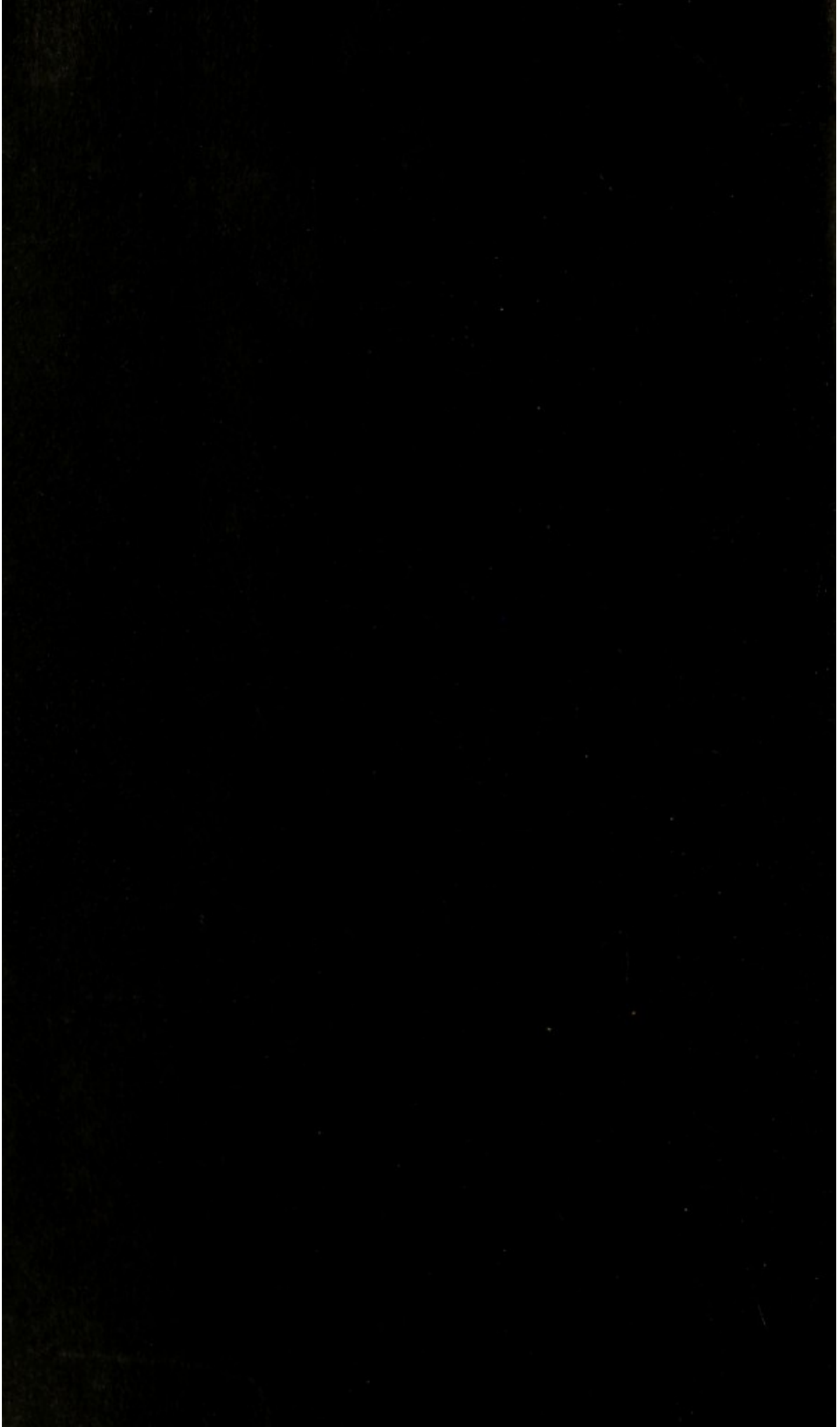
On the nature of the intestinal lesion of enteric fever / by T. J. Maclagan, M.D.



ON

THE NATURE

OF THE

INTESTINAL LESION OF ENTERIC FEVER.

BY

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INTESTINAL LESION OF ENTERIC FEVER.

THAT the intestinal lesion of enteric fever is specific in character and peculiar to that disease, and that the discharges thrown off from the bowels after the establishment of that lesion contain the poison of enteric fever, and are capable of imparting that disease to healthy individuals, are two propositions which have been abundantly proved of late years.

Whether the alvine dejections form the sole means of communicating the disease, is a question whose discussion is foreign to the object of this paper. Suffice it to say that they form at least one, and undoubtedly the most common, medium of communication.

How come the stools to have this virulent character? and in what part of them is contained the poison which produces such effects?

The source whence they derive their virulence is unquestionably the specific lesion of the solitary and agminated glands; and the sloughs and discharges resulting from these lesions are the particular parts of the stools in which the poison is contained.

The exact nature of this intestinal affection has been a matter of some difference of opinion. At the present day it is very generally regarded as being somehow or another connected with the elimination of the poison from the system. By many it is even looked upon as the result of a specific morbid deposit, the throwing off of which is Nature's mode of freeing the system of the disturbing element.

Such a view finds its chief support in the proved infectious properties of the intestinal discharges. It is, however, quite inadequate to explain many of the more striking features of the glandular lesion, to which reference will hereafter be made; and is at variance with the fact that mild cases of enteric fever do occur in which the glandular lesion terminates in resolution, and in which the so-called morbid deposit is re-absorbed into the system.

Moreover, there is no proof that the affected glands are eliminating organs at all. If they were so, it is probable that the work of

elimination would be more equally distributed, and that the glands situated at the lower extremity of the ileum would not be overworked, whilst those high up escaped altogether.

According to this view, too, the throwing off and deposition of the morbid material ought to be followed by an amelioration of the general symptoms, which is notoriously not the case. Besides, destruction of the affected glands, which commonly ensues, is not a likely means of promoting any eliminatory functions which they may possess.

Regarding the nature of these glands there are two opinions, neither of which pretends to do more than in a general way indicate the nature of the work which they do.

One is that each gland is a secreting cell, which periodically bursts and discharges its contents into the intestine. The other is that they are absorbent glands, which have no share in the production of the intestinal contents, but are somehow engaged in the elaboration of the fluid which is ultimately carried away by the lacteals.

The weight of evidence is, I think, in favour of the latter theory. The appearance which they present under the microscope is also in keeping with it. "When examined with the microscope, these bodies present a remarkable similarity in structure to the so-called medullary cords of the lymphatic glands, and have recently even been regarded as really belonging to the system of lymphatic glands."—(*Stricker's Human and Comparative Histology.*)

The pathological phenomena presented by these glands in enteric fever also support this view, and afford very strong evidence that they are not secretory but absorbent.

The pathological arguments against their being eliminating organs have just been given. Those which bear out the opposite opinion, that they are absorbent glands, will appear further on. Suffice it now to state that the recognition of their absorbent properties greatly facilitates, if it is not essential to, the explanation and proper elucidation of the diverse phenomena of the disease, and especially of the intestinal lesion.

The question naturally arises, Why should these glands suffer more than any other part of the intestine? It has been answered, "Because they are more vascular, and of more delicate structure." A most unsatisfactory reason. Better far honestly to confess our inability to answer the question, and say, "I do not know, and that for two reasons—(*a*) I do not know what is the exact function of these glands; and (*b*) I do not know the exact nature of the poison of enteric fever."

When these two obstacles are got over, the reason why these glands suffer will not be hard to discover. Till then, all attempts at explanation can be but vain theorizing.

In the meantime, a careful study of the morbid phenomena presented by the intestinal lesion, and a correct interpretation of the

facts observed, may lead to a sounder and more satisfactory knowledge of its pathology than we at present possess, and may lay the basis of a rational system of treatment. To this task I would now direct attention.

The view which I take of the nature of this lesion is, that it is a specific inflammation of the agminated and solitary glands, accompanying every case of enteric fever, complicating and intensifying, but in no way shortening the general constitutional affection, and bearing to enteric fever much the same relation that inflammation of the tonsils does to scarlatina.

I believe also that the sloughs and discharges from the ulcerated glands carry the poison of enteric fever, and are capable of conveying that disease from one person to another, just as the discharges from the mouth and nostrils in scarlatina are capable of transmitting their peculiar poison. That this mode of conveyance is so much more common in the latter than in the former disease, is to be explained chiefly by the naturally greater tendency to spread which scarlatina exhibits; but partly also by the fact that, whilst intestinal discharges, in consequence of their offensiveness, are got rid of as soon as possible, no special care is taken to remove the mucous discharges in cases of scarlatina. Allowance must also be made for the greater contamination of the atmosphere by the passage of the expired air over the surface from which the discharges come.

I hold, moreover, that the infectious nature of these intestinal discharges is not done full justice to by a simple recognition of their power to convey enteric fever from one person to another, but that their propensity to evil is coincident with their existence, and that they can, and often do, impart the specific inflammation of which they are the product to some of the unaffected glands with which they come in contact in their course down the intestine.

Some of the most striking and characteristic features of the intestinal lesion of enteric fever have hitherto baffled all attempts at explanation. The above view of the nature of that lesion suffices to explain them all, as I hope to be able to show.

Louis pointed out two different forms of intestinal lesion—the *plaques dures* and the *plaques molles*,—a distinction which subsequent observers have recognised. They are distinguished from each other chiefly by the amount of deposit in the submucous tissue, and by the appearance of the overlying mucous membrane. In the *plaques dures* the deposit is more abundant, and the mucous membrane is smooth; in the *plaques molles* the deposit is scanty and the mucous membrane has a rugose appearance.

A more careful examination of the causes of this difference is necessary to the full appreciation of the importance of the distinction.

In the *plaques dures* there takes place, in and around the glands, a morbid growth, to the presence of which is due some of their most striking physical characteristics. It imparts to them the

firmness and density to which they owe the name given to them by Louis, and tends also to give to their mucous covering the smoother appearance which distinguishes it from the rougher mucous covering of the *plaques molles.*

The precise day on which this growth commences has never been demonstrated; and, indeed, never can be, as the most virulent case of enteric fever does not prove fatal before the characteristic lesion of that disease shows itself. The probability is, that both the morbid growth and the increased vascularity which accompanies it are contemporaneous with the commencement of the disease.

Regarding its nature there has been some difference of opinion. Some look upon it as possessing no specific physical properties by which it can be distinguished from other growths. Others describe a specific "typhous cell." I am of those who regard it as a morbid growth rather than a deposit, possessing no microscopic characters peculiar to itself, and giving evidence of its specific nature only by the pathological results which it produces.

The notion of the morbid growth being a deposit *sui generis* not improbably originated in the idea that the intestinal lesion is Nature's means of eliminating from the system the poison of enteric fever. If the opinion to which I have given expression regarding the nature of that lesion be correct, there is no necessity for the supposition that any morbid material is thrown out. It is sufficient to suppose that the poison circulating in the blood causes irritation and inflammation of the glands and the surrounding tissue, and that the additional growth is only the necessary result of this action—the inflammatory products which constitute it presenting no microscopic characters by which they can be distinguished from the usual products of a non-specific inflammation.

The number of glands primarily affected, the extent of the abnormal growth, and the rapidity with which it takes place, probably bear some relation to the severity of the attack. In very mild cases it may be very slight, and recovery may take place by resolution without ulceration of the local lesions. In well-marked cases, in which there is considerable deposit, ulceration invariably ensues. The mode in which this takes place is noteworthy.

It is not by a process of superficial ulceration, or by the gradual disintegration of the glandular structure; but the glands, the morbid growth, and the submucous tissue in which these are contained, along with the overlying mucous membrane, form a slough which, on separating, exposes an ulcerated surface. Though this sloughing process may extend through the muscular, and even the peritoneal coat, there is nothing in the situation of the morbid growth to lead to its going beyond the submucous tissue; and in most cases it stops at that point, reaching but not penetrating the muscular coat.

Let us contrast with the above the formation and course of the *plaques molles.*

We have just seen that they are distinguished from the *plaques dures* by the rougher state of the mucous membrane, by their scanty submucous growth, and by their mode of ulceration. The difference in the submucous growth is one of degree only, and not at all of nature. Its scantiness accounts in part for the less smooth condition of the overlying mucous covering, though the granular aspect seen there may be due to other causes connected with the mode of production of these *plaques molles.*

In the manner in which they ulcerate, we have at once their most striking feature, and the clue to the real distinction between them and the *plaques dures.*

In the latter, as we have seen, the process commences in the interior, and the whole mass sloughs out bodily.

In the *plaques molles* the process of ulceration takes place from without inwards. "The mucous membrane may become softened, and one or more superficial abrasions may appear on the surface of the diseased patch, which may extend and unite into one large ulcer, and this ulcer may proceed to various depths through the coats of the bowel, and even to complete perforation."—(*Murchison.*)

After the sloughs and debris have separated, it is not possible to say from which form of lesion the ulcer has resulted.

No explanation of this difference has ever been given; and yet there must surely be some reason why, in the same patient, the morbid process should show two distinct forms.

The view given above of the nature of the intestinal lesion offers a ready explanation.

The *plaques dures*, in which the mucous membrane is smooth, in which there is considerably increased growth in the submucous tissue, and in which the whole diseased mass sloughs away at once, are the glands primarily involved.

The *plaques molles*, in which the mucous membrane has a granular aspect, in which there is little morbid growth, and in which the process of destruction is from without inwards, are those secondarily affected by the discharge from the previously existing *plaques dures.*

To the *plaques dures* I would therefore apply the term *primary lesions;* to the *plaques molles* that of *secondary lesions.*

The recognition of these two forms of lesion has a most important bearing on the pathology of the intestinal affection.

The explanation of the difference between the primary and secondary lesions is, that in the former the inflammatory product is very slowly deposited in the glands and the surrounding submucous tissue. This usually goes on from ten to fourteen days before the inflammation seems to reach its height, and terminate in sloughing.

In the latter (secondary lesions) the course is much more expeditious. The virus is applied directly to the glands, and (as might be expected under such circumstances) there is at once set

up a smart inflammatory action, which speedily terminates in ulceration, before there has been time for the glands to become more than slightly enlarged, and before there is thrown out sufficient inflammatory product to impart to them any of the external features of the early stage of the primary lesion. The mucous membrane at once partakes of the inflammatory action, and is quickly the seat of an ulcerative process, which rapidly involves the submucous tissue, and may also involve the muscular, and even the peritoneal coat.

It will be observed that, in the primary lesions, the process of destruction seems to commence in the submucous tissue, and involves in the slough all the superficial structures, but that there is no reason why it should go deeper; whilst in the secondary lesions it commences on the surface, and extends inwards in such a manner that there does not seem to be the same reason for its stopping short of the muscular coat. I shall afterwards have occasion to refer to my belief that perforation and profuse hæmorrhage more frequently result from secondary than primary lesions.

From the mode in which these secondary lesions are produced, it will readily be understood that they do not all come out at once, like the primary, but are developed in successive crops, or one by one, much depending on the situation of the glands which become so affected, and the facilities afforded by each for its inoculation. In this circumstance we have, I believe, the probable explanation of the protracted duration of the febrile symptoms in some cases of enteric fever.

Louis thought that the *plaques molles* (secondary lesions) were more frequent. Murchison regards the *plaques dures* (primary lesions) as more common.

There can be no rule in this matter; for it is evident that the relative extent to which these primary and secondary lesions exist in a given case, must greatly depend on the number and situation of the glands primarily affected. If these are numerous, there remain fewer to be secondarily involved, and the primary lesions are likely to predominate. If not numerous, and especially if situated high up, the secondary lesions may be a majority.

The higher up in the intestine the primary lesions are situate, the more numerous, *cæteris paribus*, will be the glands liable to inoculation by the discharges on their passage down the gut, and the more numerous, in consequence, will be the secondary lesions.

The reasons already given for my belief in the correctness of this view of the nature of the two varieties of intestinal lesion are as follows:—

1. It is consistent with all pathological analogy that the discharge from a specifically inflamed organ, applied to a like organ in a state of health, should there reproduce that specific inflammation to which it owes its origin.

2. The manner in which the primary lesions are formed is more compatible with a specific cause acting from within.

3. The manner in which the secondary lesions are produced is more compatible with a specific cause acting locally.

4. The manner in which each form of lesion ulcerates, tends to a similar explanation of the mode of production of each.

There are other reasons for holding this view, to which I would now direct attention.

It may be stated generally that the existence of primary and secondary lesions is essential to the explanation of the diverse, and hitherto inexplicable, phenomena of the disease.

To these I would refer under the following heads:—

1. The glands of the lower portion of the ileum suffer more than those higher up.

2. The extent of the intestinal lesion, as revealed by examination after death, bears no relation to the severity of the abdominal symptoms.

3. There occasionally occurs a distinct relapse, with a renewal of all the symptoms of the primary attack.

The glands of the lower portion of the ileum suffer more than those higher up.—No explanation in the least degree satisfactory has ever been given of this circumstance.

On the above view of the nature of the lesion it is very readily explained. Indeed, the greater involvement of the glands of the lower end of the ileum becomes almost a physical necessity; for, in the first place, they are more numerous there than at the upper part, and the discharge from an affected gland comes more readily and continuously in contact with the neighbouring ones; and, in the second place, the discharge from all those above passes over and comes in contact with those lower down. The ones not hitherto affected thus run the risk of having set agoing in them an action similar to that which exists in those from which the discharge comes. Of course, allowance must be made for the greater likelihood of primary lesions occurring in that locality, in consequence of the greater abundance of the glands; but something more is required to account for the very great increase of the glandular lesions found in the lower part of the ileum. This something we have in the recognition of the virulent nature of the discharges.

Careful examination of the diseased intestine tends to confirm this explanation of the more extensive disease of the lower part of the ileum. On examining the intestine from above downwards, it is found that the line of demarcation between the healthy and diseased glands is generally abrupt, and that, when once a diseased patch is reached, a healthy patch is rarely if ever found below it. Dr Murchison thus expresses it:—"At the upper part, the transition between the diseased and the healthy patches is usually rather abrupt, *and, proceeding downwards, after the first diseased patch, all are usually diseased.*" (The italics are mine.)

The transition between the diseased and healthy glands is abrupt

because the discharge from the highest primarily affected gland passes downwards, tending to inoculate in its course those below, but not affecting those above it; and hence, "after the first diseased patch, all are usually diseased."

The discharges from the secondary lesions are, of course, as potent for evil as those from the primary.

The further down the small intestine we go, the greater is the amount of specific discharge in a given quantity of the contents, and the less the likelihood of any gland escaping.

At the same time the band of muscular fibres, arranged like a sphincter at the lower extremity of the ileum, probably contracts more vigorously in consequence of the inflamed condition of the intestine, and so tends to retain the accumulated discharges longer in contact with the glands situated nearest the ileo-colic valve. The glands in this locality, which may have primarily escaped, thus run an unusual risk of being secondarily involved. The contraction of this sphincter ilei (if I may call it so) I believe to be a ~~fact~~ of considerable importance; and am disposed to think that what is called cæcal gurgling would often, perhaps, be more correctly termed ileac gurgling—the sound being produced in the ileum rather than in the cæcum.

In the cæcum the discharges are also probably retained for some time, and hence the glands of that portion of the large intestine suffer more than those further on.

It is true that the greater extent of disease presented by the cæcum is partly to be explained by the greater abundance of the solitary glands in that locality; but the other agency which I have indicated is not altogether without its influence.

The solitary glands of the large intestine, as compared with those of the small, suffer very little, though one might naturally expect them to be frequently inoculated by the discharges on their passage downwards. Their comparative exemption is to be partly explained by the diminished risk which they run in consequence of the dilution of the intestinal contents by the secretions of the large and numerous tubular glands of the large intestine, the fluid poured out by which may, to a certain extent, also afford a protective covering to the mucous membrane, and facilitate the passage onwards of the contents of the bowel, and may even by its acidity tend to counteract some of the noxious properties of the alkaline contents of the small intestine. Their chief safeguard, however, is to be found in their small size and sparse distribution, it being evident that the risk of a portion of slough, or a drop of virus-bearing discharge, resting in contact with a small solitary gland in the capacious large intestine, is very much less than the chance of its lodging over a good-sized patch in the attenuated small intestine. For not every gland over which the discharges pass is injuriously affected by them. No doubt they come into momentary contact with many sound glands without doing them harm. For the display of their virulent properties, it

is necessary that time should be afforded to the gland to take up the virus. When this is done, its absorption, and the consequent participation of the gland in the local mischief, almost necessarily result.

It may be objected to this view of the matter that post-mortem examination of fatal cases shows the ulcers near the cæcum to be as far advanced as those higher up. There is reason to believe, however (as has already been indicated, and as will be more fully explained when the subject of relapse is considered), that a gland which becomes directly inoculated in the above manner, inflames and ulcerates very rapidly, and is in three or four days as far advanced in its pathological course as its neighbours which were primarily affected a fortnight earlier. Just as a second vaccine vesicle, resulting from a puncture made several days after the first one, comes to maturity at the same time as the first, so these secondary lesions rapidly get abreast of the primary.

The extent of the intestinal lesion bears no relation to the severity of the abdominal symptoms.—This also admits of a ready explanation.

The severity of the abdominal symptoms is judged of very much by the amount of diarrhœa.

In cases in which the bowels are moved several times a day, the sloughs and discharges are carried off as quickly as they separate, and thus do their minimum of harm. Where constipation exists, however, they are retained, and so have greater scope afforded to them for the inoculation of glands not primarily involved. There may thus be produced in these cases an amount of local disease greater than would have existed had the abdominal symptoms been more marked, and the discharges carried off more speedily.

It is by no means an uncommon occurrence for a case in which the symptoms have all been very mild, to be suddenly terminated by perforation and speedy death. Such cases are every now and then being recorded.

Sometimes the symptoms are so equivocal that not till the onset of fatal signs is the real nature of the ailment recognised.

Occasionally this accident occurs after the primary fever has ceased.

Perforation, indeed, seems to occur in two classes of cases—those in which, prior to the accident, there are really no abdominal symptoms, or in which they are very mild; and those in which they are severe. The majority of cases in which this accident happens belong to the former class. How is this? It seems very like a paradox to say that perforation, the acme of all that is severe in the intestinal complication, is most frequent in cases in which the evidence of that complication is almost or altogether awanting. Paradoxical as it appears, it is nevertheless true. The explanation I believe to be, that in such cases the perforation is the result, not of a primary, but of a secondary lesion. For if in these mild cases the number of glands primarily involved is comparatively small (as

I believe it is), there remains a larger number of sound glands liable to secondary inoculation; and as the risk of perforation is directly as the extent and number of the secondary lesions, it follows that the probability of that accident occurring, as a consequence of such a lesion, bears a direct relation to the mildness of the attack.

I have already referred to the different mode of production of the ulcer in the two forms of lesion, and have pointed out that, while in the primary there is (especially in the comparatively benign cases to which I now refer) good reason for supposing that the sloughs will not extend beyond the submucous coat; in the secondary, partly in consequence of the more active inflammatory process, and partly in consequence of the manner in which destruction of the tissues is effected, there are not the same grounds for expecting the ulceration to stop at a given point. It is not unreasonable, therefore, to suppose that, in mild cases of enteric fever, the primary intestinal lesion partakes of the mildness of the general symptoms; and that, when perforation occurs in such a case, it is due to a secondary rather than a primary ulcer.

It is a question also whether the lodgement of a slough in a harmless or healing ulcer may not set agoing a fresh destructive action, and so lead to perforation, without the formation of a secondary lesion in the true sense of the term.

This view of the mode of production of perforation is quite in keeping with the fact that the accident generally occurs low down in the ileum, where we have seen that secondary lesions are likely to be most common and most severe.

To perforation occurring in severe cases, it is not necessary to apply the same explanation. The primary lesion, in a virulent case, may produce that result; though it is not unlikely that, even in such cases, a secondary lesion may sometimes be the offender.

The probability is, that when the accident occurs before the seventeenth or eighteenth day it is the result of a primary ulcer; when after that time, of a secondary. In cases in which the peritoneum is laid bare by the extension of the ulcerative process through the muscular coat, perforation seems occasionally to be the direct result of accidental rupture of the denuded membrane.

What has been said regarding perforation applies equally to peritonitis.

I have a distinct recollection that in my own case, in which the intestinal and general symptoms were mild, there occurred, at the end of the third week, slight but distinct symptoms of peritonitis in the right iliac region. This was the only anxious feature in the case; and, I have no doubt, was the result of a secondary lesion approaching dangerously near to perforation.

For some weeks after convalescence micturition was followed by a disagreeable dragging sensation in the lower part of the abdomen, which I attributed to the formation of slight adhesions between the peritoneal coat of the bladder and that of the intestine.

Profuse hæmorrhage too generally results from a secondary lesion: to this more detailed reference will be made further on.

I hold, then, that the extent of the primary lesion does bear a direct relation to the severity of the attack; but that it is not possible after death subsequent to the twentieth day to tell, in even a majority of cases, which glands were primarily, and which secondarily involved.

An incidental reference has already been made to the possibility of the intestinal lesion terminating in resolution. This result I believe to be more frequent than is usually supposed.

There is a form of fever very common in this country, in which the symptoms are all mild, and occasionally remittent in character, and in which convalescence commences from the eighth to the fourteenth day. It is possessed of no distinct eruption, though one or two rose spots may now and then be detected. The bowels are usually regular or constipated. The pulse is not unfrequently natural, or only slightly quickened in the evening. The tongue is clean, or thinly coated in the centre. The morning temperature is seldom above 101°, and is often lower; that of the evening is one or two degrees higher. Not unfrequently the temperature is, apart from the patient's complaints, the only evidence of the existence of "fever."

So slight indeed are the symptoms presented by many of these cases that it is often difficult to induce the patient to keep his bed, or even to abstain from following his usual occupation. They sometimes so closely resemble a bilious attack, or some temporary derangement of the digestive organs, that the use of the thermometer is necessary to the formation of a correct diagnosis. To such cases is usually applied the name "common continued fever."

In a paper on the Thermometry of Enteric Fever, published in the *Edinburgh Medical Journal* for August 1868, I expressed my conviction, founded on careful observation of the symptoms, and especially of the temperature of a number of such cases, that they were really mild cases of enteric fever. Subsequent observation has tended to confirm this view. Indeed, I think it may be stated generally that a febrile attack which is too long to be febricula, which is neither typhus nor relapsing fever, which is not ague, and which is not due to local disease, must be enteric.

In a recent number of the *Lancet* (10th December 1870) a similar opinion is expressed by so high an authority as Dr Murchison.

If convalescence commences by the tenth or eleventh day, we may safely conclude that no ulceration has taken place. If the febrile symptoms continue after that time, the patient cannot be too carefully guarded; though I am disposed to think that in such mild cases resolution of the intestinal lesion is possible at any time during the second week.

Cases of enteric fever which prove fatal during the second week are very severe, and we know that in such ulceration seldom com-

mences before the tenth day. In these mild cases it is not likely to commence for some days later; and the probability is, that in every one of them which recovers within the fortnight, resolution of the intestinal lesion has taken place.

A faulty diagnosis in such cases is fraught with considerable risk to the patient. For if mistaken for a bilious attack, and treated by purgatives, the irritation of the intestinal glands may be so increased as to greatly diminish the chance of its terminating in resolution.

This mistaking of the early stage of enteric fever for a bilious attack is no imaginary error. I have on more than one occasion seen the most disastrous effects produced by such a fault in diagnosis. We have in the thermometer so ready a means of discriminating between the two that its employment in doubtful cases should never be omitted.

In the early stage of such cases the symptoms are so slight and equivocal that the physician is seldom consulted before the end of the first or beginning of the second week, by which time the patient has usually had recourse to the ordinary domestic purgative remedies, possibly with the effect of causing increased inflammation, and consequent ulceration, of the intestinal glands, and so transferring the case across the boundary line which separates the so-called "common continued fever" from enteric fever usually so called.

It may be objected that, with the absence of all positive evidence of the occurrence of inflammation of the intestinal glands, we are not justified in assuming its existence.

I hold, however, that the occurrence every now and then of such a case as I have described in a house in which others are suffering from well-marked enteric fever, the occasional presence of ochrey stools and symptoms of intestinal irritation, the appearance in some of them of lenticular spots coming out in crops, and the identity of the mode of defervescence, as evidenced by the thermometer, suffice to indicate their real nature. Even in cases in which constipation exists, as it very commonly does, it is found that a dose of castor-oil, which in health would have no effect, is sufficient to produce free evacuation of the bowels.

The early period of those long-continued but mild cases of enteric fever which are frequently met with, and in which perforation occasionally occurs, differs in no respect from these cases of so-called common continued fever. There is positively no means by which, prior to sloughing of the glandular lesions, they can be distinguished. It therefore behoves us to treat every case as if resolution were possible, till we are quite sure that sloughing has commenced. It is possible, seeing that the difference between them is only one of degree, that the lengthy course of the former may be due to the (possibly accidental) termination in ulceration of one or more glands; and that the continuation of the febrile symptoms in their mild form may be the result of a series of secondary inoculations of healthy glands.

How far these secondary lesions tend to increase and prolong the febrile symptoms is an interesting subject of inquiry, but one regarding which no satisfactory conclusion can be arrived at.

They commence before the primary lesions have run their course, and hence, whatever symptoms they produce, are so mingled with those of the primary lesions that no distinction can be made between them. At the end of the third week of the disease both sets are equally well developed.

Though its exact effects cannot be determined, it is extremely improbable that so important a lesion should produce no constitutional symptoms; and I am disposed to attribute to the constitutional irritation resulting from the secondary inoculation of healthy glands, those variations (or rather the rises which cause those variations) in the pulse and temperature which so frequently occur in the course of enteric fever; and which, be it observed, are most common and most marked in mild cases, in which the secondary lesions are probably most numerous.

Whether any of the other usual symptoms of that disease (other than the intestinal) bear any relation to the successive invasion of the individual glands by the local disease, it is difficult to say; but I cannot help drawing attention to the fact that the eruption comes out about the time that the process of sloughing commences in the primary lesions, and that the successive crops of lenticular spots may possibly bear more than an accidental relation to the successive ulcerative lesions of the intestinal glands. It may here be noted too, that in cases of relapse the abdominal and other symptoms are all developed very rapidly, and that the eruption comes out often as early as the third or fourth day.

Be that as it may, there can be little doubt that, in some cases at least, these secondary lesions tend to prolong the febrile symptoms. Their existence after the cessation of the primary febrile attack serves also to explain the very gradual manner in which defervescence sets in, and the consequent difficulty which is sometimes experienced in determining the exact day on which convalescence commences.

How come they to prolong the febrile symptoms? Is it by simply causing that amount of constitutional disturbance which would result from a non-specific inflammation of the affected glands? Or are the constitutional symptoms increased in consequence of the re-absorption into the system of some of the poison of the disease?

I think that such symptoms as would result from a non-specific inflammatory action may fairly be attributed to these secondary lesions; but that they are lost in those of the primary fever, or only manifest themselves by those variations in the pulse and temperature to which reference has already been made. Their extent also must depend on the number of glands secondarily involved. If only one or two are thus affected, the resulting disturbance will be slight. If eight or ten are involved, it will be correspondingly in-

creased. As it is impossible in any case to gauge the exact extent of the secondary lesions, it follows that we cannot, with any certainty, say what symptoms are due to them and what to the primary. But where we find all the symptoms of the disease unusually prolonged, we may at least suspect the existence of numerous secondary lesions.

It is probable that in mild cases which run a short course, but in which sloughing of the glands has taken place, the primary ulcers are situated low down in the ileum, and are consequently less likely to give rise to secondary lesions; and that those in which the symptoms are prolonged have one or more of their primary ulcers situated high up in the intestine, and in consequence suffer more from the inoculation of healthy glands by the discharges on their course down the gut.

I do not think that re-absorption of the poison during the continuance of the primary fever (supposing it to occur) is likely to be followed by an increase of the febrile symptoms greater than may be explained by the increase of the intestinal affection; any more than a second inoculation of vaccine matter, made before the first is mature, tends to increase the constitutional disturbance which accompanies the maturation of the vesicle.

That this belief in the possibility of the poison being again taken into the system through the bowel is not altogether groundless, however, will be presently shown when considering the subject of relapse, which I now proceed to do.

There occasionally occurs a distinct relapse, with a renewal of all the symptoms of the primary attack.—The occasional re-appearance, after a short period of convalescence, of the symptoms which characterized the primary attack, forms one of the most interesting features of enteric fever.

These relapses have not been much studied in this country. In France and Germany they have attracted more attention, and have been the subject of some very interesting papers; but, so far as I am aware, no satisfactory explanation of their occurrence has been given.

They are by no means of frequent occurrence. I have notes of 128 cases, of which 13 relapsed. Many men of large experience have never met with a single instance. I saw a large number of cases before I ever met with a relapse, and the 13 cases which I have seen all occurred within a period of two years; and most of them during one outbreak of the disease, spreading over a period of fifteen months. The first case which I saw occurred in my own person, and no doubt led me to take additional interest in the accident occurring in others.

The rarity of these relapses, and their greater frequency in some outbreaks of the disease than in others, lead to the suspicion, if not to the inference, that they form no essential part of the disease, but are accidental, and due to some peculiarity either of the primary attack or of the period of convalescence from it.

One or two cases are recorded in which a second relapse—*i.e.*, three attacks of the fever—occurred. Such an occurrence is extremely rare; but one instance (Case III. of Appendix) has come under my own observation.

They are commonly ascribed to errors of diet, no doubt in consequence of their generally occurring at a period of convalescence, in which it is customary to make some change in the regimen; the *post hoc* being regarded as a *propter hoc*. This belief is probably strengthened too by the fact that symptoms of gastric irritation generally exist at the commencement of the second attack.

That they are not due to such a cause, in every instance at least, I am quite satisfied, as I have on more than one occasion observed a true relapse in a case in which there had been no departure from the milk diet which formed the regimen during the primary attack. But, indeed, it requires no elaborate argument to prove that an error of diet is incapable of producing such a disease as enteric fever.

The mode of onset of the relapse is usually as follows:—After convalescence from the primary attack has gone on for ten or fourteen days, and when both patient and friends are congratulating themselves on his satisfactory progress, and perhaps even after he has been up and moving about for some days, there comes on a feeling of cold and general discomfort, accompanied by headache, and pains or dull aching in the limbs; the patient complains of thirst, and loathes his food, or is actually sick; vomiting may even be troublesome for several days. The tongue becomes furred in the centre, and red at the tip and edges. As during the primary attack, the expression is languid, the sclerotics clear and pearly, and the pupils natural or dilated. The pulse and temperature get up very quickly; and generally within twenty-four hours of the first feeling of discomfort, the febrile symptoms are well developed. Indeed, I am not at all sure that a rise of the temperature does not take place before the patient begins to complain. In one of my own cases at least, in which the temperature was noted morning and evening all through the case, without the omission of a single day, the range had been at or below the normal standard at both observations on the 43d, 44th, 45th, and 46th days, and had been from 98° to 100° for nine days before that. On the 47th day it was in the morning 98·4°, and in the evening 102·6°, and yet the patient did not complain. On the following day, however, he felt the usual symptoms of commencing relapse; the temperature was 101·2° in the morning and 104·4° in the evening. In this instance a rise in the temperature was the first symptom of a recurrence of the fever. It may be so in every case, but this is the only one in which the fact was demonstrated by actual observation. The probability is that the temperature begins to rise coincidently with the onset of the other symptoms.

In the second attack the symptoms are all developed more rapidly than in the first. The patient seems to be as ill after the first day

as in the primary attack he was at the end of a week. By the time that the relapse has lasted twenty-four hours the pulse and temperature are often as high as at any period of the illness. Diarrhœa sets in very speedily, and the eruption comes out on the fourth or fifth day—maybe even earlier. Wandering and delirium too, when they do occur, set in early.

The second attack is shorter than the first, generally lasting for about a fortnight.

Defervescence takes place in a manner very similar to that which is observed in the primary attack. Whilst the general symptoms show signs of improvement, there occur the very remarkable morning fall and evening rise of the pulse and temperature, which characterize the first few days of convalescence from enteric fever. After the relapse, as after the primary attack, the temperature in the evening does not fall to the normal standard for some days after the commencement of convalescence.

Seeing that the second attack occurs while the patient is still suffering from the debility and exhaustion resulting from the first, it might naturally be expected that the second would be the more severe and the more fatal of the two. Such, however, is not the case.

Murchison indeed says that he usually found the relapse more severe than the primary attack. My experience is just the reverse. I have generally found the second attack to be the milder of the two. Certain it is, that the relapse very rarely proves fatal. All my own cases recovered. In Murchison's one fatal case, death was due to abortion.

"Post-mortem examination of fatal cases discloses the recent intestinal ulceration of the relapse coexisting with the cicatrices of the first attack; but as those glands only are attacked which formerly escaped, the recent lesions are usually less extensive than after death in ordinary cases."—(*Murchison.*)

There have come under my own observation, as I have already said, thirteen cases in which a true relapse occurred. (See Appendix.)

The first few, I thought, might be attributed to some indiscretion or error of diet, and accordingly took every care to guard against the operation of such a cause in the future. The patients were kept in bed for an unusual length of time, and the diet was limited to milk, or milk and beef-tea, till all danger was considered over. These precautions seemed to be of no avail, for in several cases in which they were taken a relapse occurred.

There seemed, indeed, to be no external circumstance which could at all account for their occurrence. With the object of finding out whether there existed in these cases any peculiar internal circumstance adequate to the production of such a result, I took the cases of which I had notes, separated those which had relapsed from those which had not, and carefully studied these records to see whether the former presented any peculiarities not observable in the latter. This inquiry was not, I think, altogether fruitless.

The mode of conducting it was as follows:—I dissected each case into the component parts or symptoms, whose sum total made the case; took separately those presented by the pulse, temperature, tongue, skin, nervous system, bowels, and viscera, and tried to find out whether any of these presented during the continuance of the primary attack, in cases which relapsed, any peculiarity not observable in those cases in which there was no recurrence of the febrile symptoms.

To give the details of this inquiry would be superfluous. Suffice it to say that it was entirely negative, that no peculiarity was found in any one system. The varieties presented by each symptom in the cases which relapsed were (relatively to their number) as great as in those which did not. Apart from the relapse, indeed, there seemed to be nothing to distinguish them from the mass of ordinary cases of enteric fever met with every day.

The primary attack may therefore be regarded as presenting no peculiarity, and as having nothing to do with the later re-accession of symptoms forming the relapse.

To the period of convalescence intervening between the two attacks we must look for any peculiar symptom, or aggregation of symptoms, capable of producing the effect referred to.

Here was adopted the same mode of investigation. The symptoms presented by the pulse, temperature, skin, tongue, nervous system, bowels, and viscera, in the interval between the two attacks, were contrasted with those presented by the non-relapsing cases during a corresponding period of convalescence.

It was found that the mode of defervescence was similar in both; and that neither the pulse, temperature, skin, tongue, nor nervous system presented, in the cases about to relapse, any peculiarity not observable in those in which no such occurrence took place. The diet also was the same in both.

In the condition of the bowels alone did any noteworthy difference exist.

In the non-relapsing cases (so far as the scanty notes of a satisfactory convalescence indicate) they were regular, and there was no necessity for the administration of laxatives.

In the cases which relapsed they were invariably constipated, and castor-oil had to be administered, in some of them two or three times, during the interval between the attacks.

In every case, without a single exception, this condition of the bowels was noted as having existed for some days prior to the onset of symptoms of relapse. The administration of a small dose of castor-oil was always the first part of the treatment.

This is the sole peculiarity (other than the relapse) which these cases presented in common. And in this condition of the bowels we have, I believe, a clue to the explanation of the occurrence of these relapses.

We have seen that the retention of the sloughs and discharges

in cases in which the bowels are constipated during the primary attack, leads to the more frequent inoculation of healthy glands, and the consequent extension of the intestinal lesion.

That which occurs in the relapse is similar in character.

It is impossible in any case to fix the exact time at which the sloughs and debris from the glandular lesions are all discharged from the intestine; but there can be no doubt that they are not quite got rid of for at least some days after the febrile symptoms have declined.

When convalescence commences, therefore, there are still in the intestine both recently detached sloughs and some in which the process of separation is not complete, and from which a discharge still takes place. If the bowels are moved once or twice a day these are not allowed to remain in one locality, but are soon carried off, and in a few days no injurious matter remains. If, however, they are constipated, this noxious material is retained; and, if it happen to lodge over an absorbent gland, may be taken up into the system, and so produce a fresh attack of enteric fever.

The risk of this accident occurring bears a direct relation to the quantity of noxious matter in the intestine, to the degree of constipation which exists, and to the number of unaffected glands situated below the discharges and sloughs, and which in consequence run the risk of inoculation.

This explanation of the occurrence and mode of production of the relapse is in keeping with, and corroborative of, the view already advanced regarding the nature of the intestinal lesion, and the function of the affected glands. Indeed, it was a careful study of these cases of relapse which led me to the larger and wider generalization regarding the specific lesion of enteric fever to which I have given expression.

Their rarity is to be explained, partly by the rarity of decided constipation after an attack of enteric fever, but chiefly, I believe, by the protective influence of the primary attack.

That one attack of enteric fever confers immunity from a second, is generally believed; and I think rightly so; for though instances of a second attack are not wanting, they are comparatively rare.

A careful study of the primary attacks of cases which have relapsed, fails to reveal any reason why they should not exercise the usual protective influence. That they do not have this salutary effect, however, is proved by the occurrence of the relapse; for this is really a second attack of enteric fever, whose peculiarities are all to be explained by the mode in which it is produced.

I believe that in enteric, as in other forms of idiopathic fever, there is a certain number of individuals on whom one attack confers either no immunity at all, or only a temporary one.

Such individuals form but a small minority of mankind; and the chance of their contracting a second attack of typhus, scarlatina, or variola, bears a direct relation to the smallness of their number

plus the remoteness of the chance of their being a second time exposed to such an influence as produced the first attack.

In enteric fever the chance of a second attack bears a direct relation to the smallness of the number of individuals on whom one attack confers no immunity, *minus* such remoteness; for the chance of being a second time exposed to the influence of the poison of the disease (in its most concentrated form, too) is almost a certainty, seeing that that poison exists in the intestine during the early part of convalescence, and runs a great chance of coming into direct contact with some of those absorbent glands which are specifically affected by it.

The risk of a relapse occurring also bears a relation to the severity of the primary attack. The more severe that is, the fewer will be the sound glands remaining, and the less the risk of inoculation. In none of my thirteen cases was the diarrhœa severe, and in most of them there was none at all. In only one case was the administration of an active astringent called for, and there it was to check hæmorrhage.

It is quite possible that those cases in which a relapse occurs, though not proof against inoculation of the disease, may be so far protected as to be insusceptible to the ordinary influences by which a primary attack is produced; the immunity to the disease conferred by the first attack not being complete, but quite sufficient to protect from the ordinary chances to which they may be exposed after the intestine is quite free from virus.

The view which I take of the matter is, that the proportion of cases in which a relapse occurs represents with tolerable accuracy the percentage in which one attack does not confer complete immunity from a second. At the same time, I believe that the risk of a second seizure is considerably increased by the existence of constipation during the early period of convalescence from the primary attack.

This view of the mode of production of the relapse is borne out by the fact that such an accident never occurs in those mild cases of enteric fever in which the intestinal lesion terminates in resolution, though constipation often exists all through the attack, and for some time after.

The relapse differs from the primary attack in some important points, all of which are to be explained by its mode of production.

The period of incubation in enteric fever is uncertain, and varies in different cases.

In the relapse, as in the primary attack, its duration cannot be fixed; but seeing that the second seizure is produced by the inoculation of the poison in a concentrated form, one would expect the period of latency to be shorter than in the first. From the somewhat analogous case of inoculated variola also, such an inference might fairly be drawn. My own opinion is that it is very short.

We know that in some severe cases of enteric fever, the intensity of the poison seems to strike the patient down at once, even when it is received indirectly through the atmosphere. It is not, I think, unreasonable to suppose that the latent period may be nearly as short when the poison, though less virulent, is introduced by inoculation.

The period of invasion is also short.

It has already been observed that in the second attack the symptoms are all as fully developed in two or three days, as in the first they are in eight or ten. The temperature may then be as high as at any other period; the abdominal symptoms are already manifest; and the eruption is generally out by the fourth or fifth day—occasionally even earlier.

The greater frequency of symptoms of gastric derangement, which is usually observed at the commencement of the second seizure, is probably a consequence of the more rapid production of the intestinal lesion.

When once established, the symptoms present no peculiar features by which they may be distinguished from those of the primary attack. As a rule they are milder. This mildness may be partly due to the diminished scope for intestinal mischief, in consequence of the destruction of a number of glands during the first attack. Or it may be that, as is the case in variola, the inoculated disease is milder than the natural.

The duration of the febrile symptoms is shorter than in the primary seizure. They generally last from ten to fifteen days.

This diminished duration, however, is more apparent than real; and is to be explained, not by the striking off of the third week, but by the omission of the first; in other words, the symptoms are all so rapidly developed that the period of invasion is curtailed by seven or eight days, and the patient leaps at once, as it were, *in medias res.* This more rapid development of the symptoms may be due, as already indicated, to the mode in which they are produced; or it may be that they are accelerated in the same manner as the vaccine vesicle is in cases of re-vaccination.

The mode of defervescence is very similar in both.

At this point the question naturally arises, "Are the glandular lesions in the second attack primary or secondary? are they *plaques dures*, or *plaques molles?*" The lesion of that gland through which the poison was absorbed must be a *plaque molle;* but in others there is no such necessity, for if the relapse be a true second attack of enteric fever (as it most undoubtedly is), consequent on the re-absorption into the system of the poison of that disease, there is no reason why its characteristic lesion should not be reproduced with the other symptoms. Indeed, the re-absorption of the poison through a gland is a surmise not at all necessary to the elucidation of the causation of the relapse. It is quite possible that the poison may be taken up by some other portion of the intestinal mucous

membrane than that situated over a gland, the glandular lesion running exactly the same course as in the primary attack. The rapid development of the abdominal and other symptoms, however, seems to point to re-absorption through one or more glands. From these glands, and from any *plaques dures* which might be formed, would come discharges which would produce the same specific inflammation in any healthy glands with which they might rest in contact. Obviously, however, the chance of this mishap would not be so great as in the primary attack.

What practical lessons regarding the management of those suffering from enteric fever are to be drawn from this view of the nature of its most important and characteristic lesion?

There is an amount of scepticism abroad in the profession regarding the benefits to be derived from treatment in febrile diseases, which is as unjust to medical science as it is likely to be injurious to the sick. I believe that in no class of diseases is the watchful care of an intelligent physician, cognisant of all the dangers with which the patient is threatened, more necessary than in continued fevers.

In enteric fever, in which the risks are so insidious and so varied, the value of such care cannot be over-estimated. In no disease is a correct knowledge of its pathology of more importance in treatment, and especially is this the case as regards the intestinal lesion.

It may naturally be supposed that the views which I have expressed regarding its nature are not without their influence on the treatment which I think it necessary to adopt. They do influence it very materially.

First, with regard to the very mild cases in which resolution of the intestinal lesion may be hoped for.

It is of the utmost importance in them to avoid (*a*) everything in the least degree calculated to increase the general excitement, and (*b*) every possible source of intestinal irritation. For this reason the diet should consist of milk, with such farinaceous articles as arrowroot, sago, corn-flour, etc., and even these should not be given too freely. No other solids should be allowed. All animal food is to be eschewed. The patient must be kept quietly in bed, and should, to ensure compliance with the instructions given to him, be warned of the risk attending any departure from them. Should there be any tendency to diarrhœa, all solids should be omitted, and nothing but milk be given. Even beef-tea should be prohibited. The addition of lime-water to the milk (nearly equal parts of each) is not ungrateful to the patient, and is of use in consequence of its slight astringent properties. Of this he may drink freely. If the looseness continue, the administration of frequently-repeated small doses of Dover's powder, with an additional equivalent of ipecacuan, has a most salutary effect; from $1\frac{1}{2}$ gr. to 3 gr. of Dover's powder, with $\frac{1}{8}$ gr. of ipecacuan, may be given every two or three hours.

It is seldom, however, that diarrhœa occurs. More commonly we have to deal with the opposite condition; and here the utmost nicety is required.

It must be borne in mind that some of the glands of the small intestine, and perhaps also of the large, are inflamed, and consequently more than usually prominent and tender. Under these circumstances the contact with them of the insoluble indigestible matters of which the fæces are composed, is to be avoided as much as possible. The less fluid the fæces are, the more likely are they to irritate the tender glands, and diminish the chance of termination in resolution. It is necessary, therefore, when the bowels are constipated, to counteract that condition by the administration of laxatives. For this purpose nothing is so suitable as castor-oil: one, or if necessary two, drachms should be given, so as to secure a stool, if possible, every day. The rule which I adopt in these cases is to give to an adult one drachm of castor-oil on the evening of every day on which the bowels have not been moved; if, by the morning, there is no stool, the dose is repeated. Occasionally it is necessary to give double that dose. Ipecacuan in frequently-repeated small doses—$\frac{1}{6}$ to $\frac{1}{4}$ gr., with a little sugar or aromatic powder, every two hours — is often beneficial, not only by its action on the skin, but by acting also on the mucous membrane of the small intestine. If there is much heat of skin it may advantageously be given in the form of wine, along with Mindererus' spirit.

Such are the means calculated to favour the termination in resolution of the intestinal lesion.

It is not very often that the physician has the opportunity to put them in practice, as the patient is generally ill for some time, and has undergone an injurious amount of medication at his own hands, before he applies to a medical man. But when in attendance on one member of a family suffering from enteric fever, the opportunity sometimes offers of treating such cases from the very commencement; and I feel that it is impossible too strongly to insist on the immense advantage which the patient may derive from the recognition by the medical attendant of the possibility of the glandular lesion terminating in resolution, and the early adoption of all measures calculated to aid in the production of such a result.

All our endeavours to attain this end may be fruitless, and the glandular inflammation may go on to sloughing and ulceration.

Even when this has taken place, much may still be done by judicious treatment to modify the severity of the intestinal lesion, and promote the patient's chance of recovery.

In order to know by what means this may best be done, it is necessary to bear in mind what has already been said regarding the nature of the intestinal affection, and the mode of production of the primary and secondary lesions, but especially of the latter.

The opinion generally entertained (founded on unsound views, or insufficient knowledge of the pathology of the intestinal affection) is, that looseness is an unfavourable, and constipation a favourable symptom. To check the former, and favour the continuance of the latter, are regarded, within certain limits, as the main objects of treatment, so far as the abdominal complication is concerned.

If all the lesions were primary this would be legitimate enough; but the recognition of the occurrence of secondary lesions alters the whole question.

All that can be done to prevent the primary lesions going on to ulceration has already been done.

Our object must now be to limit as much as possible the production of the secondary.

How is this end to be attained? Certainly not by shutting up in the intestine the sloughs and discharges which produce those lesions. For what is taking place during this quiescent state of the bowels? The sloughs are separating, the discharges continue to be given off by the primary lesions, and the healthy glands situated further down the gut are being subjected to the influence of a poison which is hourly increasing in strength and in quantity, so long as constipation exists. They are, in short, entirely at the mercy of a virulent agent, which is having everything its own way.

By encouraging constipation, therefore, we actually favour the production of what we fondly fancy we are guarding against—an increase of the intestinal mischief; for the longer these sloughs and discharges are retained, the greater is the chance of their inoculating the glands not hitherto involved.

To husband the patient's strength, to check any tendency to diarrhœa, and to guard against the dangers of the third week, are generally regarded as the great principles of treatment. The means usually adopted for these ends are calculated to increase the dangers of the third week, and to prolong them into the fourth and fifth. By encouraging constipation we do all we can to promote the formation of secondary lesions, which I believe to be more dangerous and troublesome than primary.

What we ought to do is to make ourselves sure that the sloughs and discharges are being regularly carried off from the bowels as they are formed. When constipation exists it should be overcome by castor-oil. One teaspoonful generally suffices for an adult. To females and children less should be given.

It is well to secure a stool every day. *Under no circumstances* should a patient be allowed to go three days without one.

I regard as most favourable those cases in which there are two motions in the twenty-four hours. When there are three, I do not interfere, unless they are very copious and watery. But when they go beyond that it is too much for the patient, and it is well to check them by means of astringents. For this purpose I usually employ the milder means already indicated. When these are insufficient, I

have recourse to acetate of lead, dilute sulphuric acid, or solution of pernitrate of iron. The two last are my favourites, the iron being called into requisition when the acid fails in having the desired effect. The administration of an acid astringent seems to me particularly well adapted for a disease in which the intestinal contents have lost their usual acid reaction, and have become alkaline. The combination of a small dose of tincture of opium, or solution of morphia, with the acid, is often beneficial.

From what has been said regarding the causation of the relapse, it may be inferred, and rightly so, that the prevention of constipation during the early part of convalescence tends, to a certain extent, to diminish the risk of a recurrence of the febrile symptoms. It is well, therefore, that the patient, during the first few weeks of convalescence, should not go two days without a stool.

Be it ever borne in mind that constipation, though a less apparent, is perhaps as great a source of ultimate danger as diarrhœa.

A few words on intestinal hæmorrhage.

The opinion usually entertained regarding this symptom is, that it is one of the most formidable complications of enteric fever.

Graves and Trousseau, on the other hand, have recorded their belief that it is to be regarded as rather a favourable symptom. To a certain extent both opinions are correct, and the truth lies between the two.

Bleeding from the bowel is to be regarded as a trivial or as a serious event, according to the time at which it takes place.

Occurring in the early part of the case it is usually slight, and is generally the result of capillary oozing, rather than the giving way of any one vessel. Such hæmorrhage is often productive of temporary good, by relieving the congested condition of the mucous membrane. It need never cause any anxiety unless it continues for some time, or is accompanied by bleeding from other organs (the nose, stomach, kidneys, or skin), indicating a general hæmorrhagic tendency (*fièvre putride hémorrhagique* of Trousseau).

Coming on late in the case, however, when the patient is much exhausted, when it is due to the giving way of some vessel, and when there is a risk of its recurring, perhaps more profusely, the appearance of blood in the stool is always calculated to cause anxiety. It may be that the quantity passed does little harm—good it cannot do then—but its occurrence at that time indicates the existence of a still active ulcerative process, the result of one or more secondary lesions, the destructive tendencies of which are greater than those of the primary.

So long as the mucous and submucous coats only are involved, profuse hæmorrhage is not likely to occur, there being in them no vessels sufficiently large for the production of such a result. When the muscular coat is invaded, however, the risk is much increased, for between the transverse and longitudinal fibres there run vessels of considerably larger size than those found in the submucous

tissue. These vessels run a great risk of being opened into by an ulcer which eats into the muscular coat.

This it is which imparts to even a slight hæmorrhage occurring late in the case an importance which would not attach to it at an earlier period. It indicates a still progressive secondary ulcer; and there is no saying where such an ulcer may stop. It may open into other vessels, or involve the peritoneum in its destructive course.

As a prognostic sign, I put such hæmorrhage nearly on an equality with slight peritoneal symptoms; it is a threatening of a still greater danger, and bears to profuse hæmorrhage much the same relation that peritoneal symptoms do to perforation.

Cases occasionally occur in which, after the symptoms have continued in a mild form for maybe three or four weeks, the patient, when apparently progressing most favourably, is suddenly seized with profuse hæmorrhage, which may even prove fatal.

The explanation already given of the mode of production of perforation in such cases, applies equally to hæmorrhage coming on thus suddenly and unexpectedly. The bleeding is caused by a secondary ulcer opening into one of the muscular branches to which I have referred, or at least into a larger vessel than is to be found on the mucous side of the muscular coat.[1]

From what has been said, it will be apparent that I regard the secondary lesions as a greater source of danger than the primary. When a patient dies of enteric fever within the first fourteen days, he is killed by the severity of the fever, and the result would be the same (in most cases at least) were there no intestinal complication at all. No doubt, cases do occasionally occur in which perforation and profuse hæmorrhage result from the direct destructive action of the primary lesions. These are exceptional. In the vast majority of cases in which death is to be ascribed to the abdominal complication, the fatal symptoms are manifested late in the case, when the primary lesions have reached the full extent to which they are likely to go, when the local danger arising from them may be regarded as over, and when the secondary lesions, though well developed, may still be progressing; for, as these latter are not all produced at once, like the former, those that are last developed may still be a source of danger, after all the primary and many of the secondary ulcers are clean, and in the way to undergo reparation.

Such is the view which I take of the nature of the intestinal lesion of enteric fever. I claim for it the distinction of being the only one which is capable of explaining the diverse phenomena of that disease. It shows how the stools carry the infection of enteric fever, without in any way exaggerating the importance of the local intestinal affection, or depriving that disease of its title to be ranked among the idiopathic fevers, and yet without detracting

[1] In the treatment of such an accident I should be disposed to try the subcutaneous injection of ergotine.

from the serious nature of the intestinal lesion. It explains why that lesion is greatest at the lower end of the ileum, and is quite in keeping with, and indeed serves to explain the fact, that the extent of the intestinal mischief, as revealed by examination after death, bears no relation to the severity of the abdominal and general symptoms. It serves also to explain the phenomena of the relapse.

I should have wished to have applied to this view of the nature of the intestinal lesion of enteric fever that crucial test which post-mortem examinations alone can supply. Since the above view presented itself to me, however, I have only had the opportunity of making one such examination. In it the highest lesion was a *plaque dure*, and, so far as one case could, it bore out my opinion. I must delegate to those who have more extended opportunities than I at present possess, the task of determining whether the highest lesion is always a *plaque dure*, and whether *plaques molles* ever exist prior to the commencement of the sloughing process in the *plaques dures*. If it is found that the highest affected gland is always a *plaque dure*, and that *plaques molles* are never found till the inflammation of the *plaques dures* has had time to go on to sloughing, I hold that my case is proved. If such is not found to be the case, I would yield the point that *plaques dures* and *plaques molles* are synonymous with primary and secondary lesions, and would look for some other explanation of the difference between them, but would still maintain, what is the chief point in this paper, that the recognition of primary and secondary lesions is essential to the explanation of the varied phenomena of the disease. In making such post-mortem observations, it must be borne in mind that, according to my view, a *plaque molle* cannot be formed prior to sloughing of at least one of the *plaques dures*, and that, subsequent to separation of the sloughs, it is impossible to say from which form of lesion the ulcer has resulted. It is obvious, therefore, that many post-mortem examinations can afford no evidence in the matter. The cases most likely to be available for this purpose are those in which death takes place about the beginning or middle of the third week.

The above facts may thus be briefly summarized:—

1. The intestinal lesion of enteric fever is specific in character.
2. It may terminate in resolution or ulceration.
3. When it goes on to ulceration there are two sets of lesions, primary and secondary.
4. The former are an essential part of the disease.
5. The latter are accidental, and the result of the inoculation of healthy glands by discharges coming from the former.
6. The recognition of these two forms of lesion is necessary to the explanation of the diverse phenomena of the disease.
7. Their relative frequency varies in different cases.

8. The extent of the primary lesions bears a direct relation to the severity of the attack.

9. That of the secondary bears no such relation, they being more likely to predominate in cases in which the general symptoms are mild, and the primary lesions few.

10. One primary lesion is sufficient to produce, directly or indirectly, many secondary.

11. The discharges do not necessarily inoculate every gland over which they pass.

12. The longer they remain in contact with a gland, the more likely is it to suffer.

13. The higher up in the intestine the primary lesions are situated, the more numerous, *cæteris paribus*, will be the secondary.

14. Fatal abdominal symptoms are more often the result of secondary than of primary lesions.

15. Relapses are caused by a re-absorption of the poison into the system, probably by one or more absorbent glands which escaped during the primary attack.

16. Constipation is to be regarded as a source of ultimate danger.

17. No one suffering from enteric fever should go more than two days without a stool.

Appendix.

I.—A male, aged 30, had a well-marked but mild attack of enteric fever. The eruption came out on the twelfth day, and presented its usual characteristics. The pulse ranged from 96 to 108, and the temperature from 102·5° to 103·8°. There was no tympanitis or abdominal tenderness: the bowels were somewhat relaxed, but there were never more than three stools a day, generally only two; they were ochrey, but not very liquid. There was no delirium, but the patient did not sleep well at night. He was put on milk diet. There was no other treatment.

On the twenty-eighth day defervescence began. On the thirty-third it was noted—"Continues to improve; has had no stool for three days; to have two drachms of castor-oil; fish for dinner."

On the thirty-ninth day he complained of chilliness, headache, pains in limbs, and a feeling of sickness. The skin was warm; the tongue slightly furred; pulse, 96; temperature, 100·8°. Stated that he had had no stool for several days; he thought not since last dose of oil. Was ordered two drachms of castor-oil. To have milk diet. The febrile symptoms recurred. A fresh eruption of rose-coloured spots came out on the fourth day of relapse. The pulse and temperature rose to about the same height as during the primary attack. The bowels became slightly relaxed on the fifth day, but were never so much so as to call for remedial interference. After continuing for fourteen days the febrile symptoms again showed signs of abatement, and the patient slowly but steadily convalesced.

II.—A female, æt. 32, had an attack of enteric fever, characterized chiefly by the mildness of all the symptoms. She was ill for a fortnight before she took to bed. When first seen she had a scanty eruption of rose-coloured spots; the tongue was thinly furred in the centre, and red at the tip and edges; the pulse was 76, and the temperature 102·4°; the bowels were said to be regular. She continued much in the same condition till defervescence began. The pulse ranged from 72 to 88, the temperature from 101·8° to 103·4°: both showed throughout the whole duration of the febrile symptoms a tendency to rise in the evening and fall in the morning. The bowels were never moved more than once a day; on several occasions a day was passed without a stool. These were never liquid. On what was thought to be the thirty-first day defervescence began, and continued for fourteen days.

On the fifteenth day of convalescence it was noted—"Complains of cold, headache, and a feeling of sickness. Skin warm; tongue slightly furred; pulse, 84; temperature, 101°. Has been up for an hour the last two days; for last three days has had chicken for dinner. Has had no stool for four days. Ever since convalescence began the bowels have been very costive. To have two drachms of castor-oil; and to go back to milk diet." All the symptoms of the primary attack recurred, and in much the same degree: rose spots reappeared on the sixth day of relapse in a very scanty manner, five being the highest number which existed at one time, and that only on one day—the ninth. On the thirteenth day defervescence again set in, and was progressive.

III.—A male, æt. 27, came under observation on the eighth day. On the tenth the eruption appeared. The case proved a smart one. The pulse was generally from 130 to 140, and on one occasion was as high as 160. The temperature ranged from 103° to 104·8°. Epistaxis occurred on several occasions, but to no great extent. The bowels were troublesome for a time, but were kept in check by lime-water, and frequently-repeated small doses of ipecacuan and opium. After the third week they were not so loose, and the ipecacuan and opium were omitted. The patient, however, was very weak, and required to be pretty freely stimulated, taking for some time a daily allowance of six ounces of wine and four ounces of whisky. The nervous symptoms were not a source of anxiety. He wandered at night, but was rational during the day. Defervescence began on the twenty-fourth day.

On the thirteenth day of convalescence it is noted—"Has been shivering this morning; complains of headache and general aching; has no appetite. Skin warm; tongue slightly furred; pulse (which had never fallen below 112), 128; temperature, 101·2°; has had no stool for three days. To have milk and beef-tea only for diet. To have two drachms of castor-oil."

The febrile symptoms continued; the pulse did not reach so high

a standard as during the primary attack, its highest being 136; the eruption came out on the fourth day of relapse: the bowels again became loose, but were easily kept in check by the means formerly adopted; the stools were pale and ochrey. On the nineteenth day of relapse defervescence again began, and the patient continued to improve for six days. On the seventh there was again a fresh onset of febrile symptoms. The condition of the bowels prior to this second relapse is not noted, but it is to be presumed that they were costive, as two drachms of castor-oil were ordered. The pulse and temperature again rose; the bowels became slightly relaxed; the stools were ochrey; and the patient had the circumscribed flush, the languid expression, the pearly sclerotic, and the dilated pupil of enteric fever. On the ninth day from the third onset of febrile symptoms, or the sixty-seventh day from the commencement of illness, convalescence again began, and continued uninterruptedly. No eruption appeared during the last attack.

IV.—A male, æt. 12, regarding the duration of whose illness no satisfactory information could be got, had a smart attack of enteric fever. The pulse was generally 132; the temperature varied from 103·1° to 104·5°; the eyes were clear, and the pupils dilated; the tongue was dry in the centre, and the lips cracked and bleeding; the bowels were relaxed, and the stools ochrey; there was no abdominal distention or tenderness; the nervous symptoms were marked; the patient wandered much at night, but during the day was quite capable of understanding all that was said to him, though he took no notice of what went on around him. No eruption was observed. Eight days after he came under notice, and probably about the twenty-fifth or twenty-sixth day of the fever, defervescence began.

On the eleventh day of convalescence, after the patient had been up for an hour or two, but before the diet had been changed at all, the following note was made:—"Has been sick this morning; complains of headache and a feeling of cold; skin warm; tongue furred in the centre; pulse, 120; temperature, 101·8°; the bowels have not been moved for several days; to have one drachm of castor-oil." All the symptoms of enteric fever were again developed; this time with the addition of the eruption, which came out on the third day of relapse. The nervous symptoms were less prominent, but in other respects this attack presented very much the general characteristics of the primary seizure.

On the thirteenth day defervescence again set in, and the patient made a satisfactory convalescence.

V.—A female, æt. 20, had a mild attack of enteric fever. The eruption came out on the tenth day; the pulse ranged from 96 to 108, the temperature from 102·1° to 103·3°; the bowels were regular throughout the whole course of the febrile symptoms, and the stools were of fair consistence. There was no delirium or wandering. On

the twenty-second day defervescence began. On the ninth day of convalescence it was noted—"Complains of headache and loss of appetite; tongue slightly furred; pulse,100; temperature,101·2°; has had no stool for some days; has not been up, and has had no change made in her diet. To have two drachms of castor-oil." The pulse and temperature had much the same range as during the primary attack; the bowels were again regularly moved once a day, but the stools had not so much consistence. The eruption did not reappear. After continuing for fourteen days the febrile symptoms again declined, and the patient made a satisfactory convalescence.

VI. A female, æt. 26, had a well-marked attack of enteric fever, without any alarming symptoms. The pulse was never above 108, and was generally between 80 and 90; the temperature ranged from 102·3° to 103·6°. Both pulse and temperature showed all through the case a tendency to fall in the morning and rise in the evening. The eruption appeared on the twelfth day. There were neither nervous nor abdominal symptoms sufficient to call for notice. The bowels were generally moved once, sometimes twice a day, but never oftener than that; the stools were never liquid. Indeed the case was in all respects mild, though somewhat prolonged, and presented little variety from day to day.

On the thirty-first day defervescence began.

On the forty-fourth day, or fourteenth of convalescence, it was noted—"Complains of headache, loathing of food, and chilliness; tongue slightly furred; pulse, 96; temperature, 101·4°. No stool for four days. Has been up for a short time for last five days; yesterday had a chop; on the two previous days chicken for dinner." The symptoms were generally similar to those of the primary attack; the chief difference being a slightly more relaxed condition of the bowels during the relapse. The eruption came out on the seventh day. On the ninth day, and again on the eleventh, there was slight epistaxis. On the nineteeenth day of relapse, or sixty-second from commencement of illness, convalescence began and continued.

VII.—A female, æt. 18, came under observation on the fourth day of what proved to be a well-marked attack of enteric fever. The febrile symptoms ran pretty high, the pulse ranging from 120 to 132, and the temperature from 103·3° to 104·8°. There was considerable wandering at night, but the patient was quite rational during the day. The bowels were relaxed, but never so much so as to call for the administration of any astringent more potent than lime-water. The stools were ochrey. The eruption appeared on the ninth day. Once or twice epistaxis occurred to a slight extent.

On the twenty-fifth day defervescence began. On the thirty-sixth (twelfth of convalescence) it was noted—"Has been shivering, complains of headache and pains in limbs; tongue thinly coated;

pulse (which has never been below 112), 124; temperature, 102°. For two days has been up, and has had fish for dinner. Four days ago had two drachms of castor-oil, which operated once. Since then has had no stool; to have again the same quantity of oil, and to go back to milk diet."

The second attack lasted for fifteen days, and presented much the same features as the primary seizure. The bowels were relaxed, and the stools ochrey; the eruption appeared on the fifth day. The nervous symptoms were again marked, and set in very early. Convalescence began on the sixteenth day, and was satisfactory. Patient was greatly emaciated.

VIII.—A female, æt. 20, had a smart attack of enteric fever, the peculiarity of which was that, while the febrile symptoms ran high, there was little or no diarrhœa. The eruption appeared on the eleventh day. The pulse ranged from 128 to 144, and the temperature from 103·6° to 104·8°. The bowels were never in the least relaxed, and at times were rather costive. There was considerable wandering at night, but none during the day. The urine was slightly albuminous. On the twenty-third day defervescence began.

On the sixth day of convalescence she was ordered fish for dinner, and to have two drachms of castor-oil, the bowels not having been moved for several days. Two days later she got chicken for dinner.

On the thirteenth day of convalescence the note was—"Had slight rigors this morning; complains of headache, debility, and loss of appetite; tongue slightly furred; pulse, 120; temperature, 102·3°. No stool for three days; to have two drachms of castor-oil, and milk diet." Another drachm of castor-oil had to be given before the bowels were moved. The febrile symptoms increased; the pulse and temperature were not so high as during the primary attack; neither was there so much wandering at night. The bowels, though not loose, were not so costive as before. The eruption reappeared on the fourth day. The patient was much enfeebled, and required a daily allowance of six ounces of wine. This second attack lasted for seventeen days. On the eighteenth (or fifty-second from commencement of illness) defervescence again set in. Patient made a slow but satisfactory convalescence. The pulse was long in regaining the natural standard.

IX.—A female, æt. 28, had a sharp attack of enteric fever. The eruption came out on the twelfth day, and was very abundant. The pulse ranged from 120 to 132, the temperature from 103·2° to 104·5°. She wandered much at night, but was generally sensible enough during the day. There was no abdominal distention; but slight tenderness, on pressure, existed on the right iliac region. The bowels were loose from the first day that she came under notice (seventh of illness). At first they were kept in check by

lime-water and frequently-repeated small doses of Dover's powder. On the twentieth day about two or three ounces of blood were passed by stool. By acetate of lead in three-grain doses every three hours the diarrhœa was checked, and the hæmorrhage did not recur. The patient was considerably depressed, and required from this time eight ounces of wine per diem. On the twenty-third day defervescence began. For ten days improvement continued. On the evening of the tenth day she was ordered a drachm of castor-oil, as the bowels had not been moved for three days. On the eleventh day she was suffering from the usual early symptoms of relapse. The oil had not acted, and she got another drachm, which had the desired effect. This second attack was decidedly milder than the first. The eruption came out on the fourth day, and was very scanty, generally only three or four spots. The pulse was much the same as during the primary attack, but it had fallen very little during the interval of convalescence; the temperature ranged from 103° to 104·1°. There was wandering at night, but to a less extent. The bowels were moved twice a day as a rule, and the stools were ochrey. There was cæcal gurgling, but no tenderness. On the fourteenth day of relapse (forty-sixth of illness), she again began to convalesce, and made a good recovery. The diet administered during the primary attack had never been departed from.

X.—A female, æt. 19, had a well-marked attack of enteric fever. The eruption came out on the ninth day. The bowels were never so loose as to call for the administration of astringents, but the stools were ochrey, generally two a day. The pulse varied from 96 to 108, and the temperature from 102·8° to 104°. There was slight wandering at night. There was little variety in the symptoms from day to day.

On the twenty-second day defervescence began.

On the ninth day of convalescence it was noted—"Complains of sickness, headache, and pains in neck and back; has been shivering; tongue thinly furred; pulse, 100; temperature, 101·2°. No stool for several days. Has had no solid food, except bread. To have two teaspoonfuls of castor-oil."

All the symptoms of enteric fever came back. The eruption came out scantily on the fifth day. The pulse and temperature were both much the same as in the first attack. The bowels were not so relaxed, but the stools were ochrey. There was again slight wandering at night. These symptoms continued for thirteen days. On the fourteenth, patient again began to convalesce, and made a good recovery.

XI.—A female, æt. 17, had all the symptoms of enteric fever well marked. The eruption appeared on the eighth day. The pulse generally ranged from 120 to 132, and the temperature from

103° to 104 ; once it was as high as 105·3°. The bowels were never troublesome ; usually one, sometimes two ochrey stools a day. There was some tenderness on pressure in right ileum. At night she wandered a good deal, but was quite rational during the day. There is a difficulty in saying exactly when defervescence commenced in this case. At the end of the third week the morning temperature fell a couple of degrees for a day or two, and the expression was also improved; but the onset of parotid swelling seemed to have the effect of keeping up all the febrile symptoms. Not till the thirty-third day, when the parotid began to discharge, was there any decided amelioration of these. After the third week the stools were well formed, and the bowels so costive that castor-oil had to be given on several occasions. On the forty-third day it is noted—"Bowels confined; to have two teaspoonfuls of castor-oil." On the evening of the forty-seventh day, the temperature was 102·6°. On the forty-eighth day the note says—"Complains of headache and feeling of sickness; did not rest well last night; tongue slightly furred ; pulse, 120 ; temperature, 101·2° ; has had no stool for four days; to have a teaspoonful of castor-oil." The febrile symptoms recurred, the pulse ranging from 120 to 132, and the temperature from 102° to 104·4°. For several days patient was much troubled with sickness. During this second attack the bowels were so confined that an enema had to be frequently administered. On the eleventh day of relapse (fifty-eighth of illness) two rose-coloured spots appeared. These were the only ones observed during the second attack. Defervescence began on the seventeenth day of relapse (sixty-fourth of illness).

Of the two other cases I have not complete notes.

XII.—A female, aged 20, was during the primary attack under the care of Dr Harvey of Aberdeen, who informed me that the case was a well-marked one of enteric fever, with eruption and general symptoms proper to that disease. Immediately after recovery she came to Dundee. Two days after her arrival she had shivering, headache, and sickness, followed by febrile symptoms. I saw her on the third day of this illness. The skin was then hot; the tongue furred in the centre, and red at the tip and edges; pulse, 104 ; temperature, 102·5°. The bowels were freely moved shortly before she was seen, but had been confined for some days previous to that. There was slight bronchitic wheeze in both fronts. The eruption came out on the fifth day. The symptoms were all mild. The pulse was never above 116, nor the temperature above 103·8°. The bowels were slightly relaxed from the fourth day. On the thirteenth day defervescence began.

XIII.—This case occurred in my own person. I have no detailed notes of its progress from day to day, but as I was sufficiently sensible to watch its course with the interest which one is likely to take in his own case, I can give its leading features with tolerable accuracy.

It was a well-marked one. The pulse ranged from 120 to 132; the temperature was not noted; the tongue was furred and sometimes dry in the centre; the eruption presented its usual features; there were troubled dreams, but no distinct wandering at night; the bowels were generally moved twice a day, and for a time the stools were ochrey. During the third week there was considerable tenderness in the right iliac region. These peritoneal symptoms formed the most anxious feature in the case; and to a patient conscious of the danger, a very unplesant feature it was. Symptoms of improvement first showed themselves on the twenty-third day.

During convalescence from the primary attack, the bowels were so costive that a small dose of castor-oil had to be taken more than once; and I have a distinct recollection that a dose taken shortly before the symptoms of relapse appeared got the credit of having something to do with their production. After convalescence had continued for about a fortnight (of the exact time I cannot be sure), and after I had been up on several occasions for a few hours, and had been ordered a more generous diet, symptoms of relapse showed themselves. The pulse got up, the eruption reappeared, the bowels became slightly relaxed; and for about a fortnight I was again in the same condition as during the primary attack, except that the peritoneal symptoms did not recur.

The exact day on which convalescence began I do not know. On this occasion there was no interruption.

These scanty notes suffice to show that the second attack was in every case a true relapse, as worthy of the name enteric fever as the primary seizure.

The following table shows at a glance the chief points of interest presented by these cases:—

No.	Sex.	Age.	Duration of 1st attack.	Duration of Interval.	Duration of 2d attack.	Total Duration.	Day on which eruption appeared in 1st attack.	Day on which eruption appeared in 2d attack.
1	M.	30	27 days	11 days	14 days	52 days	12th day	4th day
2	F.	32	(?) 30 ,,	14 ,,	12 ,,	56 ,,	bef. 14th ,,	6th ,,
3	M.	27	23 ,,	12 & 6 ,,*	18 & 8 ,,	67 ,,	10th ,,	4th ,,
4	M.	12	(?) 25 ,,	10 ,,	12 ,,	47 ,,	None	3d ,,
5	F.	20	21 ,,	8 ,,	14 ,,	43 ,,	10th day	None
6	F.	26	30 ,,	13 ,,	18 ,,	61 ,,	12th ,,	7th ,,
7	F.	18	24 ,,	11 ,,	15 ,,	50 ,,	9th ,,	5th ,,
8	F.	20	22 ,,	12 ,,	17 ,,	51 ,,	11th ,,	4th ,,
9	F.	28	22 ,,	10 ,,	13 ,,	45 ,,	12th ,,	4th ,,
10	F.	19	21 ,,	8 ,,	13 ,,	42 ,,	9th ,,	5th ,,
11	F.	17	Uncertain	Uncertain	16 ,,	63 ,,	8th ,,	11th ,,
12	F.	20	,,	,,	12 ,,	Uncertain	Not known	5th ,,
13	M.	26	22 days	,,	Doubtful	,,	Uncertain	Uncertain
Average		22·6	24·27	10·9	14·5	52·4	10·3	5·27

* Two relapses.

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