagium reproduced. We accordingly find that, with a large propagation of the contagium, or in other words, in a severe attack of fever, the heart's action is not only rapid, but, after a time, feeble: the feebleness being partly the result of defective power of the muscular walls. This malnutrition often gives rise to change in the cardiac structure, as we shall see when considering the changes noted after death from fever.

CHAPTER XIII.

PRÆTERNATURAL HEAT.

Calor praeter naturam has ever been looked upon as the most essential phenomenon of the febrile state. Regarding its mode of production different views have at various times been advanced. That generally held at the present day is the one propounded by Virchow. According to that distinguished pathologist 'the elevation of temperature must arise from an increased consumption of tissue.'

In attributing the rise of temperature to this agency, there can be no doubt that Virchow has fixed upon its true cause. We know that the old views as to the action of various inflammatory processes in the specific fevers were inaccurate: we know that in idiopathic fever there is, as a rule, no local lesion competent to give rise to such a phenomenon: and we know of no more probable cause than that to which it has been attributed by Virchow—exaggeration of those changes which keep up the normal temperature of the body. Moreover, we have, in increased formation of excretory products, very strong evidence that during the continuance of the febrile state, there is increased consumption of tissue.

This explanation of the most prominent and striking phenomenon of the febrile state is the strong point of Virchow's theory: and it is the ready explanation of this phenomenon which his theory affords that has led to its general adoption. It is obvious, however, that if increased consumption of tissue

be the cause of the præternatural heat, we must go further than Virchow's theory takes us, and inquire into the causation of the increased tissue change. 'This,' says Virchow, 'appears to have its immediate cause in alterations of the nervous system.' But whence these alterations in the nervous system? To this question, Virchow's theory gives no answer.

That the nervous system does play an important part in keeping up the normal temperature, there can be no doubt; that the nervous system is often deeply involved during the course of fever, is equally certain. But it does not follow therefrom that all the phenomena of that state result, either directly or indirectly, from alterations in that system. It is quite possible (to us it seems very probable) that the changes which take place in the nervous system are secondary to, rather than causative of, the increased consumption of tissue. When more fully considering these symptoms we shall see that such is the case with many of them; and that there is no evidence to show that any change which takes place in the nervous system exercises the primary influence in the production of the febrile state, which Virchow attributes to that supposed cause of disturbance.

The whole of the phenomena of the febrile state, as they present themselves in the specific fevers, are due directly or indirectly to one cause, the contagium. To this, therefore, we must look for an explanation of each and all the phenomena which constitute that state; and among others, the præternatural heat.

This, we have seen, must be due to increased tissue action. Can the contagium give rise to such increased action? We have already seen that it can.

First, when inquiring into the causation of the increased tissue waste, we saw that it was mainly due to the consumption by the contagium particles of the nitrogen and water destined for the nutrition of the tissues. We further saw that the

moment at which these elements were appropriated by the contagium, was that at which they were normally taken up by the tissues themselves; and that the nutritive changes which normally result in the formation of tissue, were well advanced before this abnormal agency stepped in to prevent their completion.

Secondly, when inquiring into the cause of the increased elimination of nitrogen, we saw that the process of nutrition consisted of retrograde, as well as of constructive changes; and we further saw, that the retrogressive and constructive steps progressed *pari passu*, and were at any given moment, equally far advanced, so that, when the changes which normally result in the formation of organ albumen from the constructive store albumen, were interrupted by the action of the contagium, those which normally result in the formation of retrogressive from the organ albumen, were in full swing. As nothing interferes with the completion of the retrograde changes, the formation of urea continues as in health.

Thirdly, when inquiring into the cause of the increased frequency of the circulation, we found that it resulted from the increased demand for nutrient material consequent on the propagation of the contagium in the tissues, and the consumption by it of the nitrogen and water destined for their nutrition.

From the propagation of the contagium there thus result (1) an increase in the quantity of blood sent to the tissues, and (2) a corresponding increase in their retrograde metamorphosis. The propagation of the contagium thus becomes the cause of the increased consumption of tissue; which, in its turn, gives rise to the præternatural heat. The propagation of the contagium is, therefore, the ultimate cause of the *calor praeter naturam*.

The increased tissue metamorphosis thus produced is confined to no particular organ, but takes place in all the organs and tissues of the body: wherever blood flows, and wherever nitrogen

and water are required, there the contagium appropriates these elements, and there, there is produced that increased tissue metamorphosis which we have seen to result from the changes to which the propagation of the contagium gives rise.

Such being the mode of production of the increased body heat, it might be supposed that the extent of the abnormal rise of temperature would bear a direct relation to the quantity of excretory products eliminated. That there is, however, no direct relation between these two results we have already seen: but we have also seen that the quantity of the excreta eliminated cannot always be regarded as representing with accuracy the quantity formed. In many cases of fever in which the temperature is very high the amount of excreta eliminated is below the normal standard. When considering the cause of this defective elimination of urea, we saw that it was due, not to decreased formation of that substance, but to the difficulty which the kidneys experienced in getting the quantity of water necessary to its elimination. The same excessive growth of the contagium which produces the prominence of all the febrile symptoms, gives rise also to an excessive consumption of water. While it leads to great increase of tissue metamorphosis, the propagation of this large quantity of contagium produces also such a consumption of water, that the eliminating organs are deprived of the fluid which is requisite to enable them to throw off even the normal quantity of excreta. These are, therefore, retained in the system; and are believed to produce many of the more alarming symptoms which occur in severe cases of fever. This retention is believed to account for the absence of any definite relationship between the abnormal rise of temperature, as indicated by the thermometer, and the increased tissue metamorphosis, as indicated by the quantity of excreta eliminated.

But there is yet another way in which this relationship might be disturbed. If there were at work in the system any other

agency capable of producing elevation of temperature, it is evident that the body heat might thus be raised, without a corresponding increase of tissue metamorphosis. And there is some evidence to show that, in the eruptive fevers, an agency does operate which may have some effect in thus elevating the temperature.

The poison whose propagation in the system is the ultimate cause of all the phenomena of the eruptive fevers, is a parasite, requiring a special nidus for its development. This nidus is the seat of the local lesion: and in it there takes place an action peculiar to the locality. The contagium particles consume nitrogen and water all over the body; but in the nidus they do something more. When considering the nature of these local lesions, we shall see that they essentially consist in hyperæmia of the affected part; and that there takes place in their seat an action which takes place nowhere else, which is essential to the propagation of the contagium, and which corresponds to the process of fecundation in plants and animals. Now this is a process which, in animals, is accompanied by increased afflux of blood to, and increased temperature of, the part in which the action takes place; and in some plants is accompanied by a distinct elevation of temperature. Under these circumstances, there is nothing improbable in the supposition, that the fecundation of the organisms with which we are now dealing, may be accompanied by an elevation of temperature analogous to that which occurs under similar circumstances in the case of other organisms; and that some of the increased body heat of the eruptive fevers, may be due to this cause.

The exact influence of such an agency it is impossible to calculate. It would, of course, be greatest in cases in which the contagium particles were most abundantly reproduced; and in which the local lesion was most marked. But these are also the cases in which the other agencies which produce the phenomena of fever are also most operative. While recognising

the possibility of its existence, we cannot determine the extent to which this agency would operate. The existence of such a possible cause of increased body heat might, however, be another reason why 'the rise of temperature theoretically due to increased tissue change, is not enough to account for the elevation of temperature in each case separately.'

Such is the explanation which the Germ Theory offers of the mode of production of the most prominent and essential phenomena of the eruptive fevers. In consistent completeness, and in freedom from the uncertainties of conjecture and surmise, it surpasses any theory of fever hitherto advanced.

But to explain the essential phenomena of the febrile state is not enough. There are other phenomena and changes, which are more or less constantly observed in this condition; and which, though not regarded as essential, are sufficiently constant in their occurrence to make it incumbent upon us to consider their causation too; and to apply to their explanation the theory which we have found capable of explaining those whose co-existence constitutes the condition to which we apply the term 'Pyrexia.'

These phenomena may be considered under the following heads:—

1. The nervous symptoms.
2. Typhoid symptoms.
3. The mode of death.
4. The changes noted after death.
5. Treatment.

We shall take them in the order in which they are enumerated.

CHAPTER XIV.

THE NERVOUS SYMPTOMS OF FEVER.

To changes occurring in the nervous centres, Virchow ascribes a primary influence in the production of fever. That the nervous system is somehow profoundly involved, there can be no doubt. Symptoms referable thereto, occupy a prominent place in an accurate description of a case of fever. But Virchow's hypothesis that alterations in the nervous system are the 'immediate cause' of the fever, seems to me to attribute to that system an action which there is no proof that it exercises. That the nervous system exercises a powerful influence in the maintenance of the normal temperature, there can be no doubt: that, as a consequence of lesion in certain parts of that system, the normal range may be very greatly altered, is equally true. But the conditions with which we have to deal in the eruptive fevers, are altogether peculiar, and present, besides the increased body heat, no analogy with those cases in which rise of temperature is due to definite lesion of the nervous centres. In these latter, there is the definite lesion to account for the change: but, in the specific fevers, there is nothing of the kind. Beyond the existence of nervous symptoms during life, there is, indeed, nothing to indicate that the nervous system is seriously involved. After death there can, as a rule, be found no lesion competent to produce the

symptoms noted in life. The nervous centres are practically unaltered; and, even in cases in which nervous symptoms were most marked, show, as a rule, no trace of lesion.

But even the adoption of Virchow's hypothesis, would not better our position: for it would still remain for us to say, why alterations take place in the nervous system; and that fresh difficulty would have to be got over, before our knowledge of the mode of production of the febrile state could be regarded as satisfactory.

Virchow has, in short, failed to recognise the influence of the *abnormal* agency which is at work in the system in idiopathic fever, and has concentrated his attention too exclusively on the excess of *normal* action, which leads to the increased tissue metamorphosis on which his theory is founded.

It has already been shown, that this increased metamorphosis, the elevation of the temperature, and all the phenomena which he attributes to changes in the nervous system, are, directly or indirectly, the result of the propagation of the contagium in the tissues.

It remains for us to show, that to the same cause are to be attributed the nervous symptoms. These are rigors, headache, delirium, convulsions, and coma.

Rigors. The first symptom of the onset of the stage of invasion of fever, the first decided intimation of the presence of the contagium in the body, is the occurrence of a feeling of cold.

In accordance with the humoral pathology, which held sway in his time, Boerhaave ascribed the cold stage of fevers to viscidity of the blood, leading to its stagnation in the minute vessels. For a long time this doctrine was maintained by his followers. Hoffman, discarding the doctrines of the humoralists, and turning to the solids, regarded the nervous system as the seat of the mischief, and attributed the phenomena of the cold

stage to spasm of the extreme vessels, resulting from a pre-existing morbid state of the blood.

Cullen adopted, and gave popularity to, this doctrine; but attributed the spasm, not to the remote causes of the fever, but to the *vis medicatrix naturae*. 'It is, therefore, presumed that such a cold fit, and spasm, at the beginning of the fever, is a part of the operation of the vis medicatrix; but, at the same time, it seems to me probable that, during the whole course of fever, there is an atony subsisting in the extreme vessels, and that the relaxation of the spasm requires the restoring of the tone and action of these' (First lines of Practice of Physic, 'Pyrexiæ').

Recently, rigors have been attributed by Dr. Geo. Johnson to anæmia (spasm of the minute arteries) of the spinal cord.

The theory which we have to advance, is the same as that of Hoffman and Cullen, that the cold stage of fever is due to spasm of the minute arteries: it differs from theirs in attributing this spasm to a more definite and satisfactory cause.

Rigors essentially consist in a feeling of cold: this, be it remarked, is a mere feeling, for while the patient is shivering, the temperature of the body is really above the normal standard. How is this brought about? How is the feeling of cold produced? And how can such a decided sensation be accompanied by an actual rise of temperature in the part which feels cold?

When a substance having a lower temperature than the body comes in contact with any part of its surface, caloric passes from the body to this substance, producing in the former a loss of heat, and consequent sensation of cold at the point of contact. Here there are two factors at work; first, the external agent or cold body; second, the internal change produced by contact therewith. What is the nature of the latter? It is something quite apart from the ordinary sense; and Brown-

Séquard holds that there are special thermic nerves for the transmission of such impressions as those which result in the sensations of heat and cold. Be that as it may; be the mode of transmission to the nervous centres of these impressions by special nerves or not, there can be no doubt that the internal local change produced in any part of the body by contact with a cold substance, essentially consists in contraction of the minute arteries of the part in which the sensation is experienced. The contraction of these vessels, the transmission of the resulting impression to the nervous centres, and the passage back to the cold part of the resulting sensation, are so instantaneous, that no appreciable interval elapses between the application of the cold body and the resulting sensation. Nevertheless all these changes do take place.

The internal change which gives rise to the feeling of cold under ordinary circumstances essentially consists in contraction of the minute arteries of the skin; and this, in its turn, results from stimulation of the nervous apparatus which controls the movements of these vessels, the vasomotor system of nerves. The ultimate internal cause of the sensation of cold, is thus abnormal excitation of that part of the vasomotor system which excites to contraction the muscular coat of the minute arteries. Such excitement is usually due to the application of some external agent. If, however, there existed in the system any agency capable of giving rise to the same abnormal contraction of the minute arteries, it is most probable that the sensation of cold would be produced thereby, without the intervention of any external agent, and without any actual loss of temperature on the part of the body. That there is at work in the system, at the commencement of the stage of invasion of idiopathic fever, an agency capable of giving rise to unusual contraction of these vessels, and that the rigors which mark the onset of that stage are really due to such contraction, it shall be our endeavour to show.

According to the theory advanced as to the causation of fever, its essential phenomena are the necessary result of the propagation in the system of an organism which has wants and demands identical, in the main with those of the tissues, and which lays hold of the material essential for their nutrition, at the moment at which it is about to be appropriated by them. The propagation of such an organism in the tissues, necessarily leads to increased demand for blood in them, and yet to coincident diminution of the material necessary for their nutrition. There is an increased demand for blood, because the contagium particles require the same materials as the tissues; there is diminution of nutrient material, because the contagium particles appropriate what is destined for the tissues. There result from this, a quickening of the circulation through the capillaries, increased retrograde tissue change, and yet diminished formation of tissue. Such derangement of the circulation, of the whole process of nutrition, and of the normal tissue changes, cannot fail to make itself felt in that part of the nervous system which presides over the muscular elements of the minute arteries, whose duty it is to regulate the supply of blood to the tissues. These vessels, by increase or diminution of whose calibre the blood supply to a given part is increased or diminished, are accordingly excited to increased contraction, with the object of checking the abnormal haste and waste, and of bringing matters to a more natural state. Contraction of the minute arteries thus becomes the first step in the production of the stage of invasion, and symptoms referable thereto, the first subjective phenomena of fever. As the cause which gives rise to this (the propagation of the contagium) is confined to no particular part of the body, but acts with equal force wherever the blood penetrates, it follows that the resulting contraction of the minute arteries is also general. It is this general contraction of the minute arteries of the skin which gives rise to the general feeling of cold which ushers in the

febrile attack; and it is its general diffusion over the surface of the body, which imparts to this sensation the features by which it is distinguished from a similar sensation produced by external agencies. In the latter case the feeling of cold is most felt at the point of contact with the cold body; in the former it is at no point predominant. Ask a man suffering from a rigor where he feels cold, and his answer is 'all over;' he cannot point to any one part in which the sensation predominates, because the contracted state of the vessels which gives rise to the sensation, exists in an equal degree all over the body.

It is thus that we would explain the occurrence of the shiverings which mark the onset of the stage of invasion of fever. They are due to a general contraction of the minute arteries of the skin, resulting from the effort which is made to control and stay the too rapid flow of blood through the capillaries, to which the propagation of the contagium in the system gives rise.

But, if the sensation of cold which marks the onset of the stage of invasion of fever, be due to a contraction of the minute arteries similar to that which results from the application of a cold body to the surface, how comes it that this subjective phenomenon is accompanied by an actual rise of temperature in the part which feels cold? It happens thus. The contagium, at the time at which the rigor occurs, is being largely and rapidly formed in the system. According to the theory advanced as to the causation of the essential phenomena of fever, the præternatural heat which forms the most striking of these phenomena, results (in the manner already explained) from the increased tissue metamorphosis to which the propagation of the contagium indirectly gives rise. This action, of course, commences as soon as the contagium begins to be propagated. Such being the case, it follows that the quantity of contagium reproduced up to the time of the occurrence of the rigors (i. e. during the period of incubation), must have

some effect in raising the temperature; so that when the rigor occurs the feeling of cold is accompanied by an actual increase of body heat. Not, in short, till the propagation of the contagium particles has gone so far as to cause derangement of the nutrition of the tissues, increased rapidity of the capillary blood flow, increased tissue change, and *increased production of heat,* does it make its presence felt in such a way as to cause contraction of the minute arteries.

Headache. The contraction of the minute arteries is, of course, not confined to the vessels of the skin, but affects those of the whole body. We accordingly find that the feeling of cold, which ushers in the febrile attack, is accompanied by other symptoms referable to anæmia of this or that organ.

The headache, which is the most constant of these symptoms, is usually attributed, either to the action of the morbid poison on the brain, or to the circulation through it of impure blood. That it does not result from either of these agencies is sufficiently attested by the fact that the headache is most severe during the first few days of the febrile attack, and diminishes in intensity, or even altogether disappears, at a later stage, when the morbid poison is more abundant, and the impurity of the blood more marked. The true cause of the headache is to be found in anæmia of the brain resulting from contraction of the minute cerebral arteries, produced in the same way, and by the same cause, as the contraction of the same vessels in the skin and other organs of the body.

That cerebral anæmia is a frequent and potent cause of nervous symptoms, is an established fact in the pathology of nervous diseases. The headache of the early days of a febrile attack is due to this cause. The anæmia which produces it, is due to a diminution of the calibre of the minute arteries of the brain. The cause which gives rise to this (the propagation of the contagium) acts with equal force on all parts of the

organ, and first makes itself felt by producing a hastening of the blood flow through the capillaries; it declares its presence, not by a morbid action, but by an increase of a natural action. The contraction of the minute arteries to which it gives rise is, therefore, due, not to an effort to exclude a morbid agency, but to an effort to bring under control the excessive action which is going on in the tissues, and to moderate the too rapid flow through the capillaries, which the propagation of the contagium induces. The contraction of the vessels being equable, and equally distributed, it follows that the symptoms resulting therefrom are general, and in no organ necessarily predominant. Those referable to the skin and nervous system are most prominent, because these organs are more sensitive and impressionable than the organs generally, and consequently give subjective evidence of derangement in a more decided manner. But the other organs also suffer from the general contraction of the minute arteries. To anæmia of the muscles thus produced are to be ascribed the muscular tremors which, superadded to the sensation of cold, constitute true rigors. To a similarly induced contraction of the minute arteries of other parts of the body, are due other of the early symptoms of a febrile attack. Anæmia of the spinal cord thus induced causes aching in the back and limbs: contraction of the minute vessels of the heart and lungs, gives rise to the feeble pulse and oppressed breathing so commonly noted: defective supply of blood to the digestive organs, due to contraction of their minute arteries, gives rise to loss of appetite; and the general result of this generally defective supply of blood, is that undefined feeling of misery and general *malaise*, which is one of the earliest indications of commencing illness.

Anæmia of the brain we know to be a potent cause of nervous disturbance. Even violent convulsions may result from sudden and copious loss of blood; and it is a recognised fact in pathology, that the direct cause of an epileptic seizure is

frequently contraction of the minute cerebral arteries. The analogy between the condition which induces such a seizure, and that which gives rise to the headache of the early days of a febrile attack, is evidenced by the fact, that it happens occasionally in the adult, and frequently in childhood (when the nervous system is particularly active and susceptible) that the headache of the stage of invasion is replaced by well-marked convulsions. The convulsions, in such cases, are due to the same cause which gives rise to the convulsions of epilepsy, and to the headache which usually ushers in the febrile attack, cerebral anæmia resulting from contraction of the minute arteries of the brain.

After continuing for a time which varies from a few hours to as many days, the evidence of arterial contraction passes off, and a corresponding change is noted in the symptoms. The sensation of cold is replaced by a feeling of heat; depression and languor give way to restlessness; and the headache is usually replaced by other symptoms referable to deranged action of the sensorium—wandering and delirium.

Delirium is usually attributed to blood-poisoning, to the action on the nervous centres of retained excreta. That blood-poisoning is a possible cause of delirium there can be no doubt: the action of many toxic agents, and the occurrence of this symptom in cases of Bright's disease, in which there is defective elimination of excretory products, sufficiently attest this.

There are good reasons, however, for not attributing the delirium of fever to this cause alone. In the first place, this symptom is frequently found in cases in which there is being eliminated more than the normal quantity of urea, and in which there is no reason to suppose that excretory products are retained in the blood. In the second place, retention of urinary excreta is not necessarily followed by delirium. And, in the third place, there is at work another agency which affords of

the change in the nervous symptoms of fever, an explanation which is more satisfactory than that to which such change is usually attributed, and is, at the same time, more in accordance with what we have seen to be the mode of production of the other symptoms which precede the occurrence of delirium.

The headache which precedes it, we have seen, results from cerebral anæmia due, directly to contraction of the minute cerebral arteries, indirectly to the propagation of the contagium. But when headache is merged in delirium, the propagation of the contagium does not cease: on the contrary, it continues to be formed in increased quantity, and there is a corresponding and consequent increase in the capillary blood flow, and in the tissue changes. Thus we have, in an exaggerated degree, the same changes which led to contraction of the minute arteries and the consequent rigors and headache, at the onset of the stage of invasion.

What, then, is the state of these vessels, now that the feeling of cold is replaced by a sensation of heat, and the headache gives place to delirium? Does the contraction cease, while the cause which gave rise to it is in full operation? That the contraction does give way, and that the flow of blood through the capillaries is greatly increased and accelerated, after the first few days of the stage of invasion have passed, there can be no doubt; the essential phenomena of fever, subjective and objective, afford sufficient evidence of this. The patient instead of feeling cold complains of heat: instead of being pale and pinched in appearance, his face is hot and flushed; the eyes are suffused; and the previously chilled aspect of the surface of his body is replaced by as general a glow of heat; a condition which points to relaxation of, and increased flow of blood through, the minute vessels, as surely as the previously chilled aspect indicated the opposite state.

How is this change in the condition of the minute arteries brought about? It might be due to simple exhaustion, and

consequent relaxation, of the contracted fibres. Such a cause is evidently not powerless to produce (within certain limits) such a result. It is equally evident, however, that it cannot be the chief agency; for it is difficult to see how mere exhaustion could lead to the long-continued relaxation by which, in the present case, the contraction is followed. Relaxation resulting from such a cause would not be so continuous as that which obtains in fever, but would again give place to contraction as soon as the exhausted fibres had recovered their tone.

It is evident that there must be some other and more potent agency at work. Such an agency we find in the great and increasing demand for blood in the brain and other tissues, the result of the propagation in them of the contagium particles.

When considering the cause of the rapid emaciation, and of the quickened circulation of fever, we saw that the demand for blood to which the propagation of the contagium gives rise, is practically indistinguishable from that which would result from a like increase in the natural wants of the tissues. During the period of incubation, the propagation of the contagium is so slight that it causes no disturbance. By and bye, as its propagation increases, the hastening of the blood flow, and consequent increased tissue waste, produce on the vasomotor centres an impression which leads to contraction of the minute arteries (the regulators of the blood supply) and a consequent feeling of cold. This contraction, however, is powerless to stay the course of events. The contagium rapidly increases and grows in the minute structure of the tissues; and by consuming the materials required for their nutrition, causes a greatly increased demand for blood in them, a demand which continues to increase with the growth of the contagium.

But contraction of the minute arteries is incompatible with the satisfaction of such a demand. We accordingly find that, as the growth of the contagium increases, these vessels, still in the due performance of their normal function, gradually relax, and

permit of the passage to the tissues of what they so urgently call for. As the urgency of this call increases, and the circulation through the tissues becomes more rapid (as both must do as the contagium is more abundantly propagated), these vessels pass from a state of abnormal contraction, to one of abnormal relaxation. This they do not suddenly, but in a manner which bears a direct relation to the rapidity with which the contagium is reproduced. In a severe attack of fever the onset of the rigors and headache is more abrupt, their severity is greater, and their decline is less tardy, than in a mild case, in which, coming on more gradually, they do not attain the same degree of severity, and do not so speedily give place to the more advanced symptoms of the stage of maturation. Their onset is more marked in the severe case because the propagation of the contagium is more rapid, and its effects on the system more quickly produced; their decline is more rapid, because, for the same reason, the condition which causes contraction of the minute arteries, is more speedily merged in that which leads to the opposite condition of these vessels. We accordingly find that, after a few days, the chilliness and headache pass off, and are replaced, the one by a sensation of increased heat, the other by wandering and delirium. The time at which this change in the symptoms takes place, marks the period at which the abnormal contraction of the minute arteries gives rise to relaxation.

Is it, then, the increased flow of blood through the cerebral tissue which gives rise to the change in the nervous symptoms? By no means. The change which takes place is due neither to relaxation of the minute arteries, nor to any direct result of the altered condition of these vessels, but is to be ascribed to the cause which produces this relaxation. The latter results from the excessive demand for blood, consequent on the greatly increased growth of the contagium in the tissues; the former (the change in the nervous symptoms) results from the excessive consumption of the essential constituents of the blood (nitrogen

and water) by the contagium, and the consequent malnutrition of the brain tissue. Increased propagation of the contagium is thus the cause, both of the arterial relaxation, and of the coincident change in the nervous symptoms. In the production of this change there are various agencies at work, all referable to that one cause. There is increased consumption of nitrogen and water; there is a consequent hastening of the blood flow, an unusually high temperature, and diminished nutrition of brain tissue, without corresponding diminution in its retrograde changes. There is, in short, going on in the brain exactly the same action which in the muscles leads to the wasting characteristic of fever. It is obvious that the effect of such an action in the brain must be, not so much diminution of bulk (though cerebral atrophy is a recognised post-mortem result of fever) as diminution and derangement of function.

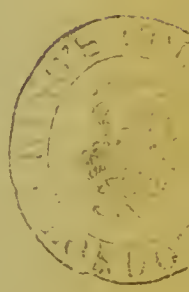
There is abundant evidence to show that malnutrition of the nervous centres is a frequent and potent cause of delirium: witness the occurrence of this symptom in case of starvation, in the debility which results from loss of blood, diarrhœa, or other exhausting discharge; and in that which accompanies many exhausting maladies, in which there is not even a suspicion of blood-poisoning.

The delirium which occurs in fever owns, as a rule, a similar causation. Blood is sent to the brain in more than normal quantity, but the organism with which it is charged seizes on the essential nutritive elements of that fluid as they are about to pass from it to the brain tissue, which is thus deprived of the elements necessary for its nutrition, and for the due performance of its functions, as effectually as if the blood flow were arrested in the minute arteries. The mode of deprivation in the two cases is, however, very different.

When due to contraction of the minute arteries, the flow of blood through the brain tissue is diminished, and there is a corresponding diminution in all the tissue changes, constructive and

retrogressive. When due to consumption by the contagium particles of the essential elements of the blood, there is increased rapidity of the circulation through the brain: but the constructive changes, which lead to the renewal of the cerebral tissue, are interfered with, and to a great extent replaced, by those which result in the formation of the protoplasm of the contagium particles. The retrograde changes, however, take place even to a greater extent than in health. We thus have, at one and the same time, defective nutrition, and increased metamorphosis of cerebral tissue. Such a state of matters must, in so delicate an organ as the brain, give rise to marked derangement of function.

Functional disturbance of the brain generally declares itself by wandering and delirium. We accordingly find, that delirium is of frequent occurrence at that stage of a febrile attack at which the nutrition of the brain is seriously interfered with in the manner indicated. In mild cases, in which comparatively little contagium is formed, the nutrition of the brain is not seriously affected, and there may be no more than a tendency to wander at night: in severe cases, in which there is a large reproduction of the contagium, greatly impaired nutrition, and increased cerebral waste, the delirium is constant, and often violent. The ultimate cause of all these symptoms, is the propagation of the contagium.



Convulsions. These occur at two different stages of idiopathic fever, (1) at its commencement, and (2) at its height.

(1) The convulsions of the stage of invasion are almost peculiar to childhood, and generally pass off without bad effects. In childhood the nervous system is particularly delicate and susceptible, and consequently suffers more severely than that of the adult from any disturbing cause. When considering the cause of the rigors and headache which usually usher in the stage of invasion, we found that these were due to anæmia, resulting from contraction

of the minute arteries of the skin and brain. The contraction of the cerebral arteries, which, in the adult, gives rise only to headache, may, in the highly suseeptible nervous system of the child, cause well-marked convulsions, which, however alarming in appearance, are rarely a source of danger; they generally pass off without bad effect so soon as the disease is fully developed, and so soon as the minute arteries pass from a state of contraction to one of relaxation. The convulsions of the stage of invasion, instead of being (as is usually supposed) the direct result of the action on the brain of a morbid poison, are really due to cerebral anæmia, similar in character to that which, in the adult, gives rise only to headache, lassitude, and *malaise*.

(2) The convulsions of the fully developed disease are much more serious, and form one of the gravest complications of idiopathic fever. They are generally regarded as of uræmic origin, as being due to the action on the nervous centres of retained excretory products, chiefly urea. The reasons for this belief are, (*a*) that in cases with such marked head symptoms, there is defective elimination of urea; (*b*) that in such cases the blood and other fluids have frequently been found to contain an excess of that substance; (*c*) that the urine in such cases is not only scanty, but is nearly always albuminous; (*d*) that the kidneys of those who die of convulsions generally present morbid appearances; and (*e*) that there is no other cause competent to produce such a result.

Of the fact that there is almost, if not quite, invariably, retention of excretory products (chiefly urea) in cases in which convulsions occur, there can be no doubt. The question which we have to consider is the connexion which exists between this state of the blood, and the nervous symptoms.

As already stated, the view generally held is that the retained excreta exercise a direct toxic action on the nervous centres; and that the nervous symptoms are due to such action. The reasons for this belief have just been given.

But there are difficulties in the way of accepting this view of the matter. In the first place, it is to be noted, that urea may exist in excess in the blood, and may be injected into the circulation, without producing disturbance of the nervous centres. Impressed with the strength of this objection, Frerichs[1] advanced the hypothesis that the real toxic agent is carbonate of ammonia. Rosenstein[2] supports this view. Oppler[3], on the other hand, believes that the real toxic agent is neither urea, nor carbonate of ammonia, but simply increased metamorphosis of the central organs of the nervous system. This view has much to commend it, but does not probably express the whole truth.

In its ultimate bearing, the opinion of Frerichs differs very little from that which was generally held before it was advanced; and it is open to the same objections. The pathological question which presents itself for our consideration, is not whether excess of this or that product of tissue metamorphosis may give rise to serious nervous symptoms; but whether *any* product of such metamorphosis is the cause of the disturbance with which we have to deal.

We believe that the view generally held (that the nervous symptoms are due to the direct toxic action on the nervous centres of some direct or indirect product of tissue metamorphosis) is an erroneous one. The reasons for this belief are:—

(1) That the products which are supposed to produce this toxic action, may accumulate, and be injected into, the circulation, without producing disturbance of the nervous centres: (2) that nervous symptoms are not peculiar to cases in which excreta are retained; but are more or less observed in all cases of fever; and, therefore, probably result from some cause which operates in all cases: (3) that there is in operation, during the course of the eruptive fevers, an agency, whose competence

[1] Die Brightsche Nierenkrankheit. 1851.
[2] Virchow's Arch. 1873. Bd. lvi. Heft 3.
[3] Virchow's Arch. 1861. Bd. xxi. Heft 3.

to produce serious disturbance of the nervous centres, is undoubted.

Into the nature and mode of action of this agency we have now to inquire. We shall find that it is the same cause as that to which all the phenomena which have hitherto come under observation have been attributed.

We have already seen that the blood-impurity, to which the nervous symptoms are ascribed, results mainly from defective action of the kidneys, consequent on the consumption by the contagium particles of the water which these organs require for the due performance of their eliminating function. We have further seen that the delirium which precedes the occurrence of convulsions is due to serious derangement of the nutrition of the brain, also resulting from the propagation of the contagium.

Cases in which convulsions occur are, *caeteris paribus*, more severe than those in which there is only delirium. Their greater severity is due to a larger propagation of contagium particles. It is evident, therefore, that the symptoms which they present may be due to an exaggerated degree of the same cause which gives rise to the less prominent symptoms of milder cases; that, in short, the disturbance in the cerebral circulation and nutrition which, in an ordinary case, suffices only to cause delirium, may, in a severe one, be sufficiently great to induce convulsions.

The severity of an attack of fever is directly as the quantity of contagium produced. When little is formed, there is little interference with the nutrition of the brain, and the nervous symptoms are correspondingly slight: when much is produced, there is marked impairment of its nutrition, and delirium is constant, and even violent: when the contagium is produced in excessive quantity, there is a corresponding interference with the nutritive changes in the brain, and a proportionate increase in the violence of the nervous symptoms, which may

even culminate in well-marked convulsions. The convulsions, then, which occasionally complicate the advanced stages of idiopathic fever, may be due to an excess of the same cause which gives rise to the delirium of ordinary cases. This latter results from malnutrition of the brain consequent (*a*) on the consumption by the contagium of the materials requisite for its nutrition, and (*b*) on the continuance in more than normal degree of those retrograde changes which result in the formation from the cerebral tissue of excretory products.

But this is not the complete history of the pathology of convulsions. We have already seen that the same cause to which we now ascribe an important part in the production of serious cerebral symptoms, also produces serious interference with the eliminating action of the kidneys: so that, coincidently with increased formation, there is decreased elimination, and consequent retention, of excretory products.

Now what is the effect of all this? and what part does such retention play in the production of those alarming nervous symptoms in connexion with which it is chiefly noted? To assert that the retention in the blood of excretory products does not cause disturbance, would be to run counter to all clinical experience and observation. We believe that such products do materially aid in the production of the nervous symptoms noted in connexion with their retention in the blood; but that the part which they play is not primary, but secondary to, and adjuvant of, that played by the agency to which we have just ascribed the delirium. In other words, retained excreta do not produce convulsions in fever by a direct toxic action on the nervous centres: they merely aid in the production of such symptoms by increasing the already existing malnutrition of these centres.

The mode in which they do so must now be explained.

The process of nutrition consists, as we have already seen, of two steps—a constructive, and a retrogressive: these advance

pari passu, and are mutually dependent; neither ever being ahead of the other. Now it is evident that the presence in the blood of an extraneous and abnormal agency, may diminish its nutrient properties to a degree which is directly as the extent to which this abnormal agency exists. The more the retrogressive products accumulate in the blood, the smaller is likely to be the relative proportion of constructive ingredients in a given quantity of that fluid. In this way the presence in the blood of retained excreta, may diminish its nutrient properties, and so lead to direct interference with the constructive nutritive changes: but such is not their principal action.

It is chiefly by producing interference with the retrogressive changes (and so indirectly with the constructive) that retention of excretory products aids in the production of those alarming nervous symptoms, whose causation we are now considering. These retrogressive changes consist in the separation from the tissues of their worn out material. Now, if the blood be unduly loaded with these excretory products, it is but reasonable to suppose that the interchange of material, which takes place between the tissues and the blood (and which constitutes the process of nutrition) will be, to some extent, hindered; the presence in the blood of an excess of the products of tissue metamorphosis, being, by the ordinary laws of diffusion, a bar to their continued free passage back into it, and, consequently, a bar to the due nutrition of the tissues.

To put it otherwise. Defective elimination by the kidneys leads to retention of excretory products: retention of excretory products leads to defective retrograde tissue change: the tissues, not throwing off their old and worn out material, are unable to take up new: the whole process of nutrition is thus deranged from behind forwards; and that, too, at a time when, by the direct action of the contagium on the liquor sanguinis, it is being seriously disturbed from before backwards. The candle,

in short, is being burnt at both ends, and with the usual result of such an operation. It is to this twofold interference with the nutrition of the brain tissue, that we have to look for an explanation of those alarming nervous symptoms, which are noted in cases in which the febrile symptoms run high, and in which there is marked diminution in the quantity of excreta eliminated.

The constructive changes are interfered with, because the constructive materials are deficient; and the retrogressive changes are interfered with, because excess of excreta in the blood, renders their continuance in due force impossible. Let us consider this latter point a little more in detail.

Retained excreta are generally supposed to exercise a direct poisonous action on the nervous centres, and different opinions have been advanced as to the real toxic agent. But there is, as we have seen, no proof that any product of retrograde tissue metamorphosis, direct or indirect, is capable of exercising such an action. They are believed to do so, because their retention in any quantity is followed by uræmic symptoms.

The way in which they act in the production of these symptoms, is quite different from that which is generally held to be their mode of action, and is readily explained, and illustrated, by what occurs when an animal is placed in an atmosphere of carbonic acid. An animal placed in such an atmosphere speedily dies asphyxiated; but it is not killed by any direct poisonous action of that atmosphere: it dies because, by the ordinary laws of diffusion, carbonic acid cannot be eliminated from the system in such an atmosphere.

Retention of excretory products in the blood, acts on the tissue respiration, in the same way as an atmosphere of carbonic acid acts on the pulmonary. The excreta which are in the blood, exercise no direct toxic action on any tissue; they simply put a stop to the tissue respiration: they are as effectual a bar to the passage back into the circulation of the products of

tissue metamorphosis, as an atmosphere of carbonic acid is to the passage outwards of that gas from the system. The more they accumulate in the circulation, the greater will be the interference with the tissue changes, and the more marked the symptoms produced. All the symptoms thus induced, must be attributed to interference with the process of nutrition. The organ which suffers most from any such interference, is the brain. It is so delicate, and so active an organ, and requires so large a supply of blood, that any general interference with the process of nutrition, is almost certain to declare itself primarily, and chiefly, by symptoms of cerebral disturbance. In accordance with this, we find that such interference with the process of nutrition, as results from the retention in the blood of excretory products, declares itself by nervous symptoms, headache, giddiness, delirium, convulsions, and coma.

The same symptoms may be induced by defective supply of the nutrient fluid. No matter whether the nutrition of the brain be interfered with from before backwards, or from behind forwards, it declares itself by like symptoms.

By uræmia, therefore, we understand a condition in which nutrition is interfered with from behind forwards; a condition, in short, of tissue-asphyxiation. And by uræmic symptoms we understand those nervous symptoms which must result from such asphyxiation of the cerebral tissue.

Coma. It is evident that if the cause which gives rise to delirium and convulsions, be of sufficiently long duration, or exist in a sufficiently marked degree, it must ere long prove fatal. When such is the case, death is brought about mainly by coma. This condition may, of course, exist in a more or less marked degree: the comatose symptoms may come on gradually, may be comparatively slight, and the patient may all through the attack be capable of being roused to a certain extent: from such a state of partial coma, recovery is

common. But when the coma is profound, and (preceded or not by convulsions) comes on rapidly, the case generally proves fatal.

Post-mortem examination of cases which prove fatal in this way, discovers no constant local lesion, or change in the intra-cranial contents, competent to the production of such a result. There may in some cases be an appearance of congestion of the pia mater, or rather more than the usual quantity of subarachnoid fluid, with some degree of cerebral atrophy; but these appearances are far from general, and are never so marked as of themselves to offer a sufficient explanation, either of the nervous symptoms noted during life, or of the occurrence of death. It is to uræmia, to the retention in the blood, and action on the brain, of the products of tissue metamorphosis that death is attributed. The true cause of the coma we believe to be that which has been offered in explanation of the occurrence of the delirium and convulsions, which so often usher it in—malnutrition of the brain, induced in the manner just explained in the case of convulsions.

That there is at work in the system an agency competent to the production of such a condition has, I think, been sufficiently shown. That anæmia of the brain is competent to the production of such symptoms as those whose causation we have been investigating there is no doubt. To what other cause can be attributed the convulsions, and even profound coma, which may follow the sudden diminution of the blood supply to the brain, consequent on compression of the carotids? To what else are to be ascribed the same symptoms occurring as a consequence of profuse hæmorrhage? And how otherwise, than by defective nutrition of the nervous centres, can we account for the occurrence of like symptoms in exhausting diseases such as diarrhœa, (especially in children with their susceptible nervous systems), and in that more slowly induced state of exhaustion which results from defective supply of food, or from actual starvation?

The most undoubted and most potent cause of such head symptoms as present themselves in the course of idiopathic fever is defective nutrition of the nervous centres. No matter how this defective nutrition is brought about; be it by compression of the large, or contraction of the minute, arteries; be it by loss of blood, or exhausting diarrhœa; be it by the cutting off at the threshold of the system of the materials requisite to the formation of blood, or by the consumption of the nutrient ingredients of that fluid by some foreign agency, while circulating through the system,—by whichever cause produced, the result is the same, so far as the nutrition of the nervous centres is concerned; it is the same also so far as concerns the symptoms by which this malnutrition of the nervous centres declares itself. These symptoms are chiefly delirium, convulsions, and coma. The degree in which these occur depends partly on the nervous constitution of the individual, and partly (and in most cases chiefly) on the extent of the malnutrition from which the nervous centres suffer, and on the rapidity with which this malnutrition is developed.

In children, and in adults of delicate nervous constitution, serious head symptoms are induced by causes which produce comparatively slight effects on the nervous systems of more robust individuals: witness the occasional occurrence of convulsions, instead of only rigors and headache, at the onset of an inflammatory, or febrile attack—the tendency to the development of the so-called hydrocephaloid disease in children as the result of exhausting diarrhœa—and the readiness with which serious head symptoms are developed in those of insane or epileptic parentage.

The constitution of the individual, then, is an important factor in the production of serious nervous symptoms in some cases in which their exciting cause is malnutrition of the nervous centres. The extent of this malnutrition and the rapidity with which it is induced are important factors in all.

In other words, the more complete and the more rapid the production of the anæmic condition of the nervous centres, the more marked the nervous symptoms. In anæmia, (or more correctly speaking spanæmia) of the brain, resulting from a slowly acting cause, such as improper and insufficient food, diarrhœa or other exhausting discharge, the head symptoms are slowly induced, and pass through the various stages of listlessness, languor, irritability, restlessness, mental torpor, and confusion, up to a state of wandering and delirium, from which the sufferer may gradually lapse into a state of more or less complete coma: the gradual development of the nervous symptoms coinciding with the slow production of the spanæmia. In the rapidly induced anæmia which results from profuse hæmorrhage, from sudden compression of the carotids, or from sudden spasm of the minute arteries of the brain, there is no time for the development of the slighter symptoms of defective nutrition which result from mere spanæmia: the deprivation of blood is so complete and so rapidly produced, and the consequent disturbance of the nervous centres so great, that it at once gives rise to well-marked convulsions and coma. So it is with the nervous symptoms of fever. These, we have seen, are due to impaired nutrition of the brain, resulting from the action of the contagium. The extent to which the brain is deprived of its nutriment, and the extent to which this deprivation declares itself in nervous symptoms, depends on the amount of contagium produced. When comparatively little is produced, there is a correspondingly slight interference with the nutrition of the brain, and the symptoms resulting therefrom are also slight. When there is a great and rapid propagation of contagium, there is an equally great and rapid deterioration of the nutrient fluid, a corresponding interference with the nutrition of the brain, and a consequently rapid development of serious nervous symptoms. Hence it is, that in mild cases of fever, in which

comparatively little contagium is reproduced, the participation of the nervous system in the general disturbance declares itself only by slight wandering; while in severe cases, in which there is a large reproduction of contagium particles, it declares itself by violent delirium, convulsions, and coma.

That there is during the course of the febrile attack very serious impairment of the nutrition of the brain is further evidenced by the mental, as well as bodily, state of the patient during the early weeks of convalescence. The mental faculties are indeed generally restored in a few days; but there is for a time, which varies according to the severity and duration of the febrile attack, a degree of listlessness and incapacity for mental effort, and an excitability of the emotional faculties, which sufficiently indicate that the brain has suffered seriously during the continuance of the fever. Sometimes the indications of cerebral weakness are very marked, and the patient may, for weeks, say and do things, which, but for the preceding febrile attack, would be regarded as evidence of insanity.

There is too a form of post-febrile delirium, to which Graves first prominently directed attention, which comes on after the patient has been convalescing satisfactorily for some days. While all is apparently going on well, the patient suddenly, and often without apparent cause, becomes violently delirious. This state generally continues for a few days, and then passes off: but it may persist for weeks; and Murchison alludes to two cases convalescent from typhus in which the maniacal excitement was so great, and so lasting, as to require temporary restraint in a lunatic asylum. This form of delirium is anæmic in nature. 'There is no evidence that either the fatuity or the maniacal attacks depend on softening or inflammation of the brain or membranes; they are attended not by fever or headache, but by anæmia and nervous depression, and are therefore benefited by sedatives and stimulants; and they are chiefly observed in cases where the primary fever has been characterized by great

and protracted delirium, and where there has no doubt been an unusual degree of cerebral atrophy' (Murchison op. cit. 2nd ed. p. 205). They occur chiefly in those cases in which there has been great and protracted delirium during the primary attack, because such delirium occurs only in cases in which there is a large reproduction of contagium particles, and a correspondingly great interference with the nutrition of the brain.

The propagation of the contagium in the system gives rise, in the brain, to exactly the same effect which it produces on the muscles; allowance being made for such differences as must result from the difference in the nature and function of the brain and muscular system. In both there is produced a serious amount of malnutrition, from which neither recovers for a considerable time; which in the muscles gives rise to weakness, and loss of bulk; and in the brain to weakness, and impairment of function, and such atrophy of the organ as is frequently found in fatal cases.

It is thus evident that all the nervous symptoms which occur in idiopathic fever, the rigor which ushers it in, as well as the coma which terminates it, and the mental weakness which follows it; the headache of the mild case, and the violent convulsions of the severe one, are all ultimately due to one cause, defective nutrition of the nervous centres, the more or less direct result of the propagation in the system of the contagium particles.

That one cause should be capable of affording a reasonable explanation of phenomena so varied, is a strong argument in favour of its being the true agency which leads to their production. And the probability of its being so is greatly enhanced by the fact that this cause is not only operative, but is the primary agent, in the production of the phenomena of every case of fever.

Of the other agencies to which these phenomena have been attributed not one is so constant in its operation, or so capable of giving rise to such varied phenomena.

Retention of excretory products is regarded by many as an adequate cause of the marked nervous symptoms by which such retention is frequently accompanied. That this is not the sole cause of their occurrence we have seen good reason to believe.

But granting for a moment the competence of the retention of excreta to produce the nervous symptoms of fever, how, on this view, are we to explain the occurrence of those nervous symptoms which precede such retention? And is it in the least degree probable that such an agency, acting by a direct toxic action on the brain, and being in operation for only a few days, could give rise either to such decided evidence of cerebral inanition and debility as we find persisting, sometimes for weeks after this cause has ceased to operate, or to such cerebral atrophy as is noted in some fatal cases? The inadequacy of a temporary and transient retention of excreta to produce such results is evident. Nothing could produce them except an agency which is capable of causing rapid and extensive malnutrition of the nervous centres. Its operation must be rapid, because no slowly-acting cause could develop, so quickly as we find they spring up, the symptoms with which we have to deal: it must be extensive, because no partially acting cause could give rise to such general disturbance as presents itself. Such an agency is present and operating in every case of fever. That agent is the contagium, to whose propagation in the system the fever is due. Its competence to produce, more or less directly, all the phenomena with which we have to deal has been shown. Fever, as formerly said, is not a distinct entity, but a collection of separate and individual phenomena, the occurrence of which at the same time in the system constitutes the febrile state. That which causes the fever necessarily causes the individual phenomena which go to constitute that state. The nervous symptoms whose causation we have been investigating are not extraneous phenomena grafted on to an attack of fever; they are part and parcel of the

attack during whose course they occur; they are the evidence of the severity of the seizure, and are as much a characteristic feature of the case as are the high temperature, and scanty elimination of urine, which are noted at the same time. Such being the case, it is but reasonable to attribute their occurrence to the same cause which, we have seen, gives rise to the so-called essential phenomena of the febrile state. The competence of this agency to produce them has, we think, been fully shown [4].

[4] The great argument in favour of the view which regards the nervous symptoms of fever as of uræmic origin, and the chief objection to that which we have advanced as to their causation, is the occurrence of similar symptoms in advanced cases of Bright's disease.

Here it is found that the kidney disease leads to the retention in the blood of excretory products. Following, and evidently consequent on, such retention, serious nervous symptoms are developed. Naturally, the retention of the excreta is looked upon as the cause of the nervous symptoms: and so, no doubt, it is: but that is a bald and misleading statement of the facts of the case. There can be no question that retained excreta do produce disturbance of the nervous centres. The point of discussion is not their competence to do so, but the manner in which they act in the production of such symptoms.

Different views have been advanced in explanation of their mode of action. The demonstration by Christison (1829) of the presence of excess of urea in the fluids of the bodies of those who died of Bright's disease, led to the belief that the nervous symptoms which preceded death were due to the direct toxic action on the nervous centres of retained urea. It was found in time, however, that urea might be retained in, and even injected into, the circulation without producing disturbance of the nervous centres. Impressed with this fact, Frerichs advanced the view, that the real toxic agent was carbonate of ammonia, produced by decomposition of urea in the blood. But the same objections have been urged against the capacity of carbonate of ammonia to produce such a result, which were previously urged against urea. Oppler recognising the force of these objections, but still impressed with the view that retained excreta are somehow the cause of the nervous symptoms, attributes them to the retention in the nervous centres of the products of their own waste.

Owen Rees thought that some other cause than retention of excretory products, probably a watery condition of the blood, had something to do with their production.

Traube very ingeniously elaborated this view. He believed that the impoverished state of the blood, and the coincident occurrence of cardiac hypertrophy, led to the exudation of water through the coats of the minute vessels; that there was thus produced œdema of the central substance; that the capillaries and veins were pressed upon by this effusion; and that this pressure gave rise to anæmia of the brain. To this anæmic condition of the brain he ascribed the nervous

symptoms. The great objection to this ingenious theory is that nervous symptoms are most common in that form of Bright's disease (the contracting granular kidney) in which œdema is least apt to occur.

Rommelære believed that the uræmic symptoms resulted from a combination of different causes, retention of excretory products, retention of water, and consequent blood impoverishment, and increased tension of blood vessels.

Dr. George Johnson 'assumes it to be indisputable that the nervous symptoms are the result of the blood being deteriorated, partly by diminution of its normal constituents, but chiefly by retention and accumulation of urinary excreta. There are two ways in which it is probable that the brain and its functions may be injuriously affected by this blood deterioration. First, the cerebral tissues, fed with poor and poisoned blood, may have their nutrition impaired, and may in various parts undergo structural changes, analogous to those which are often demonstrable in the texture of the retina. Second, it is probable that some of the cerebral symptoms, more especially those which come on and pass away suddenly, are directly due to temporary interruptions or hindrances of the circulation through certain regions of the brain, consequent on excessive contraction of the minute arteries . . . . . It is in a high degree probable that uræmic vertigo, amaurosis, delirium, convulsions, and even coma, may in some cases be explained by partial or general cerebral anæmia, the result of excessive arterial contraction excited by the presence of impure blood.'

There can, we think, be little doubt that this is the true explanation of the mode of production of the nervous symptoms of Bright's disease. A consideration of the cases in which such symptoms are most apt to occur, will render this more evident.

The form of Bright's disease in which nervous symptoms are chiefly noted, is that which is associated with a small, red, granular kidney. The exact pathagonesis of this form of kidney disease has been matter of much discussion. On one point, however, all are agreed: the malady is not a local disease of the kidney, but a constitutional affection, whose most marked local manifestation is the production of renal mischief. There is decided impairment of health before, generally for some considerable time before, there is evidence of kidney disease: the characteristic feature of this constitutional derangement is an impoverished state of the blood. 'There is no disease of a chronic nature which so closely approaches hæmorrhage in its power of impoverishing the red particles of the blood' (Christison).

There is thus in operation, in that form of Bright's disease in which nervous symptoms are most common, the cause which of all others is most competent to produce functional disturbance of the nervous centres—cerebral anæmia. As the general constitutional derangement advances, the impoverished state of the blood becomes more marked: the renal disease likewise advances; and the already existing blood deterioration is increased by the retention in that fluid of excretory products. We thus have the process of nutrition interfered with in a twofold manner, just as we found it to be in bad cases of fever. There is a constitutional anæmic condition, producing defective nutrition of the nervous centres: and there is the presence in the blood of retained excreta, interfering with, and impeding, the normal retrogressive changes.

The other form of Bright's disease in which serious nervous symptoms are

most apt to occur is the acute inflammatory form, occurring either *per se*, or grafted on to one of the chronic forms. Serious nervous symptoms are apt to occur under such circumstances because, as a consequence of the renal mischief, there is produced a sudden and rapid accumulation of excretory products in the blood, and because such rapid accumulation is apt, in the manner explained by Dr. Johnson, to cause sudden spasm of the minute arteries of the brain. Here, too, the nervous symptoms are due to cerebral anæmia, rather than to any direct toxic action on the nervous centres of retained excreta.

A careful consideration of the phenomena which precede and accompany the development of the nervous symptoms of Bright's disease thus leads to the conclusion that they are due, not to any direct irritant action on the nervous centres of retained excreta, but to faulty nutrition of these centres—the same cause to which we have ascribed the occurrence of like symptoms occurring in the course of the eruptive fevers.

The typhoid symptoms occasionally noted in advanced cases of Bright's disease own a similar causation.

Retained excreta do not act directly on the brain substance; they simply render impossible the continuance of the normal tissue changes. Their presence in the blood puts a stop to the changes which normally take place in the tissues, in the same way, and as effectually, as an atmosphere of carbonic puts a stop to the changes which normally take place in the lungs.

CHAPTER XV.

TYPHOID SYMPTOMS.

The sunken and depressed aspect of the patient, the moist clammy skin, the listless expressionless eye, the sordes-coated teeth and lips, the dry brown tongue, the feeble flickering pulse, the twitchings and subsultus, the low muttering delirium, the involuntary evacuations, sufficiently indicate the adynamic nature of that aggregate of phenomena to which the term 'typhoid state' is applied. This state is common to the advanced stages of various diseases; and in all it is attributed to one cause, retention in the system of excretory products. Such retention is assumed to be the cause of the typhoid symptoms in fever, because almost identical symptoms are noted in advanced cases of renal disease; because in fever, as in renal disease, there is, when such symptoms occur, excess of urea in the blood; and (perhaps chiefly) because no other explanation is forthcoming.

We shall endeavour to give of these symptoms as they present themselves in the eruptive fevers an explanation which accords with that already given of all the other phenomena of the febrile state. The latter, we have seen, are all directly or indirectly due to the propagation of the contagium, and the defective nutrition of the various organs (and especially of the nervous centres) to which such propagation gives rise; the severity of the attack, and the prominence of the various symptoms, depending mainly on the quantity of contagium produced. To say that a fever patient is suffering from typhoid symptoms,

is merely a short and convenient way of saying that there are great disturbance and depression of the nervous centres, as indicated by the muttering delirium, the twitchings of the muscles, the incontinence of urine, and the generally sunken and depressed aspect; and that there is threatened failure of the heart's action, as indicated by the feeble flickering pulse, the almost, or altogether, imperceptible cardiac impulse, and scarcely audible first sound; that, in short, the patient is in imminent danger, and that death is threatened in a twofold manner, by coma and by asthenia—by failure of cerebral, and by failure of cardiac, action.

Coma occurring in fever, we have already seen good reason to believe, is, like the delirium and occasional convulsions which precede and lead up to it, of anæmic origin, due mainly to defective nutrition of the nervous centres. The coma which supervenes in the typhoid state is due to the same cause; but presents, in its development, certain differences, due to the coexistence of other indications of danger to which we shall for a moment direct attention.

When death in fever is threatened by coma alone—when the danger is from the head symptoms, and not from failure of the cardiac action, or from pulmonary or other complication, the symptoms of coma are preceded by marked, and often violent, delirium, which may even culminate in well marked convulsions. Be it particularly noted, however, that, with such symptoms, there are not the same indications of intense depression which obtain in the typhoid state. Instead of being sunken and almost motionless in bed, the patient, until death is imminent, is restless, and even making efforts to get up, in which an often troublesome amount of muscular power may be displayed: delirium, instead of low and muttering, is acute and violent; the skin, instead of being moist and clammy, is hot and dry; the pulse is rapid, but wants the feeble character of the typhoid state; the heart's impulse is fairly perceptible, and there is no

threatened failure of its action. The danger is from the head symptoms, and from them alone, and, therefore, the coma is uncomplicated by other indications of danger than those referable to the nervous centres.

But in the typhoid state this is not the case. Death is threatened as much by asthenia as by coma; and it is the combination of these two different modes of dying which imparts to that state its distinctive peculiarities. The presence of asthenia is sufficiently indicated by the feeble flickering pulse, and failing cardiac action. It is the presence of this asthenia which takes from the nervous symptoms their sthenic character, and gives to the patient the sunken and depressed aspect which characterizes the typhoid state. Be the symptoms of asthenia present or absent, however, the nervous symptoms are due to one and the same cause, defective nutrition of the nervous centres, consequent (*a*) on the consumption by the contagium particles of the materials necessary to the nutrition of the brain, and (*b*) on the retention in the blood of excretory products.

Whether, then, in a bad case of fever, the patient becomes violently delirious, convulsed and comatose, or lapses into the typhoid state, would seem to depend on the absence or presence of asthenia—on the absence or presence of symptoms of threatened failure of the heart's action. To a certain extent this is true; but the statement is rather bald, and requires further explanation. We have, therefore, to consider why it is that coma seems to play a more constant part in the tragedy than does asthenia, and what is the difference between the mode of production of simple coma, and of that which occurs in combination with asthenia in the typhoid state.

To this question there is a twofold answer. In the first place, all other things being equal, the occurrence of typhoid symptoms indicates a severer attack, a larger reproduction of contagium particles, than does the occurrence of head symptoms alone; it being apparent that, always *caeteris paribus*, a larger

reproduction of contagium particles would be required to impair all the vital energics, than would be requisite to impair only those of the brain. To put it otherwise: the brain requires and receives a much larger quantity of arterial blood than any other organ of the body. Requiring so large, and so constant a supply of nutriment, it follows that the brain must, more than any other organ, suffer from such a deterioration of the nutrient fluid as that to which the propagation of the contagium gives rise. We accordingly find that symptoms referable to the nervous system, are among the earliest and most constant indications of the existence of fever. Now, if the propagation of the contagium reach, but do not exceed, the point necessary to produce the degree of cerebral malnutrition requisite to the production of comatose symptoms, we may have those symptoms developed without other or further indications of urgent danger: but if this point be exceeded, or if any cause of cardiac depression comes into play at the same time, then signs of defective action of that organ make their appearance; symptoms of asthenia are developed *pari passu* with those of coma; and we have induced that aggregate of phenomena to which the term 'typhoid state' is applied; a state which is simply one of great depression of all the vital energies; simple coma being one of great depression of only the nervous energies.

We have said that, *other things being equal*, typhoid symptoms indicate a larger reproduction of contagium particles than does the occurrence of head symptoms alone. But other things are not always equal; and it is often to some constitutional peculiarity of the individual that is due the special prominence of symptoms referable to this, or that organ. It is well known that those of delicate nervous organization, and those who, from hereditary or other predisposition, are liable to head affections, are, when seized with fever, more likely to have serious nervous symptoms than those in whom no such predisposition exists. So also, those in whom, from age or other cause, there is

defective power, or impaired vigour, of the muscular walls of the heart, are more likely to suffer seriously from asthenia, than those in whom the cardiac action is vigorous and unimpaired. Those in whom these conditions are combined; and those in whom, even without any special predisposition, the quantity of contagium produced is so great as to give rise, at one and the same time, to the requisite degree of malnutrition of the brain and heart, suffer from that combination of coma and asthenia to which the term 'typhoid state' is applied.

The typhoid symptoms of fever are, therefore, due to failure of all the vital energies, such as must result from that derangement of the whole process of nutrition to which we have seen that the propagation of the contagium in large quantities gives rise.

The uræmia by which they are accompanied, tends to make the typhoid state more marked, but is not the original cause of its occurrence. It acts here in the same way as we saw that it did in the production of the nervous symptoms, aiding the cause already in operation, and increasing the already existing depression.

CHAPTER XVI.

THE MODE OF DEATH IN FEVER.

In an uncomplicated case of idiopathic fever, death is brought about by coma, by asthenia, or by a combination of both.

That the malnutrition of the brain to which the propagation of the contagium gives rise, may be sufficiently great to produce symptoms of coma, we have already seen. That the same cause, operating on the heart, may cause asthenia, there can be no doubt: it is evident that such derangement of the process of nutrition as in the brain gives rise to coma, may, if it operate on the heart, give rise to failure of its action.

The cardiac walls require a large amount of nutriment: the blood impoverishment which results from the propagation of the contagium in the system operates on the nutrition of the heart as it does on that of the muscles and of the brain: the result of such action is weakening of the cardiac muscles, and consequent feeble cardiac action: this, if extreme, may lead to death by asthenia. The risk of such a result is increased by anything (such as age or previous disease) which tends to diminish the strength of the cardiac walls. This decreased force of the cardiac action is evidenced during life by the feeble pulse, the faint cardiac impulse, and the soft first sound; signs of an enfeeblement of the heart which, when it goes on to a fatal result, has its existence demonstrated by the changes noted in that organ after death, and to which reference will presently be made.

In an uncomplicated case of fever, death by asthenia alone

seldom occurs: there is nearly, if not quite, always more or less coma at the end. This intermingling of asthenia and coma gives rise, as we have already seen, to that combination of phenomena to which the term typhoid state is applied.

The mode of death in fever is, therefore, such as may clearly be traced back to the same cause which, we have seen, produces all the phenomena and symptoms presented by the patient prior to the onset of the signs of death. The fact that the explanation given of the mode of death, is so in accordance with that given of the mode of production of the symptoms noted during life, is corroborative evidence, both of the accuracy of that explanation, and of the truth of the theory on which it is founded.

CHAPTER XVII.

THE CHANGES NOTED AFTER DEATH.

As a rule, these are slight, and bear little relation to the severity of the symptoms noted during life. Even in those cases which present the most marked symptoms during life, and which prove fatal, apparently by the severity of such symptoms, there is found no local lesion sufficiently constant and important to give rise to such a result.

The chief post-mortem changes are those which occur in the brain and in the heart.

In the brain the chief changes noted are, (*a*) some venous congestion both of the brain, and its membranes, (*b*) some increase in the quantity of intra-cranial fluid, and (*c*) atrophy of the brain itself. None of these changes is constant; and pathologists agree that neither the amount of congestion, nor the amount of effused serum, bears any relation to the severity of the symptoms.

The congestion is most marked in cases in which there has been some obstruction to the pulmonary circulation: it is then partly due to such obstruction; but it often exists independently of such a cause, though seldom to any marked extent; it may be slight in cases which, during life, presented marked nervous symptoms.

The quantity of fluid effused into the ventricular and sub-arachnoid spaces also varies: and it has been abundantly proved

by the observations of Reid, Jenner, Jacquot, Barrallier, etc. that the nervous symptoms bear no relation to the quantity of fluid found in these localities.

It is indeed very probable that the increased quantity of serum noted in connexion with cerebral atrophy is, as Murchison remarks, 'merely thrown out to fill the space vacated by brain.' The same explanation may also, to some extent, apply to the venous congestion observed in the same cases.

The principal intra-cranial change observed in connexion with the head symptoms of fever is atrophy of the brain—diminished bulk of the cerebral substance. This, therefore, is the change for which we have chiefly to account. The cause most likely to give rise to such a change in the brain is defective nutrition of that organ—insufficient supply of the material required for its nutrition and the maintenance of its bulk. Diminished bulk of brain tissue, with increased serosity, is a recognised result of chronic wasting disease; and defective nutrition, such as occurs in these ailments, is the only recognised cause of cerebral atrophy. That this agency operates in the eruptive fevers, has already been shown. We have seen that many of the most striking phenomena of the febrile state, and notably the nervous symptoms, result from the propagation in the system of an organism which, in its growth and increase, not only consumes the material requisite to the nutrition and building up of the tissues, but causes also a coincident increase in their retrograde changes. Acting on the muscles, this agency produces the wasting which forms so prominent a feature of idiopathic fever: acting on the brain, it induces a similar condition of atrophy. The cerebral atrophy, then, which forms the chief of the intra-cranial changes noted after death from idiopathic fever, results (as might on *a priori* grounds be anticipated) from the same cause which gives rise to the nervous symptoms noted during life—defective nutrition, and increased disintegration, of the brain substance, consequent on that

disturbance of the process of nutrition to which the propagation of the contagium gives rise.

The changes which take place in the central organ of the circulation during the course of idiopathic fever have been studied chiefly in connexion with enteric and typhus fevers. They were first described by Laennec[1], and afterwards more accurately by Louis and Stokes. The most prominent of the changes noted, is a softened and friable condition of the heart, and chiefly of its left side. When very marked, and affecting the whole organ, Louis describes the heart as being 'very flaccid, so that in many cases it had no precise form, but, like a wet cloth, retained any shape into which it might happen to be placed. Its substance had very little power of cohesion, and was easily torn, or penetrated by the finger[2].' Stokes described a case in which the softening was so great that 'when the heart was grasped by the great vessels, and held with its apex pointing upwards, it fell down over the hand, covering it like the cap of a large mushroom[3].' These, of course, are extreme cases; but the observations of all pathologists show that such softening occurs to an appreciable extent in a large number of cases of idiopathic fever.

Regarding the nature of this softening there has been some difference of opinion. Laennec looked upon it as simply part of the general softening of the muscular fibres noted in cases of idiopathic fever accompanied by putridity of the blood. Louis, on the other hand, maintained that the cardiac softening was altogether peculiar, and that 'no such lesion was found in any other muscular organ, the voluntary muscles maintaining their normal consistence and colour[4].'

[1] Traité de l'auscultation méd.

[2] Louis, Recherches sur la Gastro-enterite, tome i. p. 330 (1829).

[3] Stokes on the Heart, p. 373 (1854); and Lectures on Fever, p. 222 (1874).

[4] Op. cit., tome i. p. 333.

Stokes adopted Louis' view, and pointed out the signs by which the softening could be detected during life, and the important indications as to treatment which such signs gave.

Rokitansky regards the softening as 'a mere symptomatic and simple diminution of consistence, not depending on any disturbance of texture[5].' While Murchison[6] and Joseph Bell[7] describe the fibres of the softened portion as having lost their natural striated appearance, and as undergoing granular, fatty, or waxy changes. Our own observations accord with those of Murchison and Bell.

Such is the cardiac lesion noted in many cases of idiopathic fever. It consists in a softened and friable condition of the cardiac walls; and in granular, fatty, or waxy change of the muscular fibres; and has for its most prominent symptom an enfeeblement of the cardiac power, which may be so great as to cause death by failure of the heart's action.

The chief points to be noted regarding the change which takes place in the heart are:—

1. That signs of its occurrence are not observed till the fever has been in existence for some time.
2. That the signs of cardiac feebleness, when once noted, increase with the progress of the fever.
3. That such signs are most decided in cases of a markedly typhoid type.
4. That they speedily disappear after the cessation of the fever.
5. That complications which prolong the illness after the cessation of the fever do not prevent recovery of the heart's tone.
6. That the softening noted after death is always more

[5] Pathol. Anat., Sydenham Soc. translation, vol. iv. p. 171.
[6] Murchison, op. cit., p. 257.
[7] Glasgow Med. Journ. 1860.

marked on the left than on the right side of the heart; and in the ventricles than in the auricles.

7. That it is more marked in cases which prove rapidly fatal than in those in which the fatal issue is more tardy. (Louis.)
8. That the normal striated appearance of the fibres of the softened portion is indistinct or imperceptible; and is replaced by granular, waxy, or fatty change.

Regarding the mode of production of this change in the heart different hypotheses have been advanced, but no satisfactory explanation has been given. Laennec regarded it as a putrid softening; but the inaccuracy of this view has been demonstrated. Louis advanced no explanation more definite than the hypothesis that the cause which gave rise to it was something the reverse of inflammation, 'une cause de lésions opposée à l'inflammation.' Since then, our knowledge on this point has made little advance.

The view generally adopted is that of Louis, that the change in the heart is altogether peculiar, and distinct from that which exists in the voluntary muscles. The contrary doctrine of Laennec, that the changes in the heart and muscles were similar in nature, seems to us, however, to merit more consideration than it has received. Laennec was no doubt in error when he attributed the softening to a putrid condition of the blood; but it does not follow that he erred in regarding the changes in the heart and voluntary muscles as similar in nature. He might err on one point without being wrong in all. Louis demonstrated beyond a doubt the inaccuracy of Laennec's etiology; but regarding the state of the voluntary muscles all that he said was that they were of natural consistence and colour. Now, in this there can be no doubt that Louis was in error; the voluntary muscles do not preserve their natural consistence and colour in all cases in which the heart is softened. Laennec and Stokes have both recorded

cases in which they were of soft and gluey consistence; while all those who have made frequent post-mortem examinations in cases of typhus and enteric fevers, know that the muscles often present a less than natural degree of coloration. They are frequently also darker than normal, but that is when there has been some obstruction to the pulmonary circulation.

Of late years the condition of the muscles has been inquired into with greater accuracy; and it has been demonstrated, more especially by the observations of Murchison[8] and of Zenker[9], that during the course of idiopathic fever the fibres of the voluntary muscles undergo a change (waxy, fatty, or granular) similar to that which is noted in the minute structure of the softened heart. With such a fact before us, we cannot fail to see that, to some extent, the views of Laennec were possibly more accurate than those of Louis; and that the change which takes place in the heart may, after all, be similar in nature to, and due to the same cause as, that found in the voluntary muscles.

The most marked of the changes which occur in the voluntary muscles, the loss of bulk, we have seen to be due to that cause to which have been attributed all the phenomena of the febrile state, the combined influence of defective nutrition, and increased retrograde metamorphosis—both consequent on the propagation of the contagium. Such microscopic changes as we find take place in these muscles during the course of idiopathic fever are exactly those which, occurring under other circumstances, we associate with defective nutrition of the muscular fibres. Finding them occur in fever in connexion with such a cause, we cannot fail to attribute them to this agency; more especially when we find, in the rapid wasting of the muscles, such decided evidence of its action.

The changes which take place in the voluntary muscles

[8] Murchison, op. cit., 1st edition, 1862.

[9] Zenker, Ueber die Veränderungen der willkührlichen Muskeln im Typhus abdominalis. 1864.

during the course of idiopathic fever result, then, we find good reason to believe, from defective nutrition consequent on the propagation of the contagium. Finding that the changes noted in the muscular fibres of the softened cardiac walls, are similar in nature; and knowing that the agency which produces the change in the voluntary muscles, acts on all parts of the system; it is evident that we have in that agency a possible, and (if possible) not unlikely, cause of the change which takes place in the cardiac walls.

Like all the other phenomena of idiopathic fever, the cardiac softening must result, directly or indirectly, from the action of the fever poison.

The change which takes place in the heart is essentially one of intense and rapidly induced enfeeblement. It has already been shown that the cause to which we ascribe all the phenomena of idiopathic fever, the propagation of the contagium, produces marked disturbance and even atrophy of the brain, and great wasting of, and interstitial change in, the voluntary muscles. If competent to produce these, there is no reason why it may not produce such a change as that whose causation we now investigate. We believe that such is the mode of production of the cardiac softening; that it results from coincident defective nutrition, and increased disintegration, of the muscles of the heart: the defective nutrition being due to the consumption by the contagium particles of the nitrogen and water which ought to go to build up the cardiac muscles; the increased disintegration being due to the continuance, in even an increased degree, of those changes which result in their disintegration.

But, it may be asked, if the same cause give rise to the changes in the heart and voluntary muscles, why are the results not identical? Why is the heart only softened, and not markedly diminished in bulk, as are the voluntary muscles? To understand aright the reason for this difference we must

bear in mind that, though similar in structure, the heart and voluntary muscles have very marked points of difference. We know, for instance, that the heart does continuously, and without any period of rest, an amount of work which no voluntary muscle could do for more than a short time; and that, in its innervation, formation, mode of action, and, indeed, in every respect except in the appearance of its fibres, it is essentially different from voluntary muscle. In no way is this difference better indicated than by the fact that while within the limits of health the bulk of voluntary muscles may vary much, that of the heart remains the same: it is not liable to vary except as the result of some morbid or abnormal agency. That under these circumstances the pathological changes which take place in the heart should differ from those which occur in voluntary muscles (even though both may result from a like cause) is no more than might reasonably be anticipated.

The circumstances of the heart and of the voluntary muscles are so different, that like results in each could scarcely be expected. Such rapid loss of bulk as we find take place in voluntary muscles could not occur in the heart without leading to fatal asthenia. That there should be some provision against such a result is what might be anticipated; wherein this provision consists we need not stay to consider: we know that it does exist, and that causes which, operating on the voluntary muscles, produce in them marked loss of bulk, do not necessarily have a similar effect on the heart. It need not, therefore, surprise us to find, that while the action of the fever poison causes (in the manner already explained) in the voluntary muscles granular or waxy change with loss of bulk, it produces, in the cardiac muscles, similar changes, with softening and friability of their substance.

To one point in which the condition of the heart and of the voluntary muscles in fever differs we would direct special attention. The heart acts with more than normal rapidity: the

voluntary muscles are more than normally quiescent. While there is going on in both, that deranged tissue-action to which the propagation of the contagium gives rise, the heart is called upon to do more work than natural; the voluntary muscles less.

That such a marked difference in their respective conditions, should lead to a difference in the results noted in the heart and muscles as a consequence of the fever, is what might be anticipated. Both being subjected in a like degree to the enfeebling action of the contagium, no great difference in the results noted could reasonably be expected, if the heart and voluntary muscles were in all respects similarly situated. But with such an important difference as that which has been indicated—with the heart subjected to an abnormal amount of wear and tear, in addition to those derangements of nutrition which are common to it and the voluntary muscles, it is all but inevitable that there should be noted in it an exaggerated degree of those changes which occur more or less in all striated muscular fibre, as a result of the action of the fever poison.

We accordingly find that the diminished striation, and the granular, fatty, and waxy degeneration, which constitute these changes, are more marked in the over-worked heart, than they are in the under-worked voluntary muscles. The softness and friability which form the coarser and more striking indications of the change which takes place in the fibres of the heart, are not altogether wanting in the voluntary muscles of those cases in which such change is marked in the cardiac walls: but the microscopic changes which are the essential and more accurate indications of its existence, are more constantly observed.

That the increased call which is made upon the heart, has some influence in producing the prominence of the changes observed in that organ, is evidenced by the fact that these changes are more marked in the left than in the right heart, and in the walls of the ventricles than in those of the auricles. Were they the result of any direct toxic action of the fever

poison, or of a putrid condition of the blood, the softening would be general, and equally marked in all the fibres of the heart. The only reason that can be assigned for the greater involvement of the ventricles than of the auricles, and of the left than the right ventricle, is that the ventricles do harder work than the auricles, and the left ventricle harder work than the right.

Those striated fibres which have most work to do, suffer most from the combined influence of defective nutrition and increased disintegration; and give the most decided evidence of so suffering. Hence the walls of the left ventricle are always more soft and friable than those of any other part of the heart: and hence also the changes which take place in striated muscular fibres during the course of idiopathic fever, are always more marked in the cardiac walls than in the voluntary muscles.

We thus find that the chief changes found in the body after death from idiopathic fever—those which occur in the brain and in the heart, are such as may clearly be traced back to the propagation of the contagium particles in the system—the same cause to which has been ascribed all the phenomena which have hitherto engaged our attention.

In the *post-mortem* changes we, therefore, find further evidence in favour of the view which regards the contagium as consisting of minute organisms; and which looks upon the propagation of such organisms as the direct, or indirect, cause of all the phenomena of idiopathic fever.

The only other *post-mortem* change which is observed with anything like constancy in the eruptive fevers, is an enlarged and hyperæmic condition of the liver, spleen, and other glands. We have seen reason to believe that one of the functions of these glands, is to form urea from the retrogressive albumen. We have seen that retrogressive albumen is formed in more than normal quantity, and that the urea-forming glands do more than their normal amount of work. The condition of these glands after death from fever, is in keeping with this view of the work done by them during the continuance of the febrile state.

CHAPTER XVIII.

TREATMENT.

The treatment of idiopathie fever is a subject on whieh the most opposite and antagonistic opinions have prevailed. At one time measures of depletion were those in which most confidence was placed. Bleeding, purgatives, and antimony, were the remedies which were supposed to be most appropriate. At the present day the opposite practice prevails; and the treatment of idiopathic fever may be said to eonsist in keeping up the patient's strength until the fever has run its course. Not to cut short the fever, but to guide the patient through it, is what the physician aims at.

Whatever view we may hold as to the propriety of the treatment adopted by our fathers, and as to the occurrence of a change of type in disease, there can be but one opinion as to the injurious influenee of depletory measures on the course of the eontinued fevers which we are ealled upon to treat now-a-days. If we were to bleed, to purge, to give antimony to, or even simply to withhold food and water from, all the eases of typhus and enteric fever which occur, there ean be no doubt that we should find the mortality from these diseases greatly increased. Clinieal experienee abundantly testifies to the faet that, in the treatment of idiopathie fever, everything is secondary to the administration of water and easily-digested food, and to the procuring of sleep. This drug may be lauded, that found useful, and a third be supposed to mitigate the severity,

or curtail the duration, of the febrile symptoms; but all medication is confessedly secondary in importance to the regular administration of milk and beef tea, an abundant supply of water, pure or in some form of diluent drink, and to the avoidance of all that is calculated to cause fatigue and excitement. In other words, we have learned from experience that when death is threatened in idiopathic fever, it is so by failure of the heart's action, or by head symptoms; and the treatment to which we have recourse, is adopted with the view of warding off these two dangers. To this position we have been led by a careful study of the phenomena of idiopathic fever as they present themselves at the bedside; and uninfluenced by any theory as to their mode of production. It is an additional argument in favour of the theory of fever which we have advanced, that it affords a sound pathological basis for that mode of treatment which clinical experience has shown to be most successful.

We have seen that, according to this theory, the symptoms referable to the heart and brain, are due to malnutrition of these organs, consequent, partly on increased disintegration, and partly on the consumption by the contagium particles of the nitrogen and water requisite for the renewal of their rapidly wasting tissues. The administration of milk, beef tea, and water, has the effect of remedying, so far as we can, the injury thus done to the tissues. Such administration simply means supplying the system with nitrogen and water, the elements which the contagium particles take from it, and the want of which leads to the most serious symptoms of fever.

The fact that the most successful way of treating idiopathic fever, consists in supplying the system with nitrogen and water, is an additional argument in favour of the theory which regards the cause of the fever as something which takes these elements from the tissues. Such an agency can only be a living organism.

Cold is an agency which has been much employed in the treatment of fever. The remedy is an old one, to which renewed attention has of late years been given. The observations of Niemeyer, Ziemssen, Liebermeister, Wilson Fox, and others, lead to the general conclusion that though the application of cold to the surface is of great value in reducing hyperpyrexia, and mitigating the severity of its attendant symptoms, it does not shorten the duration of the fever.

Such would almost certainly be the action of cold in fever induced by the propagation of millions of parasitic organisms in the tissues. The cold would reduce the temperature as a matter of course; but it could not put a stop to the propagation of the contagium, or stay the regular course of events, before the second factor was exhausted.

The only action of cold in the treatment of fever, is to reduce the temperature, and to mitigate the severity of the symptoms by which hyperpyrexia is apt to be accompanied. This very important object it does attain more certainly and more speedily than any other agency; but it does not cure, or even shorten the duration of, the fever. In the theory advanced as to the causation of the fever, we have an adequate explanation of its inability to do so.

We have now considered the various phenomena which are common to the eruptive fevers, and have found that they are all such as may reasonably be attributed to the propagation of an organism in the system.

The theory which has been advanced in explanation of these phenomena, fits into, and affords of, the facts with which we have to deal, an explanation which, for completeness and freedom from conjecture, is unequalled by that given by any theory hitherto advanced. Of the varied, and sometimes apparently contradictory, phenomena with which we have to deal, it leaves not one unexplained.

At this stage a difficulty presents itself.

The propagation of an organism in the system may explain the existence of the febrile state; but how, on this view of its occurrence, are we to explain its cessation? If all that is required for the production of the febrile state, be the propagation of an organism in the system, and if the organisms which produce this result are propagated so rapidly and so largely as has been said, why are we not all constantly in a state of fever, consequent on the propagation in our systems of the enormous number of germs which are eliminated from the bodies of those suffering from infectious fevers? And if nitrogen and water be all that is requisite for the growth of these germs, how is it that any one ever recovers from fever? Why do not the germs continue to grow and be propagated so long as these elements are to be had? And why, at the end of seven, fourteen, or twenty-one days, as the case may be, while there is still in the system abundance of these elements, do the febrile symptoms come, more or less abruptly, to an end, and the tissues again take up the elements of which they had been deprived by the contagium particles; and that, too, before these particles have been eliminated from the system?

There can be no question as to the force of these objections to the theory advanced. There is as little doubt, however, that the difficulty which they raise is more apparent than real. It is one, however, which cannot be explained by a reference to any property which the contagium possesses simply as an organism. As such we have seen that it is competent to produce the phenomena which have hitherto come under our notice. We have also seen that such competence is intimately connected with its organic growth. And we have further seen that, in its growth, the contagium appropriates the materials which are required for the nutrition of the tissues of the body in which it grows.

An organism which thus lives in, and at the expense of,

another organism, is a parasite. Contagia, therefore, are parasites. It is in their action as such that we shall find the explanation of the objections which have been noted as telling against the theory of fever which has been advanced.

Here, therefore, we drop the organism and take up the parasite.

CHAPTER XIX.

THE ACTION OF CONTAGIA AS PARASITES.

Regarding contagia as parasites, we accord to them the properties common to such organisms. One of the most distinctive and remarkable peculiarities of parasites, and that to which we would direct special attention, is that they are propagated only in certain localities, the area of which is often very limited.

Throughout the whole range of the animal kingdom, we find the liability to the occurrence of parasites. We find, too, that the parasites of one animal differ from those of another. This one is found in man, that in the horse; this in the cow, that in the sheep; this in the dog, that in the cat; this in the rat, that in the rabbit; and so on, through the animal kingdom. Each animal is liable to parasites peculiar to itself, and which are not found in any other animal.

But neither are they propagated in all parts of the animal in which they grow. Each parasite has its own nidus, its own special localized habitat, out of which it is not propagated. This one is found in small intestine, that in large; this in muscle, that in brain; this in liver, that in kidney; this on skin, that on mucous membrane. It is, in short, a general law applicable to the parasitic world, that each parasite has its own special nidus, in which it is propagated, and removed from which, it ceases to be reproduced.

Regarding contagia as parasites we accord to them similar properties. In keeping with this view of their nature, we should expect to find that each kind of animal had its own special contagious diseases; and that each contagium had a preference for some special locality. We accordingly do find that, among those animals whose ailments we have an opportunity of observing,

the special contagious diseases of each, are as peculiar to it, as are the ordinary parasites to which it shows a liability.

We further find that, as a rule, what imparts to each specific disease its distinctive features, is not so much any peculiarity of the general symptoms, as the existence of some local complication, generally inflammatory mischief, in this or that organ or tissue.

Finding this constant occurrence of the same local complication in connexion with the propagation in the system of a particular contagium; and finding that a similar lesion is never produced by any other agency, we cannot fail to see a probable connexion between the specific properties of the contagium, and the specific lesion of the disease to which it gives rise. The exact nature of this connexion will be more fully considered when these local lesions receive special attention. Meanwhile, we shall only give expression to the opinion, that the seat of these local lesions, is also the nidus in which the contagium, as a parasite, finds that something which is requisite to its fecundation and propagation, as distinguished from its organic growth.

The facts to which we now direct attention are: (1) that each animal has its own special parasites; (2) that each parasite has its own special nidus, out of which it is not propagated; (3) that each animal has its own peculiar contagious and specific diseases; and (4) that each contagious disease has, as a rule, its own peculiar local lesion. The juxtaposition of these facts cannot fail to indicate an analogy between ordinary parasites and contagia: the existence of such an analogy is additional evidence in favour of the view which regards contagia as consisting of living organisms.

Contagia, then, we regard as minute parasitic organisms, all of which, organism-like, exercise a definite action on their environment; and each of which, parasite-like, requires a special nidus for its development.

Let us consider for a moment what the possession of a nidus

implies. It implies that the locality within which the parasite finds the conditions requisite to its propagation, is a limited one: that is the main idea which the term nidus is meant to convey—a localized habitat out of which the parasite is not propagated. But this idea necessarily includes two others—first, that the parasite requires something more than the bare materials requisite to organic growth; and second, that the nidus is the seat in which this something exists. In other words, it is the presence in the nidus of this substance, which gives to it its special fitness to meet the requirements of the parasite which it sustains. In any part of the body the parasite would find the materials required for its growth as an organism; but only in its nidus does it find that other substance which is essential to its propagation and continued growth as a parasite. Of what this substance consists we do not know. Its nature no doubt varies in the case of each parasite. We simply know that this and that parasite live and increase only in this and that locality; and we infer, therefrom, that these localities contain something which is requisite to the propagation of the parasites found in them, and which does not exist over the body generally.

For the production of parasitic disease two factors are necessary: the first is the parasite; the second is the presence in the system of that special localized substance which is essential to its propagation.

For the production of the eruptive fevers two factors are necessary: the first is the contagium; the second is the presence in the system of that special, and probably localized, substance or material, which is essential to its fecundation and propagation, as distinguished from its organic growth.

The part which the first factor plays in the production of the phenomena of the eruptive fevers we have already considered; and have found that to the changes necessarily attendant on its growth as an organism, are to be ascribed the phenomena which have come under our notice.

But there are many phenomena connected with the eruptive fevers which are really as characteristic, and as constant in their occurrence, as those which constitute the febrile state. They, therefore, equally demand attention. They may be considered under the following heads:—

1. The comparative rarity of the eruptive fevers.
2. The occurrence in each of a characteristic local lesion.
3. The different degrees of severity in which the same form of fever occurs in different individuals.
4. The cessation of the febrile symptoms.
5. The fixed duration of the febrile symptoms.
6. The phenomena of the crisis.
7. Exhaustion of susceptibility, or immunity from a second attack.
8. The different degrees of contagiousness of the different eruptive fevers.

The phenomena here enumerated present an array of evidence against the germ-theory origin of the eruptive fevers, as this is commonly held, which is simply overwhelming. No view of the germ theory which regards contagia simply as organisms, and as nothing more, can possibly explain the phenomena just referred to. We have seen, however, that the mode of action of the poisons of the eruptive fevers, shows that they are not only organisms, but parasites. It is to the parasite, as distinguished from the organism,—to the second factor rather than to the first—that we have to look for an explanation of the difficulties which here present themselves.

In passing, then, from the organism to the parasite, we pass from the consideration of those phenomena which result from the action of the organism on its environment, to those which are due to the existence of, and necessity for, a second factor, without which the first (the organism, the contagium) cannot grow, and cannot operate. These phenomena we shall consider in the order enumerated.

CHAPTER XX.

THE COMPARATIVE RARITY OF THE ERUPTIVE FEVERS.

This has been addueed as an argument against the view whieh regards the poisons of these fevers as organisms whieh are largely reprodueed in the system during their course. 'If,' says Dr. Richardson, 'germs be ready to reproduee with the rapidity of reproduction assigned to them, and possess sueh persisteney of life, it is hard to see why there should not be an inerease of them for whieh there eould be no eseape, for men or animals, and by which in time the world would be depopulated.'

This objection to the germ theory we have already dealt with when eonsidering the question of the destruction of contagia (p. 15). We then saw that persistent vitality was the exception rather than the rule; and that, on free exposure to the atmosphere, the germs speedily perished. We further saw that a similar destruction of the majority, was the eommon fate of the ova and seeds of all organisms in a state of nature, only a very few ever coming to maturity. The ready destruetion of eontagia we, therefore, looked upon as an argument, not against, but in favour of, the view whieh regards them as eonsisting of minute organisms.

The eomparative rarity of the eruptive fevers, need no more be matter of surprise, than the rarity of oak trees as compared with the number of aeorns whieh are annually produced, or the disproportion which exists between the frequency of tapeworm and the number of ova whieh eaeh worm produces.

Theoretieally, there is no reason why each oak tree should not

give rise to hundreds of similar trees, and each tapeworm to thousands of its kind: in each case the requisite number of acorns and ova are produced. Practically, we find that, of the acorns produced, not one in a thousand develops into an oak, and that, of the ova of the tapeworm, not one in a million comes to maturity.

Theoretically, there is no reason why each case of each of the eruptive fevers should not give rise to thousands of others: the requisite number of germs is certainly produced. Practically, we find that only a few of the germs which are given off from the body during the course of the eruptive fevers, come to maturity: the vast majority perish undeveloped and inoperative[1].

Were a further reason required to give support to this view, we should find it in the fact that contagia are parasites as well as organisms. Parasites grow and reproduce their ova with such rapidity, and in so great numbers, that were every ovum to come to maturity, the results would be most disastrous. The possibility of such a result, is effectually guarded against by the general law just referred to, and by the further provision that each parasite has its own special habitat, out of which it is not propagated; a habitat often of such comparatively limited extent, that the chances are very much against its ever being reached by more than a fractional portion of the germs which are produced.

Two agencies thus continually tend to limit the spread of the eruptive fevers; the first is the ready destructibility on exposure to the atmosphere, of the poisons which give rise to them; the second is the limited extent of the nidus within which alone,

[1] Leuckhart has calculated that if every egg of a tapeworm eaten by a pig were to live and grow, a single joint would infect four pigs with 12,000 measles each. Practically he found that only one egg in 1340 developed into a bladder-worm. If such be the case with the ova which are eaten by the pig, there can be no difficulty in believing that the millions which are not eaten, must perish in greater numbers.

the germs which escape this first danger, find the material requisite to their propagation. The germs which get over both difficulties, must form only a fractional portion of those which are produced. And as only those which so surmount both obstacles, give rise to disease, it follows that the number of persons attacked by any of the eruptive fevers, must represent but a fractional portion of the number of germs which were produced at the same time as those which ultimately reached their nidus in the persons of those so attacked.

The comparative rarity of the eruptive fevers we, therefore, regard as an argument, not against, but in favour of, the view which attributes them to the propagation of an organism in the system.

CHAPTER XXI.

THE OCCURRENCE OF CHARACTERISTIC LOCAL LESIONS.

Though in each of the eruptive fevers, the course of the general symptoms is more or less peculiar, in none of them is it so distinctive as to form the leading characteristic of the disease.

That which imparts to each of the eruptive fevers its most distinctive features, is not so much any peculiarity of the febrile symptoms, as the occurrence of local lesions. The most characteristic feature of small-pox is its eruption; of scarlatina the eruption and sore throat; of measles the eruption and accompanying irritation of the mucous membrane of the eyes and respiratory passages; of typhoid fever, the bowel lesion; of typhus, the rash; of cerebro-spinal fever, the meningeal affection.

Now with reference to each of these lesions, it is to be noted that it essentially consists in hyperæmia of the affected part.

What is the pathological signification of this localized hyperæmia? And how is it brought about?

That the local lesions of the eruptive fevers form part and parcel of the maladies during whose course they occur, there can be no doubt; they are as constant in their occurrence as the febrile symptoms, and much more characteristic.

That a connexion exists between them and the specific properties of the contagia, is also certain. During the propagation of each contagium, there is developed a special local lesion, which is never observed under any other circumstances. The eruption of small-pox is never due to any other cause than the presence in the system of the poison of that disease. Nothing

but the poison of enteric fever produces the bowel lesion characteristic of that malady. The eruptions of scarlatina, and of measles, are always due to the poisons of these maladies, and never result from any other agency. The presence of the contagium in the system is, doubtless, the cause which gives rise to the local lesion. How does it produce such a result?

There are two possible modes of action.

(*a*) It may be that the contagium acts in the production of the local lesion, in the same way as ordinary medicinal and poisonous agencies act in the production of the local effects to which they give rise: or (*b*) it may be that its action in this respect bears an intimate relation to its organic development, and is altogether peculiar.

Either view may be correct. To determine which is so, we must carefully weigh the evidence for and against each.

That many poisonous and medicinal agencies exercise a special irritant action on certain organs, is a recognised fact in toxicology and therapeutics. No matter by what channel they are introduced into the system, arsenic acts on the stomach and rectum, cantharides on the bladder, and ergot on the uterus.

This predilection of certain ordinary poisons for particular organs, forms the main argument in support of the opinion which ascribes the local lesions of the eruptive fevers to a similar action on the part of the poisons which give rise to these maladies. And there can be no question as to the cogency of the argument. There is no reason why contagia may not so act. Even on the view that they are living organisms, there is no reason why their peculiar local action should not be due to some active principle, bearing to contagia the same relation that cantharidine does to the *cantharis vesicatoria*, or ergotin to ergot of rye.

It is an argument against, though not destructive of, this

view, that no such principle has ever been separated; and that the poisons of such contagious diseases as can be experimented with, have never been found to exist, except in a particulate and indiffusible form [1].

There are, however, many points in which a very great difference is found to exist between ordinary poisons and those which give rise to the eruptive fevers. Some of these have already been referred to when considering the mode of action of contagia. They may here be presented in a tabulated form.

Circumstances to be noted in connexion with the local effects of ordinary poisons.	Circumstances to be noted in connexion with the local lesions of the eruptive fevers.
1. A definite and appreciable quantity of the poison is requisite to the production of any effect.	1. The minutest possible quantity of the poison suffices to produce its full effect.
2. The severity of the symptoms, and the extent of the	2. The severity of the symptoms, and the extent of the

[1] That the contagia of the eruptive fevers act, in the production of their local lesions, like ordinary poisons, is the view held by the opponents of the germ theory, and advocated by them in opposition to that theory. (Murchison, Transactions of Pathological Society of London, 1875.) There is, however, no necessary antagonism between this view of the mode of action of contagia, and the theory which regards them as living organisms. This latter may be quite true: but its being so, does not negative the idea that the poisons of the eruptive fevers may produce their special local lesions in the same way as arsenic acts on the stomach and rectum, cantharides on the bladder, and ergot on the uterus. The fact that some dead organic and inorganic agencies exercise a special irritant action on certain parts of the body, no matter how they gain entrance to the system, shows that a living organism is not essential to the production of such a result; and that the occurrence of a peculiar local lesion in the eruptive fevers is not, *per se*, evidence that the poisons of these diseases, are living organisms. On the other hand, it does not militate against that view. The belief that contagia act like ordinary poisons in producing local lesions, is not inconsistent with belief in the germ theory. It is simply antagonistic to the view which regards these lesions as intimately related to the organic growth of the contagia, and altogether peculiar.

local mischief, bear a direct relation to the quantity of poison taken into the system.

3. In all ordinary poisons a small and varying, but always appreciable, quantity may be received into a susceptible system without producing effect.

4. The quantity which exists in, and is eliminated from, the system, is never in excess of that which was received.

5. The system being allowed to recover from its effects, the same action may be produced over and over again.

6. By the gradual and regular administration of many poisons the system may become so habituated to their presence, that a large quantity may be taken with impunity.

7. The poison continues to act so long as it exists in sufficient quantity in the part on which its action is manifested.

local lesion, bear no relation to the quantity of poison taken into the system.

3. The least particle taken into a susceptible system produces the full effects of the poison.

4. The quantity which exists in, and is eliminated from, the system, is always very greatly in excess of that received.

5. One attack of the eruptive fevers confers, as a rule, permanent immunity from a second.

6. In the eruptive fevers no such thing is possible: there is either a full action, or none at all; and a small dose is as potent as a large.

7. The local lesion shows signs of improvement, and the poison ceases to produce its special effects, while much of it still exists in the site of its action.

The existence of so many points of difference, creates a broad line of demarcation between ordinary poisons and those of the eruptive fevers, and renders it probable that their mode of action is dissimilar.

The peculiarities presented by the poisons of the eruptive

fevers, are very readily explained on the view that they are living organisms, which are largely propagated in the system during the course of the maladies to which they give rise, and whose action as poisons, is intimately connected with their organic development. We have seen that there is good reason for holding this view; and for further holding that the general symptoms common to the eruptive fevers, result from the propagation in the system of millions of minute organisms: we have further seen that their local lesions form, not only essential, but also the most distinctive features of these fevers. It is, therefore, probable that these local lesions also bear some relation to the growth and propagation of the germs. Certainly, with such evidence before us that contagia are organisms, it is incumbent upon us to consider this hypothesis, before we commit ourselves to any other.

The question which presents itself for our consideration is, whether the propagation in the system of the poisons of the eruptive fevers, is capable *per se* of causing the local lesions characteristic of these maladies.

We have seen that one of the chief characteristics of the febrile state, is an increased flow of blood through all the tissues of the body; and that this increased blood flow results, not from an increased demand on the part of the tissues, but from the appropriation by the contagium particles in the tissues, of the elements destined for their nutrition and repair. The propagation of the contagium in the tissues, thus leads to the passage through all the organs of the body of a more than normal quantity of blood.

The primary and essential condition of the local lesion of each of the eruptive fevers, is an increased afflux of blood to the affected part. In some cases it goes no further; but in others it goes on to congestion, inflammation, suppuration, and even sloughing: in all, however, the primary condition is one of hyperæmia. Now it is to be particularly noted, that this is

simply an exaggeration of that condition which, during the febrile state, obtains all over the body. In all the tissues there is an increased demand for blood; but in that part whose affection constitutes the local lesion, this demand exists in an exaggerated degree: the blood not only flows to it in increased quantity, but the increased demand for blood, is frequently accompanied by an amount of hyperaction which suffices to induce inflammation.

In considering the mode of production of the local lesion, then, we must not lose sight of the fact that the action by which it is produced, differs less in nature than in degree from that which is going on in all the tissues of the body during the continuance of the febrile state—that what constitutes the local lesion, is really and essentially a localized exaggeration of the generally increased demand for blood.

Is there any cause capable of giving rise to such localized hyperæmia?

We have found in the growth of the contagium particles in the minute structure of the tissues, and in the appropriation by them in that locality of the nutrient ingredients of the blood, the explanation of the general increase of the blood flow, which characterizes the febrile state: we have found, in short, that this increased flow of blood results from the growth of the contagium as an organism.

But the contagium is also a parasite; and as such, requires a special nidus for its propagation. Now it is evident that this nidus, no matter in what part of the body it be, cannot be exempt from the action of the contagium as an organism. Wherever situate, it is necessarily supplied with blood, and must be reached by the contagium particles which that fluid carries along with it: through its blood it affords to these particles the nitrogen and water requisite for their organic growth: but in addition, it is also the seat of that peculiar action which the term fecundation implies.

What takes place in the nidus, therefore, is the same action as goes on in all parts of the body, *plus* that which necessarily attends the process of fecundation. Now what is this latter?

In the absence of any definite knowledge on the subject, it would be natural to suppose that the fecundation of an ovum or seed, required a greater expenditure of force than the mere maintenance of its vitality—that a greater degree of energy was required to start those forces which the existence of life implies, than was requisite to keep them going after they had been set in motion. And we know from observation that such is the case.

The immediate consequence of the fecundation of the ovum of one of the higher animals, is an increased flow of blood to it, and increased vascular excitement of the maternal organs concerned in the process.

During the period of germination and flowering of many plants, the increased action which accompanies the process is often so great as to cause a decided rise of the temperature of the part in which the action occurs. So great is this rise in some cases (especially in some of the araceæ) that the heat produced may be felt by the naked hand.

Now, we do not for a moment mean to say that the process which takes place during the fecundation of the contagium particles, is the same as that which occurs in the impregnation of ova, and the germination of seeds; we merely say that it bears to it sufficient analogy to warrant us in founding an argument thereon. Contact with its special nidus, is as essential to the development of the ovum or germ of a parasite, as is contact with the seed of the male to the ova of the higher animals, or contact with the pollen to the pistils of plants.

The contagium particles, as parasites, find in their nidus something which is essential to their fecundation, and without which they cannot be reproduced. The poison of any of the eruptive fevers may be introduced into the system, but unless it reach

this second factor in its nidus, it is not propagated (as will be more fully shown when considering the question of immunity from a second attack).

There certainly takes place in the nidus an action which takes place nowhere else, and which must be accompanied by some evolution of force. From what is observed in the case of higher organisms, we may conclude that this evolution of force must be accompanied by increased activity in, and increased vascularity of, the part in which the action occurs. Increased vascularity is the primary and essential condition of the local lesion of each of the eruptive fevers. The part so affected, we regard as the nidus in which the contagium finds its second factor: and the localized hyperæmia which constitutes the local lesion, we regard as the necessary result of the action which accompanies the fecundation of the contagium particles. Such is the connexion which we believe to obtain, on the one hand, between the specific properties of the contagium and the local lesion; and, on the other hand, between this local lesion and the nidus of the parasite.

To recapitulate:—The poisons which give rise to the eruptive fevers are parasites: as such they require a nidus, for their propagation. The action which takes place in the nidus, has analogies with that which accompanies the fecundation of the ova and seeds of higher organisms: this latter is accompanied by increased afflux of blood to, and increased action in, the part in which it occurs.

The local lesions of the specific fevers consist primarily and essentially of hyperæmia of the affected parts. Active hyperæmia implies hyperaction. Such hyperaction as the fecundation of thousands, or even millions, of germs implies, is adequate to produce the hyperæmia, and even the marked inflammatory mischief, which sometimes constitutes the local lesion with which we have to deal.

The seat of the local lesions of the eruptive fevers we regard

as the nidus in which their poisons, as parasites, find the second factor essential to their propagation; and the hyperæmia which constitutes the local lesion, we regard as the necessary accompaniment of the hyperaction which the term fecundation implies.

The occurrence of a local lesion in connexion with the eruptive fevers, thus becomes an additional argument in favour of the view that the poisons of these maladies are living organisms.

From what has been said, it is apparent that clinical and pathological evidence favours the view that the poisons of the eruptive fevers are most abundant in, and act with greatest energy on, the seat of the local lesions characteristic of these maladies. It is in these local lesions that we find the most decided evidence of the action of the contagium; it is in the discharges which come from these lesions, or from such of them as are accompanied by discharge, that we find the most decided evidence of its existence. It is in these local lesions that, according to the views which have been advanced as to its nature and mode of action, the contagium ought to be most abundant: it is in their seat, therefore, that, if it can be detected at all, the contagium should be most readily found.

The minute morbid anatomy of the specific inflammations, has of late years been the subject of much careful investigation: and the concurring testimony of all who have investigated the subject is that these inflammations are associated with mycosis of the affected tissue—with infiltration of its substance with minute organisms.

The sore throat of diphtheria is the specific inflammatory affection to which most attention has been paid.

Though diphtheria is not classed with the eruptive fevers, it possesses so many points of analogy with them, that the observations made on its lesion may be utilized in any general investigation into the pathogenesis of the specific lesions of the eruptive fevers.

In diphtheria there is a general affection of the system, which declares itself by the occurrence of fever: there is a local lesion which forms the characteristic and distinguishing feature of the disease; and the combination of these two, the general disturbance and the local lesion, constitutes a disease which is believed to be due to the reception into the system of a specific poison, which is largely reproduced during the course of the malady to which it gives rise. The disease thus produced is, like the eruptive fevers, communicable from the sick to the healthy, occasionally occurs in an epidemic form, has a pretty definite period of incubation, exists in all degrees of severity, and is frequently followed by troublesome sequelæ. Like most of the eruptive fevers, it shows a predilection for those of a particular age; and like some of them, its occurrence is associated with sanitary defects. The constitutional disturbance and the local lesion generally make their appearance at the same time—the earliest indications of commencing illness being a feeling of general *malaise*, and a sensation of dryness and pricking in the throat.

Concentrating their attention, as some have done, on the virulence of the throat affection, the general symptoms have appeared to them consequent on, and secondary to, this; the constitutional affection being regarded by them not as an essential part of the original disturbance, but as resulting from the absorption into the blood of matter formed in the throat [2].

Such a view of the pathology of the disease we believe to be erroneous.

That the intensity of the local lesion is often a source of direct and urgent danger, and that prompt and vigorous treatment of that affection is a matter of the utmost importance, is unquestionable: but it does not follow therefrom that the constitutional affection, which accompanies this condition of throat, is secondary to, and consequent on, the local lesion.

[2] Oertel: Ziemssen's Cyclopædia of Medicine: article on Diphtheria.

More rational it seems to regard diphtheria as a general ailment, whose throat affection bears to the constitutional symptoms, the same relation that the throat affection of scarlatina, and the bowel lesion of typhoid fever, bear to the constitutional disturbance by which they are accompanied.

The poison of diphtheria is a parasite, requiring a special nidus for its development. The existence of a nidus implies the necessity for a second factor, contact with which is essential to the propagation of the contagium. In diphtheria this second factor has its seat in the mucous and submucous tissue of the nose, throat, and larynx. According as it is seated in one or other of these localities, the diphtheritic process will be most marked in the nose, in the throat, or in the larynx: and according to the extent of the second factor, will be the extent of the diphtheritic inflammation and exudation.

In the ordinary eruptive fevers we have seen (*a*) that the general febrile symptoms result, directly or indirectly, from the consumption by the contagium particles of the material destined for the nutrition of the tissues; and (*b*) that the extent of the febrile disturbance depends on the number of contagium particles circulating through these tissues: we have seen too (*c*) that the local lesions result from the propagation of the contagia in the seat of these lesions; and (*d*) that the extent of this propagation depends on the quantity of the second factor which the nidus contains. The intensity of the general disturbance, and the extent of the local lesion, are thus dependent on one cause—the quantity of the second factor which the nidus contains.

So it is with diphtheria. The intensity of the general febrile disturbance, and the extent of the local lesion by which it is accompanied, are dependent on one cause, the amount of contagium reproduced; and this, in its turn, depends on the extent to which the contagium finds its second factor in the seat of the local lesion. It follows from this, that the severity of the general symptoms, and the intensity of the local lesion, bear

a direct relation to each other, not because the mildness or severity of the one, produces a corresponding mildness or severity in the other, but because the mildness or severity of each, depends on the extent to which the contagium finds in the seat of the local lesion, the second factor essential to its propagation. An abundant growth of contagium gives rise, at once to a severe local lesion, and a correspondingly severe constitutional disturbance. A scanty growth causes a local lesion and a constitutional disturbance, whose mildness corresponds to the comparatively small quantity of contagium produced.

This view of the pathology of diphtheria affords a reasonable explanation of most of the phenomena of the disease: but not of all; and especially, not of the fact that the laryngeal form of the disease is so much more fatal than that in which only the fauces and nasal passages are involved.

But the peculiarity of the seat of the local lesion sufficiently explains the great fatality of such cases. The capacity of the larynx is so small, and its patency so essential to life, that a very slight development of false membrane in that locality, is attended with imminent danger. Even simple laryngitis, non-specific acute inflammation of the larynx, gives rise to most alarming symptoms—symptoms which are due, not to any peculiarity of the inflammation, but to the fact that the mucous membrane of the larynx cannot be much swollen without seriously diminishing the calibre of the laryngeal cavity, and even threatening death by its total occlusion.

A patch of diphtheritic exudation, which in the throat may *per se* be attended with no serious risk, becomes in the larynx a source of imminent danger: the danger, however, is not the same as that which accompanies a larger development of the disease in the fauces and nares. Death is threatened, not by the intensity of the disease, not by the development of typhoid depression, but by suffocation, by the mechanical obstruction of the cavity of the larynx by the diphtheritic exudation.

Where the disease proves fatal without invading the larynx, death is brought about by asthenia: the local lesion rapidly develops, and is accompanied in its progress by increased prostration of the vital powers: typhoid symptoms supervene, and the patient dies of asthenia, preceded or not by symptoms of blood-poisoning.

In cases in which the larynx alone is involved, the patient dies of asphyxia. His vital powers are not undermined by the intensity of the disease; but he is suffocated by the membrane which is formed in the larynx, before there is time for the development of that state of typhoid depression which precedes death in those cases in which only the fauces and nares are involved.

In cases in which the disease extends from the fauces to the larynx, there is a combination of these two modes of dying: the already existing depression is greatly aggravated by the agonies of impending suffocation, and by the addition to the blood impurity resulting from the propagation of the contagium, of that which results from interference with the process of respiration.

This view of the pathology of diphtheria seems to us the one which best explains the facts with which we have to deal. There is little doubt that diphtheria of the throat, and diphtheria of the larynx—true diphtheria, and true croup—are pathologically one and the same disease; the differences which they present at the bedside, being no greater than those which obtain between different cases of the ordinary eruptive fevers. A case of measles accompanied by a profuse eruption, but no chest complication, differs more, in its clinical aspects, from a case in which there is no eruption, but marked inflammatory mischief in the chest, than does a case of catarrhal from a case of laryngeal diphtheria: but both attacks result from the action of the same poison. The chest complications of measles are, indeed, more varied than the throat complications of diphtheria:

but we do not draw any etiological distinction between a case of measles accompanied by bronchitis, and one accompanied by pleurisy, or pneumonia.

In typhoid fever the local lesion may, in one case, be confined to the agminated glands; while in another, these may escape, and the solitary alone give evidence of inflammation: but in both cases the disease is due to one and the same cause.

In scarlatina we have seen that the poison seems sometimes to expend its action on the bowel, the throat giving little or no evidence of its action: and cases are common in which high fever (as measured by the temperature) is accompanied by profuse eruption, and little sore-throat; or the reverse, bad sore-throat, and little or no eruption.

With such variations in the mode of manifestation of the local lesions of the common eruptive fevers, it need not be matter of surprise to find the local lesion of diphtheria present varieties in its mode of development.

The difference between catarrhal and laryngeal diphtheria—between true diphtheria and true croup—is no greater than the differences which we find obtain between different cases of the same eruptive fever. And Nassiloff[3] has shown that the microscopic appearances presented by each form of diphtheria are the same; such differences as are noted, being due to the structural differences which naturally exist between the mucous surfaces of the throat and respiratory passages.

But, it may be said, the lesion of diphtheria is altogether peculiar—there is no other malady in which a similar membranous exudation is formed—it cannot, therefore, be regarded as produced in the same way, as the local lesions of the common eruptive fevers.

That the sore-throat of diphtheria is peculiar is certain; but so is the sore-throat of scarlatina; and so is that of syphilis;

[3] Virchow's Archiv. l. 1870.

and so is the local lesion of each of the eruptive fevers. The eruption of small-pox differs from all other eruptions. The bowel lesion of typhoid fever presents peculiarities which distinguish it from all other affections of the bowel. The peculiarities of each are due to the specific differences of its contagium, and to the special peculiarities of the seat of the lesion. We recognise the existence of specific differences in contagia by the peculiarities of their action, local and general, on the system; and the existence in diphtheria of a peculiarity in its local lesion, serves only to indicate that the poison which produces this lesion is specifically distinct; while its mode of action, and its large reproduction in the system during the course of the ailment to which it gives rise, indicate that it is an organism, and that, as such, it is generically allied to the poisons of the eruptive fevers.

Regarding diphtheria as being, etiologically and pathologically, closely allied to, if not worthy to be ranked among, the eruptive fevers, we may utilize the observations which have been made on the minute anatomy of its local lesion, in the prosecution of our present inquiry, as to whether or not organisms can be detected in those localities in which clinical and pathological evidence shows the contagium to be most abundant—the seat of the local lesions.

The microscopic anatomy of the tissue involved in the diphtheritic lesion has been carefully studied by Oertel, Hueter, Nassiloff, Klebs, von Recklinghausen, Eberth, Weber, Hetzerich, and others[4]. The general result of their observations, is to show that the diphtheritic lesion is essentially associated with

[4] For a general summary of the observations of these authors, and for references to their original communications, the reader is referred to Oertel's article on Diphtheria in von Ziemssen's Cyclopædia of the practice of Medicine; to Dr. Burdon-Sanderson's 'Report on recent researches of the Pathology of the Infective Processes,' in the report of the Medical Officer of the Privy Council: New Series, No. iii. and to Wagner's Manual of Pathology.

infiltration of the affected tissue with granular matter, which, on minute examination, is found to consist of micrococci.

At all stages of the disease, and in all the affected tissue, these organisms are detected.

Nassiloff regards the changes which constitute the diphtheritic lesion as probably due to the occupation of the channels of absorption by masses of micrococci.

According to Eberth, without micrococci there can be no diphtheria.

Oertel says there can be no doubt that these organisms are not of accidental occurrence, but are inseparable from the diphtheritic process. 'We find them,' he says, 'in the very smallest and most superficial plaques, we see them in immense collections in the tissues, we meet with them again in embolism as the cause of metastatic abscess, and the intensity of the toxic affection increases with the number of these organisms.'

The concurring testimony of all observers is, that the local lesion of diphtheria is associated with the development of micrococci in the affected tissue, and that these organisms exist at all stages of the disease, and in all the tissues involved, increasing in numbers with the advance of the lesion.

Various attempts have been made to communicate diphtheria to the lower animals by inoculating their tissues with matter derived from a diphtheritic sore in man. The general result of these experiments, has been to demonstrate that by such inoculation there may, though by no means invariably, be induced a destructive inflammatory action, which seems to be associated with the development in the inflamed tissue of organisms which cannot be distinguished from those found in true diphtheria.

Referring to these experiments, Dr. Sanderson[5] says, 'I am not indeed certain that any of the experimenters have kept in

[5] Op. cit. page 17.

mind in their investigations the distinction between the property of communicating a specific disease, e.g. diphtheria with its sequelæ, in its entirety, and that of merely ingrafting by inoculation, a particular local process.'

In this there can be no doubt that Dr. Sanderson is correct. The German observers have concentrated their attention too exclusively on the local process. They have, beyond question, succeeded in inducing by inoculation with diphtheritic matter, a destructive inflammatory process associated with the development of micrococci in the inflamed tissue: but such a process does not constitute the disease to which we apply the term diphtheria.

Oertel 'found that a disease having well-defined pathological characteristics, and in particular associated with nephritis, could be produced by such inoculation; and further, that it could be communicated from one animal to another without losing any of its distinctive features. He further showed that the disease in question, whatever were the local peculiarities given to it by the tissue in which it was ingrafted, was always a mycosis; in other words, that all the localisations of the disease were associated with the presence in the affected part of innumerable microzymes [6].'

The observations of the German experimenters all tend to show that serious disturbance may follow inoculation of healthy tissue by diphtheritic matter: but they also show that true diphtheria, as we find it occur in man, is not a disease which is communicable to the lower animals. In none of the animals experimented on was there induced a disease presenting an aggregate of phenomena, such as, occurring in man, would lead us to regard the malady as true diphtheria. The general symptoms induced were those, not of diphtheria, but of septicæmia, or embolic pyæmia; and were more likely due to the inoculation of the tissues by septic material derived from the diphthe-

[6] Burdon-Sanderson's Report, page 46.

ritic sore, than to their inoculation by the contagium of diphtheria.

We know that, in bad cases of diphtheria, symptoms of blood-poisoning—of septicæmia, or embolic pyæmia—are apt to occur; but we know, too, that this is not an essential feature of the disease: and we associate such symptoms, not so much with the action of the contagium of diphtheria, as with the absorption into the blood of septic matter formed in the local lesion to which the contagium gives rise. We thus associate these symptoms with septicæmia, rather than with the action of the diphtheritic contagium, first, because such symptoms are not sufficiently common in diphtheria to warrant us in attributing them solely to the action of the poison of that disease; and second, because they occur in other maladies which are accompanied by destructive local inflammations.

The poison of diphtheria we regard as a parasitic organism requiring a special nidus for its development: that nidus is the mucous and submucous tissue of the nares, fauces, and larynx of man. This seems to be the only locality in which the contagium of diphtheria finds the material necessary to its fecundation and propagation, and to the consequent development of all the symptoms of that disease.

The peculiar lesion which occurs in this locality, is always associated with infiltration of the affected tissue with minute organisms, whose quantity seems to bear a direct relation to the intensity of the local mischief.

Though the constant association of the organism and the lesion, is not sufficient to prove that they stand to each other in the relation of cause and effect, the facts (*a*) that the association is constant, (*b*) that the extent of the local lesion, and the severity of the general symptoms, are directly as the extent of the reproduction of the organism, (*c*) that the poison of diphtheria is, as we believe, an organism, (*d*) that it is largely reproduced during the course of the malady to which it gives

rise, and (*e*) that the propagation of an organism in a given locality is (as has been shown) competent to give rise to inflammation there, form a body of evidence which clearly favours the view that the organism is the cause of the diphtheria.

In erysipelas we have another disease between which and the specific fevers, there exist strong points of analogy. Like diphtheria, it possesses many claims to be ranked among them. It is contagious, and, therefore, results from the reception into the system of a poison derived from without. The appearance of the local lesion is not the first sign of illness; but, as in the eruptive fevers, the onset of the local lesion is preceded by headache, *malaise*, and signs of general constitutional disturbance.

Possessing, as erysipelas does, such analogies with the eruptive fevers, observations made on the erysipelatous process may also be utilized in our present inquiry.

The minute morbid anatomy of the local lesion of erysipelas has been carefully studied, especially by Hüeter, Orth, Lukomsky, and von Recklinghausen[7]. The general result of their observations, is to show that the erysipelatous process is invariably associated with the presence of micrococci in the inflamed skin.

Orth found that 'the infiltrating liquid of the swollen parts contained an enormous number of bacteria.'

The observations of Lukomsky and von Recklinghausen are divided into two parts: the first consists of the anatomical investigation of the erysipelatous process as it occurs in man; the second is a record of experiments made on the lower animals, with the object of contrasting the disease thus induced, with the natural disease already studied.

The result of both series of investigations, was to demonstrate the invariable association of micrococci with the inflammatory

[7] Virchow's Arch. lx: and Burdon-Sanderson's Report on Infective Processes; Report of Medical Officer of Privy Council, New Series, No. iii.

process in the skin. The lymphatics and lymphatic spaces were the chief seats of the organisms.

But the local lesions of diphtheria and erysipelas are not the only specific lesions whose minute morbid anatomy has been the subject of investigation.

That the fluid of small-pox pustules contains minute organisms, was demonstrated by Keber[8], Cohn[9], and others; and the existence of these is now generally recognised. Weigert[10] extended his investigations beyond the pustule to the surrounding skin, and found, especially in the neighbourhood of the pustules, masses of granular matter, situated probably in the lymphatics, and which, on more careful examination, presented all the appearances of the micrococci found in the fluid of the pustules.

The existence of these organisms both in the pustules, and in the tissues around them, indicates that in small-pox (as in diphtheria and erysipelas) the local lesion is associated with the development of minute organisms in the affected tissue. Believing as we do that the poison of small-pox is a minute organism, and that the propagation of an organism is competent to the production of a lesion, we regard it as at least possible that the micrococci which are so abundant in the lesion characteristic of small-pox, may be the cause of the disturbance with which they seem to be inseparably associated.

The full investigation of the connexion which obtains between these organisms, and the phenomena which accompany their development, is attended, in small-pox, with obvious and insuperable difficulties. The lesion cannot be examined at all stages of its development.

But there exists in the lower animals a disease, which, in its clinical and pathological aspects, so closely resembles small-pox,

[8] Virc. Arch. Bd. 42.

[9] Virch. Arch. Bd. 55.

[10] Centralblatt, 1871, No. 39.

that it may very well be substituted for that disease in our present inquiry. We refer to sheep-pox, the pathology of which has been carefully investigated by Dr. Klein[11]: 'Variola ovina, or sheep-pox, is a disease which, although it is not communicable to man, and possesses a specific contagium of its own, very closely resembles human small-pox, both as regards the development of the morbid process and the anatomical lesions which accompany it. This correspondence is so complete, that it cannot be doubted that the pathogeny of the two diseases is the same; that is to say, that whatever explanation can be given of the way in which the material cause or contagium produces its effects in the one case, will also serve as a key to the understanding of the other.'

Klein's investigations consisted in microscopic examination (*a*) of recent lymph, (*b*) of primary pustules produced by inoculation with that lymph, and (*c*) of secondary pustules produced by inserting some of it into the circulation. The general result of these investigations, was to show that recent lymph contained 'numerous small highly-refracting granules either isolated or in couples, which exhibited molecular movement,' and which on being kept for some time at a temperature of 32°C underwent such changes as are found only in organisms.

The changes noted in connexion with the primary and secondary pustules were practically the same in each, and were invariably accompanied by the development in the affected tissue of masses of micrococci.

Among the earliest changes noted, was distension of the lymphatics and their canaliculi with granular matter, which on careful examination was seen to consist of organized bodies 'which neither belonged to the tissue, nor were referable to any anatomical types—viz. of spheroidal or ovoid bodies having the character of micrococci and of branched filaments.'

It had already been demonstrated by Chauveau that the poison of sheep-pox consists of minute solid particles. Klein's

[11] Report of Medical Officer of Privy Council, New Series, No. iii.

observations have demonstrated that the fluid of the pustules of that disease, contain minute organisms which seem to be inseparably connected with the activity of that fluid, and which are reproduced in large quantity in the pustules of the malady; and they have further shown that the local changes which take place in the cuticle, and which result in the specific lesion of the disease, are invariably associated with a rich growth of minute organisms in the affected tissue.

Sheep-pox bears to sheep the same relation that small-pox bears to man. In its history too it so closely resembles the small-pox of man, that all that Klein has proved regarding it, may be accepted as having been demonstrated for small-pox. The observations of Weigert are, therefore, more than verified by the researches of Klein; and the eruption of small-pox we regard as intimately associated with the development of minute organisms in the affected skin.

To the same author, Dr. Klein, we are indebted for a careful investigation into the changes which take place in the specific bowel lesion of typhoid fever [12].

The general result of these investigations, is to show that the mucous membrane over and around the affected glands, is more or less thickly covered with minute organisms, which seem to find their way through the mucous membrane into the submucous tissue, and which, when closely packed, appear to be of a dark olive green colour. They are found in the Lieberkuhnian crypts, in the mucous membrane, in the veins, and in the lymphatics, and also in the fresh stools.

The result of Klein's researches, is to show that the bowel lesion of typhoid fever is associated with the development in the affected tissue of masses of minute organisms.

Such are the facts with which we have to deal. It is agreed on all hands that the specific inflammations which have hitherto been the subject of investigation, are associated with mycosis of

[12] Report of Medical Officer of Privy Council, New Series, No. vi.

the affected tissue. On this point there is no doubt; the association of the organic forms with the inflammatory process is invariable. What we have to do, is to interpret the facts, and to explain this association. Does the lesion result from the growth of the organisms, or are the organisms developed subsequently to the onset of the inflammatory process? Their relation is certainly not accidental; the organisms cause the inflammation; or the inflammation leads to the growth of the organisms.

The question as to which is cause and which effect, is a very difficult one to answer. It is so, because of the extreme minuteness of the organisms with which we have to deal; and because of the difficulty of examining the inflamed tissue at the earliest stage of the morbid process.

Evidence, however, is not altogether wanting.

Against the view which regards the organism as the cause of the inflammation, there are two principal arguments. These are, first, the fact that minute organisms, indistinguishable by the microscope from those found in the inflamed tissue, exist naturally on the mucous surfaces, and may be introduced into the circulation without doing harm; and second, the fact that the virulence of 'contagious mixtures diminishes in direct proportion to the increase of bacteria therein.'

The first argument simply means that all bacteria are necessarily possessed of similar properties, and that there exist among them no differences but such as may be detected by the microscope. This argument bears with it its own refutation; for to say that a body may possess no properties but those of which it gives evidence by its external form, and that all organisms of the same configuration, are necessarily possessed of the same properties, is to run counter to all experience and observation. As well might we say that all eight sided crystals are composed of oxalate of lime, and all cubes of chloride of sodium.

The ovum of a cat may not be distinguished from that of a rabbit, nor the ovum of a sheep from that of a cow; but we

know that each will develop into a form similar to that from which it sprung; and we do not for a moment allow the similarity in their appearance to blind us to the fact that the ova of these animals are possessed of essential and specific differences. To say that because they are identical in appearance these ova must be identical in nature, would be to make a statement which all evidence belies.

When dealing with organisms so much more minute as those which now engage our attention, such a method of reasoning is still more irrational. The negative evidence afforded by the fact that the organisms which exist in one specific inflammation, are indistinguishable by the microscope from those found in another, we, therefore, regard as inadequate to show that they are not specifically distinct.

The second argument, that contagious fluids are most potent in the fresh state, and lose their contagious properties as bacteria are developed in them, has already been considered (page 23); and the fact on which this argument is founded has been shown to tell in favour of, rather than against, the germ theory. The development of bacteria in contagious fluids coincidently with, and in direct proportion to, the loss of their contagiousness, was shown to be due to the fact that the bacteria are formed from the disintegrating elements of the contagium particles.

The arguments adduced in opposition to the view that the micrococci are the cause of the inflammation, and in support of that which looks upon these organisms as pathological products, we, therefore, regard as invalid.

The arguments adduced on the other side, i. e. in support of the view which regards the organism as the cause of the morbid process, are various.

It has been shown that the specific lesions of the eruptive fevers, are not extraneous complications grafted on to the constitutional disturbance, but are essential and characteristic features of the diseases during whose course they occur. They

are as much a part of the disease as the febrile symptoms which accompany their development, and result from the same cause which gives rise to the fever. This cause, we have seen good reason to believe, is a parasitic organism. The competence of such an organism to produce a local lesion has already been shown.

So far, therefore, the evidence favours the view that the lesion results from the propagation of an organism.

The question which we have now to consider is whether or not the organisms which exist in these lesions are those which produce the disturbance. The only way in which direct evidence on this point could be got, would be to examine each lesion over and over again, and see whether or not the same organism always occurred in connexion with the earliest symptoms of the same lesion, and never with any other. But such direct evidence is not to be had: for we have already seen that the organisms found in one lesion are indistinguishable by the microscope from those found in another.

In the absence of direct, we can only make the best use of such indirect, evidence as is available. Of this there is not a little. The missing link in the chain of evidence is the proof which would be got from ocular demonstration, of the existence of specific differences in the organisms. The absence of this link does not prove the non-existence of such difference. It has been shown that in other organized bodies, less minute than those with which we are now dealing, we recognise the existence of specific differences of which the eye can detect no sign. There is no reason why ocular demonstration should be regarded as of more importance in one case than in another.

It has already been observed that Professor Cohn of Breslau recognises the existence of specific differences between the micrococci which are found in connexion with diseased processes, and those which occur in connexion with putrefaction—differences which probably very few other men are competent to detect. If Professor Cohn can detect differences which are imperceptible

to other men, it is not too much to say, that there may exist among the micrococci which occur in connexion with the specific inflammations, differences which even he cannot detect.

It is an ascertained fact that the contagia of small-pox, of vaccinia, and of sheep-pox, consist of minute solid particles. It is equally a fact that these particles are specifically distinct. The mode in which each acts, always, and under all circumstances, producing its own special malady, during whose course the particles of which the contagium consists are always largely reproduced, proves the existence of specific distinctions among these particles, more certainly than this existence could be proved by any slight difference in their external appearance—and any differences in configuration presented by particles so minute could only be very slight.

In the case of three diseases which are accompanied by the development of local lesions, we have definite proof (1) that the poisons which give rise to them are specifically distinct, and (2) that each poison consists of minute solid particles. In addition, we have a mass of very strong evidence to show that these particles are living organisms which are propagated in the system. That the local lesions, which form the characteristic features of the maladies produced by these particles, result from the special action of the particles on the tissues in which the lesions are developed, there can be no doubt. We thus have a body of evidence, amounting almost to proof, that these lesions are produced by an organism.

With such evidence before us—knowing that an organism is competent to produce such lesions, and finding on examination that the occurrence of these lesions, is invariably associated with the development of masses of minute organisms in the affected tissue, the conclusion is almost forced upon us that the organisms give rise to the lesion.

We have definite proof that the development in the system of minute particles, possessing all the attributes of organisms,

does give rise to local lesions which essentially consist in inflammation of the affected tissues. We thus have the strongest possible grounds, short of absolute proof, for believing that organisms may cause inflammation. There is no such evidence to show that inflammation may give rise to organisms.

But there is yet another way in which evidence may be got. If the organisms cause the inflammation, they ought to be most abundant where the inflammatory process is most active: if, on the other hand, the inflammation leads to the development of the organisms, and if these latter be formed in the inflammatory products, (no matter whether by archebiosis or from a pre-existing germ) they ought to be the most abundant where the morbid process is completed, and where the inflammatory products are most plentiful. Is such the case?

On this point we have not much evidence: but such as we have is of value.

In not one of the specific inflammations whose minute morbid anatomy has been investigated, has there been found to exist a stage of the inflammatory process unassociated with the presence of organisms: the inflammation never precedes the mycosis.

(*a*) In his observations on the lesion of small-pox Weigert [13] found micrococci in greatest abundance in cases which proved fatal at an early stage of the illness, before the sixth or seventh day: when the disease was of longer duration the organisms were found in much smaller quantity, or not at all.

If the organisms were a result of the inflammatory process, they should have been most abundant in cases in which that process had lasted longest. If, on the other hand, they were the cause of that process, they ought to have been found most plentifully in cases which proved fatal while the inflammation was still active. This seems to us the true explanation of the results of Weigert's observations. He himself modestly attributes the paucity of the organisms in the advanced cases to the

[13] Op. cit.

increased difficulty of detecting them, in consequence of the abundant corpuscular infiltration of the affected tissue. This, however, can scarcely be regarded as an adequate explanation of his facts.

Their true interpretation seems to us to be, that the organisms were more abundant in cases which proved fatal on the sixth, than in those which proved fatal on the twelfth, day of the disease, because on the sixth day the inflammatory process was actively going on, while on the twelfth day it was completed.

But there is another reason why organisms should be most abundant in cases fatal at an early period.

We have already seen that a severe attack of any of the eruptive fevers, means a large propagation of contagium. A case of small-pox which proves fatal on the sixth day, is more severe than one in which the fatal event is delayed till the twelfth. There is in it, therefore, a larger quantity of contagium produced.

The greater abundance of the micrococci in the lesion of cases which proved fatal at an early stage of the illness, we attribute, in the first place, to the fact that cases which die in the first week of the disease are more severe than those which last till the second; and are, therefore, attended with a larger reproduction of contagium; and secondly, and chiefly, to the fact that death takes place while the inflammatory action which constitutes the lesion, is actively going on.

(*b*) Klein's observations on the lesion of sheep-pox[14] show that the earliest stage of the local process is associated with distension of the lymphatics and their canaliculi with granular matter, which, on minute examination, is found to consist of micrococci.

(*c*) But probably the most important observations of all, are those of Lukomsky and von Recklinghausen on the process

[14] Op. cit.

of erysipelas[15]. In the course of their investigations these observers found, first, that micrococci existed in greatest numbers at the edge of the inflamed patch, and especially at the point at which the inflammation was most actively progressing: and second, that in parts in which the inflammatory process was completed, and in which the disease was receding, there existed few or no micrococci. In other words, organisms were found in great abundance in the seat of active inflammation; but existed only in small quantity, or not at all, at a distance from that point. 'This not only serves to illustrate the intimate relation of the organisms with the process, but to show that we have here to do with a phenomenon which is connected with the beginning of the process, and cannot be considered as a *result* of the destructive changes to which the process has already given rise[16].'

The evidence with which we have to deal is:—

1. That the poisons of the eruptive fevers are specifically distinct.
2. That these poisons are almost certainly minute organisms.
3. That they are largely reproduced in the system.
4. That such reproduction causes the phenomena of the eruptive fevers.
5. That the characteristic local lesions of these fevers form an essential part of the illness.
6. That the seat of the local lesion is the locality in which the fever poison is most abundant.
7. That these lesions are essentially associated with the development of organisms in the affected tissue.
8. That such development bears a direct relation to the activity of the inflammatory process.
9. That the organisms are more abundant in the early than in the advanced stages of the inflammation.

[15] Op. cit. [16] Burdon-Sanderson: Transactions of Pathological Society, 1875.

With such evidence before us, it is difficult to see how we can come to any other conclusion than that the organisms which are found in the local lesions of the eruptive fevers, are the cause of the inflammation which constitutes these lesions; that they are, in short, the contagium particles whose propagation in the system gives rise to disease.

In favour of the only alternative view—that the inflammation gives rise to the organism—there is no evidence.

But, it may be said, if these organisms are the contagium particles, and if the general symptoms of the eruptive fevers be due to the growth of these particles in the tissues, similar organisms ought to be found in these tissues, and in the blood, as well as in the local lesion.

There are two answers to this objection.

1. It is evident that many millions of organisms such as we find in the local lesions, might be diffused in the blood and over the body without our being able to detect them. That such organisms do enter the blood, is proved by the fact that they have been traced from the local lesions, through the lymphatics, and into the veins; they could not enter the veins without getting into the circulation. It is simply their dense massing in a very limited space, which enables us to see them in the local lesions.

2. The action which takes place in the local lesion is not the same as that which takes place in the tissues generally.

In the local lesion the contagium not only grows, but is *propagated:* in the minute structure of the tissues it only *grows.* Between these two processes a very decided distinction must be drawn. This distinction will be best indicated by tracing the life history of a germ.

A disease germ is received into a susceptible system, i. e. one containing the second factor essential to its propagation, and circulates with the blood through the body: presently it comes in contact with its second factor, and at once is subjected to

that influence which leads to the formation from it of similar germs, which in their turn act in the same way as the parent from which they sprung: and so the process goes on, each germ giving rise to several more. At first they are probably confined to the nidus, but as they increase in numbers they pass from this through the lymphatics into the circulation.

Organisms such as those with which we are now dealing multiply by division. Each full grown organism which we see in the lesion may give rise to several others; in doing so, it breaks up (so to speak) into several parts, each of which in its turn becomes an organism. Now it is evident that the breaking up into three or four parts of one of the micrococci which we see in the specific inflammations, must be attended with its disappearance from the field of our vision — the particles or germs resulting from such division, being too minute for ocular examination.

It is these particles which grow so abundantly in the tissues. There they appropriate the nitrogen and water of the liquor sanguinis, and from these elements, form their own protoplasm. Many of them are given off from the body, most to perish, but some to repeat in other susceptible systems, the process and the disease during which they were formed. Of such as remain in the body, those only are reproduced which again reach their second factor in the seat of the local lesion. On reaching this point, the process which originated the disease again begins; and so it goes on till the second factor is exhausted.

The distinction between the germ properly so called, and the full-grown organism, is one of much importance; for we have to do with both during the course of the eruptive fevers.

The chief action which takes place in the local lesion, is the development from the full-grown organism of the germs to which it gives rise: that which takes place in the minute structure of the tissues is the appropriation by these germs of the materials necessary to their growth.

In the local lesion we have to deal chiefly with the full-grown organism: in the tissues, with the germ.

'A portion of the energy of the virus consists in its passage from the germ state to that of the finished organism' (Prof. Tyndall, Op. cit. p. 71).

The reasons why organisms are not so readily detected in the blood as in the local lesions are, therefore, first, that in the lesion they are densely aggregated together, while in the blood they are very widely diffused; and second, that the lesion is the seat of propagation, and, therefore, the locality in which fully developed organisms most abound; while the blood is the seat of growth, and, therefore, the locality in which germs properly so called are most abundant.

CHAPTER XXII.

THE DIFFERENT DEGREES OF SEVERITY IN WHICH THE SAME FORM OF FEVER OCCURS IN DIFFERENT PERSONS.

This is generally referred to individual susceptibility; and an analogy drawn between this, and what is observed in the case of ordinary poisonous and medicinal agencies. But we have seen good reason to believe that the poisons of the eruptive fevers do not act in the same way as ordinary poisons, but that their action is intimately connected with their organic growth.

How it is that some individuals show a peculiar susceptibility, or the reverse, to the action of certain ordinary poisons, we do not know; for to refer it to individual susceptibility, is to indicate, not to explain, the fact. Nor, indeed, do we know how it is that what we regard as the ordinary and normal action of such agencies is brought about. We know from experience that such and such a drug produces such and such an action on such and such an organ; that, for instance, digitalis acts on the heart, and cantharides on the bladder; that opium contracts, and belladonna dilates the pupil. But why each produces its own peculiar action; and why digitalis never irritates the bladder, and opium never dilates the pupil, we cannot tell.

Under these circumstances, to bound our knowledge of the mode of action of the poisons of the eruptive fevers, by what we know of the mode of action of ordinary poisons, would be wilfully to restrict and curtail it. We do not know how all

ordinary poisonous and medicinal agencies produce their peculiar effects: but that is no reason why we should not strive for a more precise knowledge of the mode of action of the poisons of the eruptive fevers. These we have seen to be essentially different in their nature from ordinary poisons. We have seen also good reason for believing that the peculiarity of their nature gives rise to a corresponding peculiarity in their mode of action.

The local lesions which characterize their action, are most readily explained on the view that the site of these lesions, is also the nidus of the parasite; while the general symptoms to which they give rise, bear an intimate relation to their organic growth. What we have now to consider is the question why, with the same dose of the poison, both the intensity of the local lesion, and the severity of the general symptoms, vary so much in different cases.

First, as to the local lesion. The hyperæmia which constitutes this, we have seen to be the necessary accompaniment of the propagation of the germs in the nidus. The degree of hyperæmia, and the extent of the action which takes place in the nidus; or, in other words, the intensity of the local lesion, will depend on the number of germs fecundated. This, in its turn, will depend on the facilities presented by the nidus for the accomplishment of that process. In other words, the extent to which the second factor exists in the nidus, is the agency which determines the extent of the propagation of the contagium, and the degree of intensity of the local lesion. If the second factor exist only to a small extent, the action which takes place in the nidus will be comparatively limited, and the resulting local lesion correspondingly slight. If it exist to a large extent, the action which takes place in the nidus will be proportionally great, and the resulting local lesion correspondingly severe.

With regard to the general febrile symptoms. We have seen that these result from the growth of the germs in

the tissues. The degree of their severity depends on the extent to which the contagium particles are reproduced: that depends on the fecundating powers of the nidus; so that the same agency which determines the extent of the local lesions, determines also the amount of febrile disturbance by which such lesions are accompanied.

In accordance with this, we find that the severity of the general symptoms, bears a direct relation to the prominence of the local lesion. In small-pox and typhus fever[1], the more severe the case, the more abundant the eruption. In measles and scarlatina, the smartness of the attack is indicated by the quantity of the eruption, or by the severity of the pulmonary and throat symptoms. In typhoid fever, the height to which the fever runs is directly as the extent of the bowel lesion. In cerebro-spinal fever, the danger is directly as the extent of the meningeal mischief.

Here an apparent difficulty presents itself. If such be the nature of the connexion which obtains between the local lesion and the general symptoms, how are we to explain the occurrence of those cases in which no local lesion is developed—variola sine variolis; morbilli sine morbillis; typhus sine eruptione?

There are two possible explanations.

It may be that such cases are instances of mistaken diagnosis. There are so many causes capable of giving rise to a febrile attack of short duration, that one of them may very readily act on an individual who has recently been exposed to one of the specific fevers; and in whom, therefore, any febrile symptoms which present themselves, are apt to be traced back to such exposure.

[1] With reference to typhus fever, we would here note that there is reason to believe that the eruption is not its only local lesion. There is not a little evidence to show that the pulmonary parenchyma is also to some extent involved in this manner. What is called pulmonary hypostasis is an all but invariable accompaniment of a bad attack, with a profuse and dingy rash; and becomes an element of danger much in the same way as pulmonary congestion is apt to do in measles.

The fatigue and anxieties inseparable from attendance on one suffering from fever, may alone suffice in some persons to produce such an attack. A febricula, accompanied by gastric irritation, in one who has been exposed to the contagion of small-pox, may thus become a variola sine variolis: accompanied by catarrhal symptoms in one who has been exposed to measles, it may be called morbilli sine morbillis: a non-eruptive febrile attack in one resident in a house in which there are cases of typhus, is typhus sine eruptione.

The main ground for the diagnosis in each case is the fact that the patient has been exposed to infection. In many cases, the diagnosis may be wrong; but it probably is not so in all. For there is good reason to believe that the poisons of the eruptive fevers sometimes produce febrile disturbance, without giving rise to the usual local lesion. Next to the absence of the local lesion, the most prominent characteristics of these cases, supposing them to be attacks of eruptive fever, are their mildness, and the shortness of their duration. Now, if it be the case that the quantity of the second factor is the agency which determines both the extent of the local lesion, and the severity of the general symptoms; and if it be true that the amount of the second factor which the system contains, varies so much in different individuals, it is evident that in some, it may exist to so slight an extent, that there may not be sufficient for the production of a characteristic attack of the disease.

In the case of typhus, for instance, there may be enough of the second factor to produce just so much febrile disturbance as exists during the first two or three days of an ordinary attack, before the eruption comes out, but not enough to produce a characteristic seizure; and not enough to lead to the amount of local hyperæmia requisite to the development of the rash.

In measles there may be an abundant eruption, and little or no

chest affection; or there may be prominent chest symptoms, and little or no eruption.

So with scarlatina, there may be a profuse eruption, and very little sore throat; or a virulent sore throat, and little or no eruption.

That is to say, that in cases in which there is apt to be a double lesion, one may predominate almost to the exclusion of the other. This shows that the second factor may be concentrated in one locality. We have already seen that it may exist to a large, or to a slight extent.

Under these circumstances, it is evident that a given individual may have in the mucous surface of his respiratory tract, enough of the second factor to enable the contagium of measles to be propagated in quantity sufficient for the production of some febrile disturbance, but not sufficient for the production of serious pulmonary symptoms. The skin of the same individual may contain none of the second factor. An attack of measles in such a person, would consist of a febrile attack of a few days' duration, and some catarrhal symptoms. It would be a feverish cold, or morbilli sine morbillis, according to the view which we took as to its origin.

It is a recognised fact, that typhoid fever may exist in so slight a form, that the duration of the febrile symptoms may be no more than ten or twelve days: in such cases, the bowel lesion consists only in some fulness and increased redness of the affected glands: there is no ulceration; and, therefore, there are no bowel symptoms.

Analogous, and equally mild, cases may occur in all the eruptive fevers. In such instances the second factor exists to an extent which is sufficient for the reproduction of the quantity of contagium necessary to produce slight febrile disturbance; but is not sufficient for the development in the locality in which it exists of an amount of hyperæmia, which is perceptible to the naked eye. There is necessarily some increased blood flow through that locality; but not enough for the development of a lesion.

The true nature of such cases is apt to escape recognition; especially if they occur sporadically. In such circumstances they are very likely to be mistaken for some slight non-specific febrile ailment: and in the symptoms presented by the patient there is nothing to guide us in discriminating between these, and very slight attacks of the specific fevers. The duration of the febrile symptoms, and the circumstances under which they occur, are our best means of doing so. But even these are inadequate; and it is most probable that many of the anomalous forms of fever which come under the notice of the physician are really very slight attacks of one or other of the specific fevers [1].

But there is yet another class of cases in which no eruption is observed; and whose characteristic is the severity of the seizure. We refer to those cases in which the poison of scarlatina acts with such virulence as to lead to the rapid development of typhoid symptoms, to collapse, and death within twenty-four or forty-eight hours of the seizure, without the occurrence of eruption, or sore throat.

If the second factor be necessary to the propagation of the contagium, how are these cases to be explained? In the first place it is to be noted that it is not always strictly accurate to say that there is no local lesion: for though there may be no throat symptoms, the fauces are often of a deep red colour—they are hyperæmic. In the second place it is to be observed, that one of the prominent symptoms of such cases is the frequent passage of watery stools. The

[1] Dr. Tweedie believes that all cases of febricula are mild cases of typhus or relapsing fever. (Lumleian Lectures, 1860.)

Murchison regards it as probable that many cases of febricula result from a small dose of the typhus-poison (op. cit. p. 187). He also says that most cases of 'simple continued fever,' or 'febricula,' are abortive attacks of enteric fever (op. cit. p. 457).

In this view (no doubt the correct one) of the pathology of many cases of febricula, we have the probable explanation of the occurrence of those cases of typhus and typhoid fever, in which the disease is believed to have originated *de novo*.

watery stools and the collapse give the patients the appearance of those suffering from cholera. Cases of scarlatina in which diarrhœa occurs are always very anxious ones; and such diarrhœa is particularly troublesome. Such cases very often prove fatal. The view which we take of this symptom is, that the bowel congestion which leads to it, is similar in nature to the throat affection, and to the skin eruption.

In other words the second factor, in some cases of scarlatina, has its seat in the intestinal mucous surface. In such cases diarrhœa is a troublesome symptom. If the second factor exist to a large extent in that locality, this symptom may predominate to the exclusion of the eruption and sore throat; and the patient, though suffering from the action of the poison of scarlatina, may die, less with the ordinary symptoms of that disease, than with those of cholera-diarrhœa, and collapse.

It is evident from all this, that the view which regards the amount of the second factor as the agency which determines the severity or the mildness of a particular seizure, is the one which best explains the facts with which we have to deal.

CHAPTER XXIII.

THE CESSATION OF THE FEBRILE SYMPTOMS.

The cessation of the symptoms which constitute a febrile attack, forms as essential a part of the illness as their onset; it, therefore, equally calls for consideration and explanation.

The propagation of the parasite in its nidus, is the cause of the local lesion: the growth of the germs in the tissues, is the cause of the general febrile disturbance. So long as the contagium particles are conveyed to, and find in, the nidus the second factor necessary to their propagation, so long do they continue to be reproduced and to grow. While their propagation and growth continue, the local lesion does not diminish in intensity, and the general symptoms show no signs of abatement. But let this second factor be exhausted, as (if not reproduced as speedily as it is used up in the process of fecundation) it inevitably must be in time, and all those actions and changes which depend on the continued propagation and growth of the germs, must come to an end.

That the second factor is exhausted, and is not again reproduced, is proved by the fact (to be presently referred to in greater detail) that the contagium, the first factor, cannot, as a rule, be propagated in the system more than once. So long as any of the second factor remains, the contagium continues to be propagated: so soon as it is exhausted, its propagation ceases, and the febrile symptoms come speedily to an end. The cessation of the febrile symptoms is, therefore, due to the exhaustion of the second factor.

It is a strong argument in favour of this view of the important part played by the second factor, that the local lesion begins to decline, or altogether disappears, and the febrile symptoms come to an end, while there is still in the system much of the poison which gave rise to them; but which is now powerless for evil to the body in which it exists, though capable of producing disease in those around.

The early days of convalescence from the eruptive fevers are, indeed, regarded by some as the most infectious period of these diseases. We do not think there is evidence to prove this: but there is abundant evidence to show that the febrile symptoms cease, and the local lesion shows signs of amendment; some time before the poison which gave rise to them is eliminated from the system; clearly showing that something more than its *presence* in the system is essential to the production of the febrile state, and of the local lesion. On the view that contagia are parasites, requiring a second factor for their propagation, and that this second factor is exhausted during their propagation, all is readily explained.

At the moment at which the exhaustion of the second factor is completed, there must be circulating in the blood a number of germs which have not completed their organic growth. These will continue to appropriate the nutrient ingredients of the blood until their growth is completed. And until they cease to grow, the febrile process will not come to an end.

It follows from this that the cessation of the febrile symptoms, and the exhaustion of the second factor, are not exactly contemporaneous. The latter is contemporaneous with the moment at which the former begins to decline—it is indeed the cause of this declension. But the complete subsidence of the febrile symptoms must necessarily, for the reason given, be subsequent to the complete exhaustion of the second factor, Hence we find that a sudden cessation of the fever is, in these days of accurate thermometry, unknown in the eruptive

fevers: the process of defervescence always occupying twelve, twenty-four, forty-eight, or more hours.

The cessation of the febrile symptoms is not due to the elimination, or destruction, of the poison which induced them; but results from the exhaustion of that second factor which is requisite to the propagation of the contagium in the system. Such cessation thus becomes an argument in favour of the view which regards the poisons of the eruptive fevers as living parasitic organisms.

CHAPTER XXIV.

THE FIXED DURATION OF THE FEBRILE SYMPTOMS.

One of the most prominent characteristics of each of the specific fevers, is the possession of a fixed and definite period of duration. Seeing a patient suffering from any one of them at a given period in its course, we can tell, with tolerable certainty, not only the past history, but the probable future course and duration of the illness. For example, seeing an ordinary case of typhus fever for the first time on the day on which the eruption has appeared, we can tell that the patient has been ill five days, and that the febrile symptoms will not begin to decline for other eight or nine days—more or less, according to the age of the patient, and the severity of the case. We can tell also the symptoms which presented themselves during the five days which preceded our visit, as well as those which are likely to present themselves during the remaining period of the illness.

In the case of no ordinary organic or inorganic poison, can we thus, without any knowledge of the quantity taken, scan the past, and prognosticate the future of its action. Seeing a man suffering from the symptoms of arsenical poisoning, for instance, we cannot, from his symptoms alone, and without further evidence that he has taken poison, at once come to a decided conclusion as to their causation. We may have a decided opinion on the point; but there can be no absolute certainty.

Again, having satisfied ourselves that it is arsenical poisoning with which we have to deal, we cannot, in the absence of

information as to when, and in what quantity, the poison was taken, tell either how long it has been acting, or for what time it may continue to do so.

The duration of the period of action of the poisons of the specific fevers is, within certain limits, fixed and invariable. That of ordinary poisons is variable and uncertain. The severity of the action of the latter depends mainly on the dose taken. In the former the dose is immaterial: that which determines the extent of its action is the amount of the second factor. The exhaustion of this, we have seen to be the cause of the cessation of the febrile symptoms. The fact that the duration of these is, in each of the specific fevers, sufficiently fixed and distinctive to form one of its characteristic features, is enough to show that there is a pretty constant average quantity of the second factor. It is the existence of this average which gives to each of the specific fevers its fixed duration.

The duration of the febrile symptoms represents the time which the contagium requires to exhaust its second factor. For this purpose the poison of typhus fever requires, on an average, from twelve to fourteen days; that of typhoid fever, on an average, from twenty to twenty-two days. Hence the mean duration of these two forms of fever is respectively two, and three weeks.

CHAPTER XXV.

THE PHENOMENA OF THE CRISIS.

Defervescence essentially consists in the cessation of those processes which constitute fervescence. These processes all result, more or less directly, from the propagation of the contagium. Their cessation, and the consequent decline of the febrile state, are, therefore, consequent on the stop which is put to this propagation by the exhaustion of the second factor.

Coincidently with the decline of the febrile symptoms, there is frequently observed an increased action of the eliminating organs, especially of the skin and kidneys.

A perspiration or a diuresis occurring at this time, is said to be critical; and is generally supposed to result from nature's efforts to throw off, either the poison which gave rise to the febrile disturbance, or excretory products which have accumulated in the blood during its continuance.

But, if such be the explanation of the occurrence of these phenomena, why do they not take place sooner? If the system possesses the power of thus throwing off peccant material, why does it not exercise that power at an earlier period of the illness, when the comparatively small extent to which such material exists in the blood, would render its elimination so much more easy? And why does it so often fail to exercise that action at all, and allow these materials to accumulate and increase till death ensues?

Assuredly the phenomena of the crisis do not result solely

from an effort to eliminate either the poison of the disease, or retained excretory products.

The cessation of all those processes which constitute the febrile state, is an essential preliminary to the occurrence of the crisis, properly so called. The cause which gives rise to the latter must be that which leads to the cessation of the febrile symptoms. This we have seen to be the cessation of the propagation of the contagium. What we have now to consider, is the competence of this phenomenon to produce a perspiration, or a diuresis.

The cessation of the propagation of the contagium implies the cessation of all those changes to which that propagation gives rise. Two of the chief changes thus induced, are increased consumption of water, and increased formation of urea: the coincident occurrence to any extent of these two effects, leads to defective elimination by the skin and kidneys, and consequent retention of excretory products.

Such is the state of matters before the crisis occurs.

With the cessation of the propagation of the contagium, all is suddenly changed. The abnormal demand for water ceases, and the organs and tissues are allowed to appropriate all that is sent to them. But, prior to the cessation of the abnormal demand, there has probably been taken into the system more water than is requisite for its bare wants; the surplus being that which would have been required for the contagium, had its propagation not ceased. Of this surplus the system relieves itself by perspiration, by diuresis, or by diarrhœa. The extent of the critical flow is, *caeteris paribus*, directly as the quantity of this surplus.

The action of the skin is aided by the generally relaxed state of its vessels; while, if there has been retention of urinary excreta, the kidneys are stimulated to increased work by the presence of these in the blood. There being no obstacle to their getting the requisite quantity of water, diuresis results.

The phenomena of the crisis essentially consist in a sudden

elimination of water from the system; and that is consequent, more or less directly, on the cessation of the increased demand for water to which the propagation of the contagium gives rise. The phenomena of the crisis we, therefore, regard as indirectly due to this cessation.

Besides increased discharge of water and of excretory products there is also, at the critical stage, increased discharge of heat, as is evidenced by the observations of Drs. Leyden[2] and Senator[3].

The fall of temperature to the normal standard, is no doubt due to the cessation of those processes which induce the abnormal rise. But the rapidity of this fall seems to bear a relation to the loss which takes place by evaporation; and that is directly as the extent of the perspiration.

To this increased evaporation from the surface may also probably be attributed, in part at least, the fact that the temperature continues to fall till it reaches a point one or even two degrees below the normal.

Increased consumption of water is one of the chief phenomena of the febrile state: its increased elimination is the chief feature of the crisis. In the eruptive fevers the former results from the growth of the contagium; the latter from the sudden cessation of that growth.

[2] Deutsch. Arch. Vol. v.

[3] Op. cit.

CHAPTER XXVI.

EXHAUSTION OF SUSCEPTIBILITY.

The immunity from a second attack, enjoyed by those who have once suffered from the eruptive fevers, is one of the most remarkable features in the history of these maladies. It, therefore, calls for careful consideration.

Of no ordinary organic or inorganic poison can it be said that it acts but once in a lifetime. Habit, indeed, renders the system less susceptible to the action of many of them: but that is quite a different thing from a single dose, suddenly and rapidly administered, totally and for ever exhausting the susceptibility of the system to the action of the poison.

Such a very remarkable feature in the history of the eruptive fevers can only be explained on the supposition that, by the action of the contagium, there is produced some peculiar and indelible impression on the system, as a consequence of which the body no longer presents to the contagium all the elements requisite to its propagation.

We have seen that, for the production of the eruptive fevers, two factors are necessary; and that the cessation of the febrile symptoms, coincides with, and is consequent on, the exhaustion of the second.

It is this exhaustion of the second factor which constitutes the permanent impression left by an attack of one of the specific fevers.

Of what this second factor consists we do not in any case

know. We infer its existence from the facts with which we have to deal; and from the same facts we conclude that, though a constant, it is not an essential constituent of the human organism. We know that it is a constant element because, speaking generally, every one is susceptible to one attack of each of the eruptive fevers. And we know that it is not essential to the wellbeing of the body, because its exhaustion is followed by no other effects than immunity from a second attack.

That the mere reception of contagium into the system does not suffice to the production of disease, has been thousands of times demonstrated practically in the case of vaccinia and variola. Matter may be taken from a vaccine vesicle, and inserted into the arm of one who has never been vaccinated, with the certain result of producing in him a similar vesicle. Some of the same matter may, at the same time, and in the same way, be inserted into the arm of one on whom the operation had previously been performed with success, with the certainty that there will either be no result at all, or only a modified one.

And so with variola: one who has suffered from the disease may be inoculated with small-pox matter over and over again, without experiencing more discomfort than would result from inoculation with the matter of a simple pustule. It cannot be that the matter is not again absorbed; it can only be that the contagium, thus taken into the system, does not find in it, the second factor requisite to its propagation.

If the phenomena which follow the reception of the contagium into a susceptible system result from its propagation in that system: and if individual *susceptibility* consist in the possession of what we have called the second factor; it follows that individual *insusceptibility* is most likely to be due to the absence of that factor.

That the second factor is used up during the course of the febrile attack, and that it is not again reproduced, is an opinion

which we have also seen good reason to maintain. Exhaustion of susceptibility we, therefore, attribute to exhaustion, and non-reproduction, of the second factor requisite to the propagation of the contagium.

If any two contagia required and appropriated the same second factor, the action of the one would probably protect against the action of the other. Thus it is, possibly, that vaccination protects against small-pox.

CHAPTER XXVII.

THE DIFFERENT DEGREES OF CONTAGIOUSNESS OF THE ERUPTIVE FEVERS.

Regarding the mode in which the poisons of the eruptive fevers act, there are two different and antagonistic views. The one is that held by the advocates of the germ theory; the other that entertained by those who hold the physico-chemical theory of disease.

These two theories, though distinct, and even antagonistic, have one feature in common; each regards the blood as the seat of the morbid changes which accompany the development of the febrile state.

According to the germ theory, as usually held, these changes result from the propagation in the blood of a living organism which finds in that fluid all the materials requisite to its propagation.

According to the physico-chemical theory, the changes which take place in the blood, result from the entrance into it of a 'fragment of dead organic matter whose elementary particles are in some occult state of chemical union, and capable of imparting their condition to other substances susceptible of the same change[1].'

On either view, all the eruptive fevers ought to be equally contagious.

But this is notoriously not the case. All experience shows that small-pox is more contagious than typhus; and typhus than typhoid fever; while cerebro-spinal fever is generally believed

[1] Dr. Dougal: Transactions of Pathological Society of London, 1875.

to be non-contagious. This is a fact which it is simply impossible to explain on any view which regards the blood only, as the field in which the contagium is reproduced. Each contagium can with equal facility gain entrance into the blood: if all that were required for the action of each, were its reception into the circulation, each of the eruptive fevers would, *caeteris paribus*, be equally contagious, and equally communicable.

The contagiousness of a given eruptive fever depends on two things: first, on the quantity of contagium which passes into the surrounding atmosphere from the bodies of those suffering from it; and second, on the readiness with which the contagium thus eliminated reaches its second factor in the systems to which it gains entrance.

In considering this question we have, therefore, to take into account the part played both by the giver, and the receiver of the contagium.

The giver. It needs no argument to show that the quantity of contagium in the atmosphere, must play an important part in determining the spread of a contagious disease. The more numerous the contagium particles in the atmosphere of a room, the greater the chance of one or more of these particles being inhaled by those who breathe that atmosphere. The question which we have to consider is, why this chance seems to vary so much in the different eruptive fevers: why, for instance, an unprotected person cannot be for any length of time in the same room as a sufferer from small-pox, without contracting the disease; while an equally unprotected person runs so much smaller a risk in the case of typhus; why, in the case of typhoid fever, he runs scarcely any risk; and why, in the case of cerebro-spinal fever, he runs apparently none at all.

On the view which has been advanced as to the important part played by the second factor, all this is very readily explained.

We have seen that the seat of the local lesion is also the

seat of the second factor, and of that fecundating action which follows contact of the contagium with its second factor, and results in its propagation. Contact with the second factor is essential to the fecundation of the organisms; and only those organisms which have been thus fecundated, grow, and produce the phenomena of disease. This fecundating action is constantly going on in the seat of the local lesion, to an extent which is directly as the amount of the second factor which exists therein. The local lesion is, therefore, the locality in which the contagium particles are likely to be most abundant: and we know from experience that such is the case. The poison of small-pox is found chiefly in the pustules of that disease; that of measles in the discharges from the mucous surfaces; that of scarlatina in the discharges from the throat, and in the peeling cuticle; that of typhoid fever in the intestinal discharges[2].

The contagium being so abundant in, and so freely given off from, the local lesion, it follows that the contagiousness of each of the specific fevers, must, to some extent, depend on the seat of this lesion. If this be on the cuticular, or respiratory surface, the contagium will readily and freely pass into the surrounding atmosphere, and every facility be afforded for its inhalation by those in the neighbourhood of the sufferer. If the local lesion be so seated that the emanations or discharges from its surface, do not readily reach the atmosphere, as in typhoid fever, there will be little chance of the air being contaminated, and an equally small chance of the contagium being inhaled by those who breathe this air.

If, as in cerebro-spinal fever, the lesion be so situated as to render impossible the direct passage of germs from it to the

[2] We have seen that microscopic investigations into the nature of the changes which take place in some specific lesions, such as those of variola, typhoid fever, diphtheria, erysipelas, and sheep-pox, have demonstrated the existence in them of minute organisms which are believed to bear an important relation to the diseased processes; and we have further seen that there are good reasons for regarding these organisms as the cause of all the disturbance.

atmosphere, such contamination of the atmosphere as occurs in measles and small-pox, cannot take place: and the disease, though communicable, in the strictest sense of that term, will not be contagious in the ordinary sense of the word. It will be communicable, because some germs are almost certain to pass out of the system by one or other of the various eliminating channels: it will not be contagious, because the number of germs which thus pass out in a given time, will be so small as to render such contamination practically inoperative.

For the same reason that typhoid fever is much less communicable than typhus, cerebro-spinal fever is much less communicable than typhoid.

The contagiousness of a given eruptive fever depends, then, so far as the giver of the contagium is concerned, on the quantity of contagium which passes off from his body into the surrounding atmosphere in a given time: and that depends very much on the seat of the local lesion. The seat of the local lesion thus becomes an important agency in determining the degree of communicability of the particular form of fever in connexion with which it occurs.

In all forms of fever a severe attack implies a larger reproduction of the contagium, than does a mild one. Severe attacks are, therefore, more dangerous to those around. But that which determines the different degrees of communicability of the different eruptive fevers, so far as the giver of the contagium is concerned, is the relation which their local lesions bear to the surrounding atmosphere.

It so happens that in all the common eruptive fevers, the seat of the local lesion has a more or less direct connexion with the external atmosphere; and, therefore, they are all contagious.

Did there exist any specific fever, characterized by the possession of a local lesion which had no relation, direct or indirect, with the external atmosphere, but had its seat in some deeply situated tissue or organ, it is probable that evidence of con-

tagiousness would, in such a fever, be entirely wanting. Such a disease we have in cerebro-spinal fever[3].

[3] Cerebro-spinal fever is now generally regarded as closely allied in its etiology to the specific fevers. We think it should be ranked among them. In the nomenclature of disease issued by the College of Physicians of London, it is called 'a malignant epidemic fever.' The disease is a specific fever which is characterized by the peculiar seat of its local lesion; and to this peculiarity is owing both its great fatality, and the very slight extent of its communicability.

Regarding it as due to the propagation in the system of a morbid poison similar in nature to those which give rise to the other specific fevers, it is difficult to separate from it the idea of communicability. That it is not contagious in the sense in which small-pox and measles are so, there can be no doubt; but neither is typhoid fever. That it is communicable has, I think, been proved by the observations of Boudin, Hirsch, and Stokes. One instance given by Hirsch will suffice to show this. 'On the 8th of February, in the township of Sczakau, K., aged 20 years was taken ill; he was nursed by a woman, W., who had come for that purpose from the village of Sullenczyn. After the death of K. his nurse returned home, and there died, Feb. 26th, of meningitis. This was the first fatal case of the disease in Sullenczyn, with the exception of a previous one on January 15th. To the burial of this maid at Sullenczyn came the family of the farm-steward K., from the township of Potgass, accompanied by a servant D. and the daughter O. (aged 4 years) of the teacher R. in Potgass. After their return from the funeral, a little child of K. sickened and died within twenty-four hours; then the servant D., who died on the 4th of March; and finally the girl R., who died on the 7th of March.' (Ziemssen's Cyclopædia of Medicine, vol ii. page 697.)

When we consider how long a time elapsed, and how much discussion took place before the communicability of typhoid fever was recognised, we need not be surprised to find considerable difficulty in settling the same point in so comparatively rare, and so slightly communicable, a disease as cerebro-spinal fever.

The view which has been advanced in explanation of the different degrees of contagiousness of the common eruptive fevers, serves to explain the peculiarity in this respect presented by cerebro-spinal fever; and to remove the difficulty raised by the large mass of negative evidence which has been advanced in support of the view that the disease is not communicable.

If it be the case, as we have endeavoured to show, that the degree of contagiousness of each of the specific fevers which is characterized by the possession of a local lesion, is dependent on the more or less direct relation which this lesion bears to the surrounding atmosphere, then it inevitably follows that a disease, such as cerebro-spinal fever, in which the local lesion is seated in a cavity which is completely shut off from the atmosphere, and has no communication with it except through the very indirect means of the circulation, must be possessed of the property of communicability in the smallest possible degree. Variola is the most communicable of the eruptive fevers, because its local lesion is seated on the surface of the body, and, therefore, readily contaminates the atmosphere. Typhus fever, measles, and scarlatina possess this quality in a high degree because their lesions, though not so widely diffused over the surface

That eruptive fever in which the largest surface of local lesion is exposed to the atmosphere, will, *caeteris paribus*, be the most contagious. Hence we find that such diseases as small-pox, scarlatina, and measles, are very contagious; while typhoid fever, with its half concealed local lesion, is very slightly so; and cerebro-spinal fever, with its wholly concealed lesion, is so seldom communicated from the sick to the healthy, that the great majority of those who have studied the natural history of the disease, have come to the conclusion that it is not contagious.

The receiver. He too exercises an important influence in determining the readiness with which he takes a given contagious fever. This influence is generally recognised; and is usually referred to under the vague term of 'individual susceptibility.' What we have to do is to explain what individual susceptibility really is.

We have seen that the contagium, the first factor in the production of the eruptive fevers, is *per se* impotent for evil; and that it may be introduced into the blood without giving rise to any deleterious effects, unless it come in contact with its second factor; the *rapprochement* of these two being essential to the production of disease.

In the varying degrees in which this second factor exists in different individuals, and in its greater or less diffusion over

as that of variola, still bear a direct relation to the atmosphere. Typhoid fever is communicable in only a minor degree, because its local lesion bears only an indirect relation to the atmosphere which surrounds the patient; and because the discharges from this lesion pass from the body in a manner and combination which ensure their early removal from his neighbourhood. In cerebro-spinal fever the local lesion has its seat in a bony cavity, which is completely and specially shut off from the atmosphere, and from which nothing can pass into the atmosphere except through the devious and indirect route of the general and pulmonary circulations. It is scarcely possible for such a disease to be contagious, in the ordinary sense of that term; though it may occasionally be communicated; and the facts of the case are exactly in accordance with this. The degree of communicability which, on this view, should theoretically pertain to cerebro-spinal fever, corresponds exactly to that which we find it to possess.

the system, we find the explanation of the varying degrees of susceptibility to the action of a given contagium, presented by different people.

Each contagium has its own peculiar second factor; each second factor has its more or less localized seat (the nidus of the parasite). According as this seat is more or less localized, it will be reached by the contagium circulating in the blood with more or less difficulty: and directly as the readiness with which the first factor reaches the second, will, *caeteris paribus*, be the contagiousness of the malady to which it gives rise. If widely distributed, and readily got at through the circulation (as in small-pox), the disease will be very infectious: if confined to narrow limits, and with difficulty reached through the circulation (as in typhoid fever) it will be slightly so.

That which determines the degree of contagiousness of each of the eruptive fevers, so far as the receiver is concerned, is simply the facility with which the first factor reaches the second through the circulation.

Here illustration will serve better than argumentation. For this purpose we shall take one of the most, and one of the least, infectious of the eruptive fevers, small-pox, and typhoid fever.

In small-pox the second factor is widely distributed over the skin, and to a less extent over the mucous membrane of the mouth and throat. Of what it consists we have no accurate knowledge; and it suffices for our present purpose to know that it is intimately connected with, and widely distributed over, the skin.

A small-pox germ being inhaled, passes through the lungs into the circulation, and is sent along with the general column of blood. It will do no harm unless it come in contact with its second factor; and it is quite possible (and, no doubt, frequently does happen) that it may make the round of the circulation once and again, and may ultimately pass out through some eliminating organ, without entering a cuticular vessel, and, therefore, without doing harm. The extent of the cuticular

surface is so great, however, and the number of vessels which go to it so numerous, that the chances are against the probability of the contagium circulating for any time with the blood, without entering one of these: if it do so, it almost certainly comes in contact with its second factor, reproduces other germs and so gives rise to small-pox.

There are one or two curious facts in the history of small-pox which are better explained on this than on any other hypothesis.

It is a fact, for instance, that, in inoculated variola, the period of incubation is shorter than in the natural disease. On no view which regards the blood only as the seat of all the changes which take place, can this fact be explained. The contagium gains entrance to the circulation as rapidly when taken in by the lungs, as when it is inserted under the skin; the symptoms to which it gives rise ought, therefore, on the view that the blood is the seat of its action, to be as speedily developed in the one case as in the other.

Two agencies tend to shorten the period of incubation of inoculated variola—agencies whose operation is readily explained on the view advanced regarding the mode of action of the contagium.

In the first place, granting that during the period of incubation the contagium is being reproduced, and that the termination of that period marks the time at which its reproduction has reached a point at which disturbance of the economy must ensue; and granting further, that the febrile symptoms result from the growth of the contagium particles in the system—granting all this, it is evident that the larger the number of contagium particles which gain entrance to the system, the shorter is likely to be the period of incubation.

That period represents the time which is required for the reproduction of the quantity of contagium requisite to produce disturbance of the economy.

Suppose a thousand to be the number of contagium particles required for that purpose, it is evident that that number will sooner be produced from twenty germs, than it could possibly be from only one. Supposing that each germ produces four others, it is quite apparent that, starting with twenty, the requisite thousand will be got sooner than if we start with only one. Now in the natural variola it is doubtful if more than one contagium particle is originally taken into the system; sometimes there may be more, but probably not often. In inoculated variola, on the other hand, it is certain that very many are introduced. The exact number it is impossible to determine, but from what we know of the relation which the small-pox poison bears to the matter of its pustules, it is probable that the quantity of matter used for inoculation would contain not less than twenty or thirty, it might be even two or three hundred, contagium particles.

In the larger number of germs which gain entrance to the system we have an adequate explanation of the fact that inoculated variola has a shorter period of incubation than the natural disease.

This is an agency which, it is evident, may operate in any of the specific fevers. The variation in the duration of the period of incubation which is noted in connexion with each of them may thus be, to some extent, explained.

In the case of variola there is another agency which may aid in shortening the period of incubation of the inoculated disease. Contact with its second factor is necessary to the propagation of the contagium. In small-pox this second factor has its seat in the skin; such being the case it is evident that contact of the two factors, and, therefore, the symptoms to which the propagation of the contagium gives rise, may be more speedily brought about when the first factor is introduced directly into the cuticular circulation, than when it reaches it indirectly through the lungs and general circulation. In the former case, it is brought into immediate contact with its second factor, and at once begins

to be propagated; in the latter, it may circulate in the blood for some time before it enters a cutieular vessel. On this view of the matter, the period of incubation of inoculated variola *ought* to be shorter than that of the natural disease.

There is another interesting fact in the history of variola, which it may seem difficult to explain in any way, but of which this hypothesis also affords a feasible explanation. Inoculated variola is gnerally milder than the natural disease. On no view hitherto advanced can that be explained; on that now advanced, we think it may. It has just been said (and, though incapable of proof, the fact is so obvious that no one will be disposed to deny the possibility of the occurrence) that a contagium particle may enter the circulation through the lungs, and may circulate in the blood for some time, possibly for days, without coming in contact with its second factor. It is evident that the larger the quantity of the second factor, the less the chance of such an occurrence. We know also that the larger the quantity of the second factor in the system, the more violent is the attack. Those whose systems contain much of the second factor are thus more susceptible, and more apt to suffer severely, when seized, than those whose systems contain less of it. Each is equally likely to inhale the contagium, but in the latter there is a greater chance of its again passing out, without coming in contact with its second factor.

There is little doubt that such an occurrence does sometimes take place, and that the small-pox poison enters, circulates in, and passes out of the system, without reaching its second factor, and, therefore, without doing harm. Those in whom this occurs most readily are those whose systems contain little of the second factor, and who, if they took the disease, would have it mildly.

Such is what obtains in the natural disease. Those who have much of the second factor, and who, when seized, suffer severely, have little chance of escape if the contagium enter their system. Those who have little of the second factor, and who, when seized,

suffer much less severely, have a greater chance of escape, in consequence of the increased chance of the contagium passing from their systems without coming in contact with its second factor.

When the poison gains entrance by inoculation, there is no such chance. Here there is no selection. All are inoculated without reference to their susceptibility. The contagium is introduced directly, and in larger quantity, into the cuticular circulation, and is thus in every case brought into immediate contact with the seat of its second factor. The chance of escape is thus done away with; all who thus receive the poison, no matter what their natural susceptibility, take the disease—those who have much of the second factor, severely; those who have little of it, mildly. It is obvious that in inoculated variola, in which all alike are seized, the proportion of mild cases, must be very much greater than in the natural disease, in which paucity of the second factor so much favours the chance of escaping the disease altogether.

The fact that the natural disease may be as mild as the inoculated, and that the inoculated may be as severe as the natural, sufficiently shows that inoculation, as such, is not the sole cause of the mildness of cases so induced.

Let us consider now the case of typhoid fever.

Of the common eruptive fevers, this is the least communicable. To so slight an extent is it so, that by many it is not regarded as contagious. There are, however, facts sufficient to show that it may thus be communicated; but the paucity of such facts, as compared with the frequency of the disease, sufficiently shows that, in the matter of contagiousness, it differs materially from the other common eruptive fevers.

We have seen that the degree of contagiousness of a given eruptive fever depends (*a*) on the quantity of its contagium which exists in the surrounding atmosphere, and (*b*) on the readiness with which this reaches its second factor through the circulation.

The former depends on the seat of the local lesion (in which the reproduction of the contagium chiefly takes place) with reference to the surrounding atmosphere; the latter on the extent of distribution of the second factor.

Typhoid fever is the only one of the common eruptive fevers in which no direct relation exists between its characteristic local lesion, and the surrounding atmosphere. Whatever is given off from its lesion, passes, not directly into the atmosphere, but gains exit from the body with the intestinal discharges; and with them is speedily removed from the atmosphere which the patient breathes. So far as the giver of the contagium is concerned, typhoid fever ought, therefore, to be the least contagious of the common eruptive fevers; and all experience shows that it is so.

Of the extent of distribution of the second factor we judge by the extent of tissue involved in the local lesion. In small-pox, the most contagious of all the eruptive fevers, the local lesion may be very extensive, involving nearly the whole of the cuticular, and part of the mucous surface. In typhoid fever the local lesion is confined to narrow limits, the glands scattered over a foot or two of the small intestine. It is only in this limited space that the contagium of typhoid fever finds that second factor, contact with which is essential to its propagation. The difficulty which the contagium experiences in reaching its second factor in so narrow a compass, is one of the chief causes of the slight degree of contagiousness which belongs to this form of fever.

Suppose that a typhoid germ gains entrance to the circulation. It will be sent from the heart along with the general column of blood; it may pass into the carotids, the subclavians, or down the aorta and into the iliac arteries, or into any of the aortic branches except those which lead to the glands specially involved in the disease, without the chance of being propagated, and, therefore, without the chance of doing harm.

Contrast with this what takes place in the case of small-pox,

and the importance of the extent of distribution of the second factor as an agency in determining the degree of contagiousness of the eruptive fevers, will be apparent.

In small-pox, the germ may pass into the carotids, the subclavians, or down the aorta and into the iliac arteries, in short, into any of the main channels of the circulation, and still reach a cuticular vessel. Only in the visceral arteries does it not have this chance. The quantity of blood which goes into the main arteries, forms such a large proportion of the circulating fluid that the chances are much in favour of its containing the contagium.

In typhoid fever, on the other hand, the quantity of blood which goes to the glands involved in the local lesion, is such a fractional portion of the general mass of the circulating fluid, that the chances must be very much against its containing the minute particle which constitutes the contagium. There are, too, so many chances in favour of the contagium passing out of the system by the lungs, skin, or other eliminating organ, that it is probable that the majority of typhoid germs which gain entrance to the circulation through the lungs, or otherwise than through the glands specially involved in the disease, are eliminated without ever coming in contact with their second factor, and, therefore, without causing disturbance.

The degree of contagiousness which, according to this view, should theoretically pertain to typhoid fever, corresponds very closely to that which experience shows it to possess.

But the lungs are not the only channel through which the contagium may gain entrance to the system. It may be taken in with the food or drink. The poison of typhoid fever does frequently enter the system through the alimentary canal, especially through the medium of contaminated water; and experience shows that, when thus received, it acts more certainly than when inhaled from the atmosphere.

This result may be due to one of two causes :—(*a*) the water may

contain more contagium than the atmosphere; or (*b*) the contagium may reach its second factor more certainly by way of the digestive canal, than by way of the circulation.

The first cause is that to which the difference is usually ascribed. The poison is believed to be so mixed up with the contents of the bowels that it does not readily pass into the atmosphere, but attaches itself to the fluids in which it exists, and with them passes into the soil, and so into the water of wells, more readily than into the atmosphere. That is a very easy, and probably to some extent true, explanation of the fact with which we are dealing; but there are reasons for not fully assenting to it.

In considering the question of the attachment of the contagium to fluids, it is necessary to take a wider view of the matter; and to study the habits of the contagium of typhoid fever in this respect, along with those of the other eruptive fevers.

In small-pox the contagium is as intimately mingled with the fluid of the pustules, as in typhoid fever it is with the intestinal discharges. The liquid secretions which flow from the mucous surface in measles contain in an equal degree the contagium of that malady. The discharges from the throat in scarlatina contain in an eminent degree the poison of that disease. But in none of these cases do we assume that the poison remains fixed in the fluid. We do not see a sufficient reason why, in this respect, the contagium of typhoid fever should be separated from the other contagia to which it is generically allied; and have assigned to it properties and habits which none of these possess; especially as the fact on which this assumption is based, is, as we shall presently endeavour to show, more satisfactorily explained in a way which does not so isolate the poison of typhoid fever from the other contagia.

Theoretically, there is no reason why the contagium of typhoid fever should not pass into the surrounding atmosphere from the stools which contain it, as readily as the contagia of small-pox, measles, and scarlatina pass off from the fluids

in which they exist. That the poison of typhoid does frequently so pass into the atmosphere, is proved by the fact that the disease is often produced by exhalations from cesspools, and by emanations from drains, into which typhoid stools have passed. If one typhoid stool may thus give off its contagium, there is no reason why all should not do so.

From a cesspool containing typhoid stools, there does not necessarily pass into the soil more of the poison than passes into the external air. But the poison which percolates through the soil into a well, is not dissipated abroad in the same way as that which passes into the atmosphere. Of a hundred germs which pass from the cesspool, seventy may pass into the atmosphere, and thirty into a well; but the seventy will be scattered abroad in the external air, while the thirty will be retained in the narrow limits of the well; and, in consequence of such retention, be a greater source of danger than the seventy which were scattered about in the atmosphere.

But, it may be said, if the typhoid stools contain so much of the contagium; and if the contagium be as readily given off from these into the surrounding atmosphere as the poisons of the other specific fevers are given off from the fluids which contain them, surely the attendants on those suffering from typhoid fever ought more frequently to take the disease; and surely it ought sometimes to spread in the wards of a general hospital in which those suffering from typhoid fever are freely mixed up with the general cases.

If the entrance of the contagium into the blood were all that was necessary, most assuredly the disease would thus be frequently communicated and spread. But we have seen that the presence of the poison in the blood is not enough: the contagium is impotent for evil until it is fecundated by contact with its second factor; and the contagiousness of a given eruptive fever, depends on the readiness with which this is reached by the first factor through the circulation.

In typhoid fever we have seen that the second factor exists only in a few intestinal glands, and that the chances are very much against a germ circulating in the blood, ever reaching so limited a locality. But it is very much otherwise if the germ be situated in the intestinal contents. In the circulation the chances are all against its reaching these glands; in the digestive canal they are all in favour of its doing so: and if it pass with the intestinal contents as far down as the ileum, its absorption by one of the glands containing its second factor, becomes almost a matter of certainty.

According to this view of the matter, water containing the poison of typhoid fever, ought to communicate the disease more certainly than an equally contaminated atmosphere; and all experience shows that such is the case. Typhoid fever is more readily communicated through drinking water than through the atmosphere, first, because the poison is more likely to be retained in a well than in an equally limited extent of the external atmosphere; and secondly, because the contagium reaches its second factor more readily, and more certainly, by way of the digestive canal, than by way of the circulation.

The magnitude of the danger which attends the reception of the poison of typhoid fever into the digestive canal, is well illustrated by what occurs when a little of that poison is mingled with milk; a very slight contamination of the milk being sufficient to produce most serious results. The history of the various outbreaks of the disease which have been traced to this cause, shows that contaminated milk is a greater source of danger than the water from which it receives the poison. It is so, first, because milk is used only as an article of diet, and is, therefore, all taken into the alimentary canal; while water is used for many other purposes: and, second, because the germs in the water are more frequently destroyed by boiling, than are those in the milk.

So marked is the infecting power of contaminated milk, that

it has been supposed by some that typhoid germs find in that fluid the pabulum requisite to their propagation, and that to such propagation taking place in the milk, is to be ascribed the intensity of its infecting power[4]. Such a hypothesis is quite unnecessary: the two reasons just given being adequate to explain all.

The reception of the poison of typhoid fever through the alimentary canal, bears a close resemblance to the production of variola by inoculation. The peculiarity in each case, is that the poison is brought into direct contact with its second factor, and is, therefore, sure to be propagated. In either case the passage of the contagium into the circulation through the lungs, involves a chance—in the case of typhoid fever a very great chance—of its passing out through some eliminating organ without coming in contact with its second factor.

But the microscopist and the chemist may say 'if the seat of the local lesion contain something which is essential to the propagation of the organism, surely we should be able to detect its presence, and demonstrate its existence, in a more certain way than by such pathological evidence as has been advanced.'

A similar objection was raised by the microscopist against the view that contagium consists of germs; but it was shown that the true reason for his being unable to see the germs was, that they were too minute to be readily brought within range of his vision; and that the particulate nature of contagium had been demonstrated in other ways, and without his aid. To his present objection the same argument applies, with the additional one, that the second factor is not necessarily particulate; and that, therefore, it does not necessarily come within his province to express an opinion upon its presence.

No such reply can be given to the chemist; but to him it may be said—Is your science so advanced, and so perfect, that

[4] Lancet, vol. i. 1876, p. 644.

you can detect by its aid the presence of everything which exists in nature? Are there not many substances whose existence you recognise, but whose presence chemical science is unable to demonstrate? Can you, for instance, by all the aids of your science tell us, what we by our unaided senses can tell you—that this is cod, and that is haddock; that this is beef, and that is mutton; that this is grouse, and that is partridge; that this is snipe, and that is woodcock? Or can you tell us what it is that gives to each animal an odour so peculiar that, by the sense of smell alone, one may distinguish a horse from a cow, a dog from a cat, a sheep from a goat, a fox from a badger? Or, more wonderful still, can you tell us what it is that enables a dog by its nose to recognise his master, and unerringly to track his course over ground which has been traversed by many other men, the scent of whom he must perceive, but at once distinguishes from that of his master?

It is a practice among shepherds, when a ewe dies, to get another one, which has lost her lamb, to suckle the one whose mother is dead. But the foster-mother at once finds out that it is not her own lamb, and refuses to suckle it; and she cannot be got to do so until the skin of her own dead lamb is fixed on the living one. She is deceived by the odour of the skin, and allows the lamb, which she before butted away, to suck her teats. One cannot watch the actions of ewes and lambs during the first few days of the latters' existence without seeing that it is by the sense of smell that the mother distinguishes her own offspring.

The various instances which have been given of the existence of substances whose presence the chemist cannot demonstrate, suffice to show that his inability to detect the presence of what we have called the second factor, in the seat of the local lesions of the eruptive fevers, cannot be regarded as a valid argument against its existence.

Such an objection on the part of the chemist, is more than met by the broad and undeniable fact that each parasite has a

special nidus in which alone it is propagated. The nidus necessarily contains something which is essential to the propagation of the parasite, and which does not exist over the body generally. The time may come when the chemist will be able to tell us what this substance is: meantime, his inability to do so cannot overturn the positive evidence of its existence, gained from a study of the natural history of parasitic organisms.

We have now considered the whole of the phenomena presented by the eruptive fevers; and have found that the view which regards the poisons of these diseases as parasitic organisms, affords an adequate explanation of the occurrence of each of their symptoms and phenomena. Their essential phenomena result from the growth of the organism; their incidental, from the peculiarities of the parasite.

CHAPTER XXVIII.

RELAPSING FEVER.

Regarding the mode of production of its essential phenomena, relapsing fever does not differ from the other forms of fever which have already come under our notice.

The increased consumption of nitrogen, the increased consumption of water, the increased rapidity of the circulation, and the præternatural heat, are all produced in the same way as in the eruptive fevers: they are all due more or less directly to the propagation of the contagium, and to the consumption by its germs, of the materials destined for the nutrition and repair of the tissues.

So far as concerns the mode of production of the febrile state in relapsing fever, there is, therefore, nothing to add to what has been said regarding the mode of production of the same state in the eruptive fevers.

But, though possessing much in common with the eruptive fevers, relapsing fever is separated from them by some very prominent points of distinction, which render it necessary for us to consider this form of fever by itself.

The peculiarities by which relapsing fever is distinguished from the eruptive fevers are as follows:—

1. It possesses no characteristic local lesion.
2. During the fever a foreign organism is found in the blood.
3. The course of the febrile symptoms forms the distinctive feature of the disease.
4. One attack confers no immunity from a second.

We shall consider these peculiarities separately and in the order enumerated.

1. *The absence of a local lesion.*

When considering the eruptive fevers we saw that the contagium of each was not only an organism, but a parasite, requiring a special nidus for its development; we further saw that this nidus was the seat of the local lesion; and that this lesion was the necessary result of the action which takes place in the nidus.

The distinctive feature of the eruptive fevers—the possession of a characteristic local lesion—is due to the fact that the nidus in which the contagium finds the material necessary to its propagation, is limited to a particular organ, or part, of the body.

If this second factor, instead of being localized in a particular part of the body, had its seat in the blood—if instead of existing only in skin, in mucous membrane, or in intestinal glands, it had its seat in the circulating fluid, and was thus equally distributed over the body—and if the contagium, instead of finding the second factor necessary to its propagation only in this or that organ or tissue, found it in the blood of all parts of the body—if such were the case, it is evident that the general phenomena to which the growth and propagation of the contagium give rise, would be produced without the development of a local lesion.

This is what takes place in relapsing fever.

The poison of that disease is a living organism, which grows in, and at the expense of, the body in which it is propagated. Thus acting, it is a parasite. As such it requires for its propagation something more than the bare materials necessary to organic growth. This something it finds in the blood of man.

If the localization of the second factor in a particular organ or tissue, play the important part which has been attributed to it in the eruptive fevers; and if, in relapsing fever, there

be no such localization, but a general distribution of the second factor over the circulating fluid, it is evident that the phenomena which, in the eruptive fevers, are due to this localization of the second factor, will, in relapsing fever, be conspicuous by their absence. The phenomenon which, in the eruptive fevers, was attributed to this cause, was the local lesion. One of the distinctive features of relapsing fever, is the absence of such a lesion.

The want of a characteristic local lesion in relapsing fever we, therefore, attribute to the circumstance that the second factor requisite to the propagation of its contagium, is not localized, but is generally distributed in the blood.

We shall find that this view also affords a ready explanation of the other peculiarities of relapsing fever.

2. *The presence of an organism in the blood.*

In 1868 Obermeier[1] discovered that the blood of those suffering from relapsing fever often contained a foreign organism presenting to the eye the appearance of minute spiral fibres.

Subsequent observations have established, first, that these organisms are never absent from the blood during the period of fever; and second, that they very speedily disappear after defervescence. They are present during the pyrexia, and absent during the apyrexia.

Such are the facts. What we seek is their interpretation.

What is the relation of the organism to the fever? That it is not accidental is certain. The organism causes the fever; or the fever gives rise to the organism.

(*a*) The view that the fever causes the organism, is that advocated by the opponents of the germ theory.

The main argument adduced in favour of this view is

[1] Centralblatt, 1873, No. 10.

'that the form taken by many minute growths depends not upon the germ, but upon the nature of the medium in which it grows[2].' And it is presumed with reference to the spirillæ of relapsing fever, 'that the soil is suitable for their development during the febrile process, and unsuitable when the febrile process is completed[3].'

But if the febrile process induce a state of the blood, which favours the development of these organisms, why are they not found in other forms of fever? There are many maladies during whose course the febrile state is as marked as during relapsing fever, but in not one of them has the spirilla ever been found.

Then again, on this view of the matter, how are we to explain the alternation of periods of pyrexia and apyrexia? And if this were explained, how are we to account for the cessation of such alternations, and the permanent restoration of health?

That the soil is suitable for the development of the spirilla during the pyrexia, and not during the apyrexia, is evident: but we shall presently give of this, an explanation which does not favour the view that the pyrexia causes the spirilla.

To support this view there is, indeed, little or no evidence. There seems to be no possibility of explaining by it the phenomena which present themselves in the course of relapsing fever.

The opinion that the fever causes the organism we, therefore, regard as unsupported by evidence, and as inadequate to explain the phenomena with which we have to deal.

(*b*) In support of the opposite, and alternative opinion, that the organism causes the fever, various arguments may be adduced.

1. Independently of the presence of an organism in the blood, there is very strong evidence that the poison of relapsing fever, like those of the eruptive fevers, is an organism.

[2] Murchison in Transactions of Pathological Society of London, 1875.
[3] Ibid.

2. The growth in the system of millions of organisms, is competent to produce the phenomena of the febrile state.

3. A peculiar and distinctive organism is invariably found in the blood during the pyrexial stage of relapsing fever.

'That a parasite so clearly determined as this, abounding in relapsing fever, and never having been found thus far in any other disease, must be closely connected with the development and spread of the affection in question, is hardly to be doubted' (Lebert).

When considering the eruptive fevers we found (*a*) that the organisms which gave rise to them were propagated in the seat of the local lesions; and (*b*) that they were propagated in that locality because it was there that, as parasites, the contagium particles found the second factor essential to their reproduction. We also found (*c*) that such of these lesions as had been examined were invariably associated with the development of organisms in the affected tissues; and we came to the conclusion (*d*) that the organisms found in these lesions, were the cause of the morbid process.

In relapsing fever we find no such morbid process, no such localization of the second factor, and no localized growth of organisms. But we find the same evidence of the introduction of an organism from without, as we found in the eruptive fevers; we find, too, the same evidence of its propagation in the system; and with this, we find an organism abundantly present in the blood. The organism is thus distributed in the circulating fluid, and not aggregated in any particular organ or tissue, because the second factor essential to its propagation as a parasite, exists in the blood, and is not, as in the eruptive fevers, confined to a particular tissue.

The spirilla of relapsing fever we, therefore, regard as bearing to that disease the same relation that the organisms found in

the local lesions of the eruptive fevers, bear to the maladies with which they are associated.

In each case the evidence is all in favour of the view that the organism is the cause of the disease.

3. *The course of the febrile symptoms forms the distinctive feature of the disease.*

The characteristic feature of relapsing fever is the relapse. There is a febrile attack of six or seven days' duration; then a period of freedom from fever of a week's duration; then another febrile attack of shorter duration than the first; and then another period of freedom from fever, which is generally permanent: but there may be as many as four or five relapses.

During each period of pyrexia, the spirilla is found in the blood; during each period of apyrexia, it is absent. The pyrexia we have attributed to the propagation and growth of the organism; the apyrexia we must attribute to its absence. And if we can explain the cessation of its propagation, and the coincident decline of the fever, we shall have accounted for the distinctive course of relapsing fever.

The absence of the spirilla during the apyrexia may be due either to some peculiarity of the contagium, or to some peculiarity of the second factor.

If the contagium were an organism which naturally went through a series of changes involving alternate periods of activity and repose; and if the phenomena of the febrile state, were the result of such changes as occurred only during the period of activity, it is evident that the propagation of such an organism in the system, would give rise to a malady characterized by alternations of pyrexia and apyrexia. The spirilla might thus give rise to relapsing fever.

But if such were the case—if each febrile attack corresponded to the advent of another period of active growth of the parasite, we should probably find some change in its external appearance,

some evidence of a further development of the organism. We should probably find, too, that it was present to some extent during the apyrexia.

But such is not the case. The spirilla is found only during the pyrexia; and presents in the second, third, and fourth seizures exactly the same appearance which it presented in the first.

Again, if such were the explanation of the distinctive course of relapsing fever, we should almost certainly find the course of the malady the same in each case. If the contagium had certain normal stages of development to go through, these stages would always be the same; and the course of the symptoms to which they gave rise would be the same also. But this is not in accordance with fact. The number of pyrexial attacks is generally two; but there may be only one; or there may be three, four, five, or even six.

For these reasons we conclude that the cause which gives rise to the distinctive features of relapsing fever, is not to be found solely in some peculiarity of its contagium.

The only other possible cause is some peculiarity of its second factor.

(*b*) The peculiarity of the second factor of relapsing fever is its general distribution in the circulating fluid. Could such a peculiarity induce the phenomenon now before us—a re-accession of fever?

In the eruptive fevers we attributed the decline of the febrile symptoms to the exhaustion of the second factor: in relapsing fever we attribute their decline to the same cause.

The permanent duration of convalescence in the eruptive fevers, we attributed to the fact that this exhaustion is permanent—that the second factor is not reproduced: the absence of such permanency in relapsing fever, we attribute to the opposite cause—the second factor *is* reproduced.

The occurrence of the characteristic second seizure of relapsing

fever is due to the circumstance that the second factor is reproduced in the blood before the first is thoroughly eliminated from it: its early reproduction leading to the renewed development of such germs as remain, and a consequent second pyrexial attack.

If such be the explanation of the relapse, it is evident that cases might occur in which, either from more rapid elimination of the first factor, or from more tardy reproduction of the second, the former might be thoroughly eliminated before the latter was reproduced: the consequence would be the absence of the usual characteristic of the disease—there would be no relapse; the attack being completed by one seizure.

That such cases do occur is an established fact in the history of relapsing fever. Of 2425 cases which occurred in 1843, and which have been collected by Murchison [4], 724 had no relapse. Of 100 consecutive cases under Murchison's own care in 1869, four were completed by one pyrexial attack. Of 400 recorded by Litten [5], six had no relapse.

Again, if the second factor be so frequently and so quickly renewed, it is evident that the process might be repeated more than once, and that a third seizure might be caused in the same way as the second, and a fourth in the same way as the third: the sole requisite to the production of a pyrexial attack, being the reproduction of the second factor prior to the complete elimination of the first.

Such cases are observed in every epidemic. Of 1500 cases collected by Murchison a second relapse, i.e. a third pyrexial attack, occurred in 109, or in 1 out of 14; a third relapse in 9, or in 1 out of 166; and a fourth relapse in one of the 1500. Of Litten's 400 cases $35\frac{1}{2}$ pct. had a second relapse (a third attack), while 7 of them had 3, and 3 had 4 relapses.

[4] Op. cit. 2nd edition, page 379.

[5] Quoted by Burdon-Sanderson, Report of Medical Officer of Privy Council, New Series, No. iii. p. 42.

The mode of production of each seizure is the same: the second factor is reproduced before the first is eliminated.

The course of events in a case of relapsing fever is as follows:—a germ is received into the system, and immediately begins to grow and be reproduced in the blood: in time a sufficient number is produced to cause pyrexia; in the course of six or seven days the rapid development of the organism leads to exhaustion of the second factor: in consequence of such exhaustion the contagium ceases to be reproduced, and there is a rapid decline of the fever. But the mass of contagium existing in the blood cannot at once, and suddenly, be eliminated. Some days must elapse before the process is completed. But before the expiry of this time, the second factor is reproduced, and the conditions essential to a pyrexial attack again present themselves.

It is probable that the second factor is not absent from the blood for more than a few days, the greater part of the interval between the first and second seizures, being really the period of incubation of the latter.

In the eruptive fevers we saw good reason to believe that the period of incubation was shorter in cases in which there were many germs received into the system than it was in cases in which there were only a few. The same reasoning applies to relapsing fever. It is evident that the germs remaining in the system at the commencement of the period of incubation of the second attack, i. e. at the time of reproduction of the second factor, are likely to be much more numerous than the number originally received from without at the commencement of the corresponding period of the first: the latter is, therefore, likely to be of longer duration than the former: and this is in accordance with the facts of the case. The period of incubation of both attacks, but especially of the first, is apt to vary in duration; but as a rule it is longer in the primary than in the secondary seizure. The variations which each

manifests, probably result from the varying quantity of contagium particles which originate the seizure.

The mode of production of subsequent seizures, is the same as that of the second.

But the question arises, Why do the alternations of pyrexia and apyrexia come to an end? Why should there be only two or three seizures, and not ten or twelve?

The probable explanation of this is, that the exhaustion of the second factor during a pyrexial attack, is so complete that it cannot at once be replaced; and that the oftener this exhaustion is repeated the more tardy the action by which it is reproduced.

In other words, after having been only once used up, the second factor is more readily reproduced than after it has been exhausted two or three times: the readiness with which it is re-formed, diminishing with each successive seizure, till a time is reached at which its reproduction is so delayed, that the whole of the contagium is eliminated from the system before the second factor re-appears in the circulation. The advent of this period ushers in permanent convalescence.

In accordance with this view we find that, as a rule, each successive attack is shorter and milder than the preceding one. It is so, because after each successive attack there is reproduced less and less of the second factor.

In Litten's cases the mean duration of the 1st attack was 6.6 days

,,	,,	2nd	,,	4.9 ,,
,,	,,	3rd	,,	3.1 ,,
,,	,,	4th	,,	3.1 ,,
,,	,,	5th	,,	2.3 ,,

4. *One attack confers no immunity from a second.*

The renewed susceptibility to the action of the poison of relapsing fever, manifested by those who have already suffered from the disease, is to be explained in the same way as the relapse.

Both are due to the fact that the exhaustion of the second factor is only temporary.

We have seen that in the eruptive fevers, in which one attack confers, as a rule, permanent immunity, the second factor is localized in some particular organ or tissue; while in relapsing fever, it is some ingredient of the blood.

Now it is evident that a permanent impression may be more readily produced on a formed and stable organ, than on a constantly changing fluid like the blood. A contagium which finds its second factor in an individual organ or tissue is, therefore, more likely to produce a permanent impression than one which finds its second factor in the circulating fluid.

Moreover, it is to be noted that some of the tissues which are the seat of lesions in the eruptive fevers, are apt to undergo permanent change in the ordinary course of nature—they are, in early life, the seat of actions and peculiarities which are normally and naturally lost as adult life and old age are reached. We would specially instance the tonsils, which are involved in scarlatina; and the intestinal glands, whose affection forms the characteristic lesion of typhoid fever.

The tonsils are in early life the seat of an activity, and of a tendency to inflammatory enlargement, which diminish as adult life is reached, and are altogether lost with the attainment of more mature years. The question of the exact function of these glands, is one which we need not stay to consider. It is sufficient for our present purpose to note the fact that in early life (from two or three years of age up to fifteen or sixteen) these glands are more active, and more liable to inflammatory enlargement, than at any subsequent period.

This period of activity of the tonsils, corresponds to the period of greatest susceptibility to the action of the poison of scarlatina. The system is then most susceptible to the action of that poison, because the particular organ which contains the second factor essential to the propagation of the contagium, is then in its state

of greatest activity and perfection. As this activity declines, it is probable that the second factor diminishes in quantity, and ultimately disappears. In this way there may be brought about a natural insusceptibility to the action of the poison of scarlatina, similar to that which results from an attack of the disease.

In keeping with this view of the matter we find that adults who are not protected by a prior attack are often freely exposed to scarlatina without contracting the disease; while young people, similarly unprotected, and much less exposed, very readily take it.

The immunity enjoyed by mothers of families, physicians, and nurses, is often attributable to their having already suffered from the disease; but by no means always. All physicians must be familiar with cases, either in their own persons, or in others, in which adults who have never had scarlatina, have been much and frequently exposed to that disease without suffering from it. Such immunity is almost unknown in children. Those of mature years enjoy a natural immunity from the disease, identical with that enjoyed by children who have already suffered from it: in neither does the system contain the second factor requisite to the propagation of the contagium; in the one, the second factor is lost in the ordinary course of nature; in the other, it is exhausted by the contagium, and is not again reproduced.

The same mode of reasoning applies to typhoid fever.

The glands specially involved in that disease, are not equally prominent and active all through life: their period of greatest activity is from ten to thirty years of age, more or less; and that corresponds exactly to the period of greatest susceptibility to the action of the poison of typhoid fever.

In infancy these glands are indistinct; but they gradually become more developed after birth, and by the age of two or three years are quite perceptible. From that time they increase in size, and presumably in functional activity, and at the end of the first decade of existence are prominent objects in the

walls of the ileum. They continue to increase in prominence, and by the end of the second decade have reached their full size. During the third decade they remain stationary. During the fourth they show signs of diminishing in size, and, therefore, probably in functional activity. They continue to decrease as life advances, and by the end of the sixth decade, are so reduced in size and importance, that it is probable that their period of functional activity has ceased.

The periods of insignificance, of importance, and of subsequent decline, noted in the development and history of these glands, correspond exactly to the periods of greater and less susceptibility to the action of the poison of typhoid fever.

In infancy, during which these glands are practically non-existent, typhoid fever is unknown. After two or three years have passed, and when the glands begin to come into notice, the liability to the occurrence of the disease, begins to manifest itself, but in so slight a form that it is apt to escape recognition. Only indeed since 1848, when West demonstrated the identity of the two maladies, has the old *febris infantum remittens* been recognised as a mild form of typhoid fever. By the end of the first decade, the susceptibility to the action of the poison is pronounced: it increases during the second; reaches its height towards the end of it: remains pretty stationary during the third: declines during the fourth: and continues to decline till, at the end of the sixth decade the susceptibility to the disease is so slight that it may be regarded as practically worn out.

Finding the liability to the occurrence of typhoid fever correspond so closely and so intimately to the period of activity of the glands whose lesion forms the characteristic feature of the malady, we cannot avoid the inference, that the presence of these glands, or of something which they contain, is essential to the action of the poison of that disease.

Regarding that poison as a parasitic organism, which is propagated in the system during the course of the malady to which it

gives rise, and whose action is intimately connected with its organic development, it seems to us that the view which regards the intestinal glands as the nidus in which the parasite finds the second factor necessary to its propagation, is the one which affords the best and most satisfactory explanation of the occurrence of the phenomena with which we have to deal.

The same insusceptibility to the action of the poison of typhoid fever, which is naturally and slowly developed as years advance, may be artificially and rapidly induced by the destruction of the intestinal glands during an attack of that disease.

What has been said regarding scarlet and typhoid fevers, and the mode of production of their local lesions, serves to illustrate the manner in which localization of the second factor may lead to permanent immunity from the disease.

It serves also to show how the absence of such localization of the second factor may, in relapsing fever, be the cause of the absence of immunity from a second attack which characterizes that disease.

We have now considered all the phenomena of the common specific fevers, and have found them to be such as may be explained by the growth and propagation of an organism in the system.

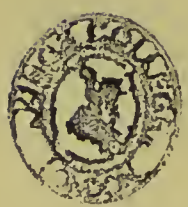
The theory as to the causation of the specific fevers, to which we must give our adherence, is not that which explains this or that phenomenon, or even this or that fever, but that which best explains the whole of the phenomena which present themselves for our consideration.

We think we may claim for the theory advanced in these pages the distinction of being the only one which fulfils this condition.

Of the phenomena presented by the contagium out of the

body, of the phenomena to which its reception into the system gives rise, of those which accompany its reproduction in the system, as well as of those which follow such reproduction, it leaves not one unexplained.

That it should be competent to explain the occurrence of phenomena so numerous, so varied, and sometimes so apparently contradictory, may be regarded as the crowning argument in favour of that theory which attributes these phenomena to the growth and propagation in the system of minute parasitic organisms.



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