Some Observations ON THE INVESTIGATION OF THE TOXAEMIAS OF PREGNANCY.*

BY

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OF late years much stress has been laid upon the great value and benefit to be derived from the medical supervision of the pregnant woman, not only to herself but to the future welfare of her child. It has been proved by experience that attention to the disorders of pregnancy has brought about a considerable reduction in foetal mortality, and of the complications of labour and the puerperium.

The subject of pre-natal care is very closely bound up with that of infant mortality, as child life begins at the conception of the ovum. The medical profession owes a debt of gratitude to the work of Dr. Ballantyne of Edinburgh, as he gave the first stimulus to the interest in ante-natal hygiene and pathology, and it is due to his enthusiasm, and also to Dr. Amand Routh,¹ that we are now alive to the vast and far-reaching importance of the subject.

Obstetrics having been rescued from the hands of the untrained midwife is now a science which has advanced more rapidly than almost any other branch of medicine.

Now, when every possible surgical method has been exhausted for alleviating childbirth, we turn our attention to the medical aspect of the subject to find that the work of the future lies in the investigation of the physiological and pathological conditions of pregnancy. By the prevention or early relief of many conditions we will soon realize that much of the operative interference advocated hitherto is unnecessary, and that by reducing the number of operations at childbirth much will have been done to diminish the maternal and infant mortality.

For the same reason puerperal sepsis will be found to have a close association with the prevention of abnormal conditions found during pregnancy.

The main work of the future lies in the investigation of the toxæmias of pregnancy. At present we only stand on the threshold of the subject and contemplate as if in a mist the difficulties and complications which confront us. Already the literature is burdened with inexactitudes, published by physiologists and pathologists who not only contradict one another but themselves in their subsequent publications. Such a condition of affairs proves the difficulties of the research. Clinicians look for guidance to the laboratory workers, but much patience will be required before the problems involved are ready for solution. Take, for example, the ammonia coefficient in the urine of pregnancy, which was looked upon as an almost infallible test of the gravity of the condition, and was employed as an indication for the termination of pregnancy. It is now admitted that it is of little value, as it is so readily modified by various factors, such as diet, vomiting, and the administration of alkalis. One discovery of vast importance is that the clinical obstetrician can no longer stand alone in his diagnosis of the complications of pregnancy, but that he must have help from various sources. The main source of help is to be found in (1) public authorities, and (2) expert laboratory workers.

1. Public Authorities.

The first named must give facilities for the observation of patients in ante-natal clinics, both outdoor and indoor, either in connexion with maternity hospital centres or associated with them. The Ministry of Health has done much to advance obstetrics, and its department of maternity and child welfare, under the direction of Sir George Newman and Dr. Janet Campbell, has raised the standard of obstetrics throughout the country. Ante-natal and child welfare centres are given grants towards their upkeep, and their work is organized and inspected. The centralization of the work is the first step in the establishment of the fact that obstetrics is a branch of the work of the public health authority.

The maternity allowance enables the working-class mother to be freed from financial anxiety, and to have skilled help and attention when required.

Maternity hospitals not only benefit their patients directly, but provide material and facilities for the training of students and midwives, who are thus made fully aware of the importance of the subject of child welfare from its ante-natal beginnings.

2. Expert Laboratory Workers.

Well-equipped laboratories are required for the investigation of ante-natal conditions; such laboratories should be within reach of all maternity hospitals and obstetricians. The great difficulty at present is the problem of finance—a serious question, and one which must be overcome if British research workers are to maintain their place with other countries.

Grants can be obtained from the Medical Research Council and other scientific bodies, such as the Royal Society and British Medical Association, but even these are threatened with the Government economy axe, authorities being unmindful of the fact that true anti-waste conditions are brought about by the provision of healthy children who will not become a subsequent burden upon the State.

The Physiology of Pregnancy.

Before entering upon a discussion of the abnormal conditions found in pregnancy it must be noted that very little is known of the normal physiological processes which take place in connexion with the physiology of reproduction and the newborn; and that a great deal of research must be carried out in these directions before we can dogmatize as to where the normal ends and aberrations begin.

The Medical Research Council is the first organized research centre of its kind in this country, and its results will be of value since it co-ordinates the work of so many investigators. Ideas should be centralized and special lines of research organized, and workers should not remain isolated and scattered in laboratories. Committees composed of obstetricians and laboratory workers should be formed to draw up schemes for investigation, and mutual help should be given in the supply of information and material.

Public health authorities and societies should appoint committees to investigate and report upon subjects requiring further work. This has been done on several occasions recently by the Obstetrical Section of the Royal Society of Medicine with very satisfactory results, and it is a step in the right direction.

Scheme for the Investigation of the Toxaemias of Pregnancy.

At present much research is being done in various teaching centres upon the origin of these toxæmias. An outline of the scheme carried out at the Royal Free Hospital may serve as an example of such work.

In connexion with the obstetrical unit of the hospital, where whole-time specialists are employed, the patients first come under observation in the ante-natal outdoor clinics, which are held four times a week. The majority of the patients are entered for admission to the wards for their confinement when it is due. The cases are examined and the appropriate treatment given, and when the patient eventually enters the obstetrical indoor department her ante-natal case sheet is incorporated with that of the ward. Before dismissal from the ward after confinement each patient is seen by one of the senior obstetricians and her condition noted on her case sheet. She is given a card to attend at least once at the post-natal clinic should any complications arise and when she is not under the supervision of her own medical attendant. The baby is brought to the infant welfare clinic, and there kept under observation if necessary. A trained sister is available for visiting the babies in their homes, and an untrained visitor keeps a register of the patients and their home conditions, and visits them when required. In this way the patients are kept under observation during the ante-natal and post-natal periods. The infant welfare clinic with its physician in charge, and also the V.D. department, work in close co-operation with the obstetrical unit. In this way the various departments are linked up, and the patients have the benefit of responsible specialists. The obstetrical and gynaecological unit is therefore enabled to devote its entire time to its own special branch. Accommodation for the reception of indoor ante-natal patients is limited. Although these cases require observation to a certain extent it should be possible to carry

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this out in rest homes where the cost of upkeep is less than in a large general hospital, and where a purer atmosphere and surroundings might be available.

Cases diagnosed as toxæmic at the ante-natal clinic are admitted to the wards for further investigation and treatment. When admitted a routine method of procedure is carried out; the patient is put at absolute rest in bed and given a carefully measured diet. The urine is collected by catheter for six, twelve, twenty-four hours, and with the blood is sent to the Physiological Department of the London School of Medicine for Women, where an analysis is carried out by Dr. Pilman Williams—a Medical Research Council Scholar—and by members of the staff under Professor Winifred Cullis. The Wassermann test is done as a routine in a very large number of cases in the outdoor department. A general scheme of treatment is carried out for those toxæmia cases which will be referred to later, and it is hoped to publish the results of the investigation of the toxæmias at a future date.

Manifestations of the Toxæmias of Pregnancy.

The developing ovum causes physiological changes to take place in the maternal organism, the evidence of which is to be found in the breast, blood serum, and endocrinous organs. These changes are said to be due to enzymes or ferments circulating in the blood and having their origin in the trophoblast and foetal portion of the placenta. Antibodies are generated in the blood at the same time which render these ferments or toxins harmless by neutralizing them. In this way auto-intoxication is prevented and the woman is immunized by her own serum. These chemical substances were investigated by Abderhalden as the result of Veit's work on the syncytial fragments found in the blood stream in pregnancy, and which are said to be destroyed by antibodies. The ferments have not as yet been isolated as far as any chemical test can be applied to their recognition, but the theory of their presence is supported by a considerable amount of circumstantial evidence. Abderhalden found by his dialysing process that from the sixth week of pregnancy until after delivery these substances could be found in the blood, but his work has been questioned by subsequent observers who obtained similar results in cases of myoma and cancer. The presence in the blood stream of syncytial fragments with villi is borne out by the *post-mortem* examination of patients dying from eclampsia where emboli composed of these structures have been found in the lungs, and also in cases of chorion-epithelioma, where there is a widespread distribution of the malignant growth fragments from the ovum. As far as our present knowledge goes the main source of the toxins is the foetal placenta, the foetus itself contributing little by its waste products to the supply. Abderhalden did not find these substances in the foetal circulation. Under normal physiological conditions the toxins when neutralized are eliminated by the various excretory channels, more especially the kidneys. If the normal process of excretion is interfered with, or if pregnancy has occurred under conditions where elimination has been defective, as, for example, in nephritis, a condition of auto-intoxication or toxæmia may result; its severity depends upon the strength and degree of concentration of the toxins and on the failure of the maternal organism to excrete them. Accumulation of toxins occurs should there be any interference with the metabolic processes of the liver, as this organ, together with the endocrinous organs, detoxicates the ferments to a certain extent and renders them innocuous when passing through the excretory channels. The liver is therefore a most important organ in the investigation of those toxæmias which are intimately concerned with its function. The kidney is secondary and acts as an excretory organ, its degree of activity depending upon its previously healthy condition and upon the virulence of the toxins which pass through its tissues. As the toxins are retained in the blood, the chemical analysis of the blood is as important as that of the urine. It is said that toxins having their origin in the syncytium are more active in the early months of pregnancy, but this is open to question, as it is a matter of clinical experience that severe toxæmic conditions, such as are found in eclampsia and accidental hæmorrhage, occur in the late months of pregnancy. As investigators advance in their researches wider fields seem to open out, and conditions such as hæmorrhage from the pregnant uterus, formerly looked upon as due to local or traumatic causes, are now classified under toxæmias. The majority of cases of interruptions of pregnancy—that is, abortion, premature births, habitual death of the foetus, etc.—are now looked upon as toxæmic in origin.

Gordon Ley² found that a large number of cases of accidental hæmorrhage showed toxic symptoms. The toxæmic origin of eclampsia is now accepted, and also of persistent vomiting, chorea, ptialism, acute yellow atrophy, and insanity.

It may be possible that in the future we will find conclusive evidence that fibroids are due to a toxin in the blood. The investigation of several cases of this condition has led me to adopt this view of the origin of these overgrowths of the uterine wall, associated as they frequently are with severe hæmorrhage which is not mechanical, and also with toxæmic complications. There is histological evidence to prove that there is some chemical irritation of the walls of the blood vessels in the substance of the growth, more especially in cases of multiple small tumours. It is quite possible that such conditions as hydatidiform mole also may owe their origin to some toxic condition of the ovum.

It is difficult to distinguish a toxæmia of pregnancy in a previously healthy individual from that of a pregnancy super-added to an already existing disease. This question affects the prognosis and also the advisability of incurring a future pregnancy. The history of previous constipation, intestinal stasis, hepatic or renal disorders is a guide. Examination of the teeth for evidence of caries or pyorrhoea, and x-ray investigation of the stomach and bowel are of value, as also the investigation of the bacteria of the bowel contents and the urine. As a rule the toxæmias of pregnancy disappear after labour. Little is known of the changes which take place in the endocrinous organs in pregnancy or of their failure in function. Epidermal changes such as pigment deposit, dry scaly skin, brittleness or loss of the nails, with thinning of the hair, point to thyroid and suprarenal insufficiency.

The Urine in Pregnancy.

The routine examination of the urine in pregnancy is essential in every case; when albumin is found to be present it should be looked upon as a danger signal, although it must be remembered that some of the most serious cases of eclampsia and coma have shown no evidence of albumin previous to the onset of the acute condition.

Albuminuria may be a transient symptom, it is not always evidence of toxæmia. It is most frequently found in the latter half of pregnancy and in primiparæ. It may be associated with death of the foetus and premature labour. If the amount of albumin is considerable the possibility of the occurrence of eclampsia must be borne in mind. When associated with oedema of the abdomen and lower extremities it points to toxæmia. If there is oedema of the face and arms the condition is more likely to be one of chronic nephritis (Eden). In some cases the toxic symptoms disappear after death of the foetus in the uterus; the toxæmia resulting from infection of the dead ovum must not be confused with the toxæmias due to placental origin. In some cases of toxæmia oedema of the foetus has been found and pathological changes in the placenta.

What is the value of the analysis of the amount of the various constituents of the urine? Mackenzie Wallis³ lays much stress upon the diastase content of the urine and blood, and advocates that the test should be made, together with the urea concentration test by Maclean's method, the ratio between the amount of globulin and albumin, and the urea content of the blood. He also investigates the blood for sugar, and when possible the cerebro-spinal fluid also. He holds the view that globulin is a direct indication of the amount of toxin eliminated, and is therefore more favourable than albumin excretion. In the urea concentration test 15 grams of urea is given to a fasting patient, and the urine examined in two or three successive hours. If the amount of urea is found to be 1 per cent. or below, damage to renal tissue is taking place; the normal amount should be 2 per cent. or more.

Mackenzie Wallis affirms that diastase is a constant factor in the urine of the non-pregnant, except in cases of disease of the pancreas, but that it is affected by toxins in pregnancy, the urine showing a high diastase content in eclampsia and other toxic conditions. This is an important danger signal if the rise in content is rapid; it sometimes persists after other symptoms have disappeared. Congestion of the capillary tufts of the glomeruli causes a rapid rise in the diastase content of the urine. The content is usually low in chronic nephritis—below ten units—and is therefore a means of distinguishing between the two conditions.

The nitrogen changes are of importance. For the meantime

the ammonia coefficient has to be left in abeyance. Urea is diminished in eclampsia and in persistent vomiting. Acetone is only of importance when associated with diacetic and β -oxybutyric acids; if these are in excess in the blood there is a condition of acidosis present. Williamson⁴ has found acidosis constantly present in severe toxæmia with albumin, but not in chronic nephritis unless toxæmia is added.

The excess of acid in the blood is neutralized partly by the ammonia or alkaline blood salts. The liver being concerned with carbohydrate metabolism is an important factor and when destruction of its tissue occurs the condition is grave. Lipoid substances are found in the blood in hepatic derangements.

The Blood.

It is essential to examine the blood in order to determine the amount of retention of the various products of disordered metabolism. The concentrated toxins of pregnancy seem to have an effect upon the tissues similar to those of some forms of snake poison. According to Mackenzie Wallis the blood changes in toxæmias are not marked. Blood sugar shows little change, and this he takes as evidence of the slight disturbance of the endocrinous organs. Blood diastase is unchanged in eclampsia but increased in nephritis. A high urea content indicates progressive destruction of kidney tissue, and in such cases induction of labour should be considered. If the urea content rises to 0.3 per cent. there is grave danger to the patient.

The Wassermann reaction has been investigated in the obstetrical department of the Royal Free Hospital in a very large number of cases by Dr. Pilman Williams, but it has been found that the results are somewhat unreliable as compared with non-pregnant cases. Positive results alternate with negative results at different periods of pregnancy, and do not correspond with the clinical evidence of the presence or absence of syphilis. It is quite possible that there is a reaction in pregnancy which may influence the Wassermann test.

In the diagnosis of toxæmia from nephritis there is much confusion and difficulty. The factors which have been put forward as a means of differentiation are: The diastase urine content is high in toxæmia, low in nephritis, while in the latter the blood content is increased. Serum globulin is more abundant in toxæmia, and serum albumin in nephritis. Acidosis is present in toxæmia, and rare in nephritis. Albuminuric retinitis is more frequent in nephritis. Primiparae suffer more from toxæmia, and nephritis is more frequent in multiparae.

The rise in blood pressure is a valuable danger signal, and in threatened eclampsia is often the forerunner of convulsions. If it rises above 150 mm. there is cause for anxiety. A high blood pressure persisting in spite of treatment is sometimes an indication for the termination of the pregnancy. It is associated with the function of the pituitary and suprarenal glands, and with the presence of amines.

Changes in the Tissues.

Bacteriological investigation of the toxæmias has contributed little to their elucidation. The histological examination of organs obtained *post mortem* and the examination of the placenta show destruction of renal and hepatic tissue with degenerative changes in the uterus. Gordon Ley, who investigated fifty cases of accidental haemorrhage, in forty-two of which albumin was present, concluded that the condition was due to toxæmia; he found marked degenerative changes in the uterine wall, with areas of necrosis, haemorrhage, and oedema of the connective tissue, and diminished elasticity, showing a tendency to rupture.

It is probable that cases of rupture of the uterus will be found to have their origin in toxæmia; this theory explains the ease with which rupture takes place after slight manipulation of the uterus, and the resistance of a healthy organ to strain in cases such as impacted shoulder presentations. The cause of atonic *post-partum* haemorrhage may be found on examination of the blood and urine. Changes in the placenta have been observed by numerous workers. Persistent vomiting and eclampsia may be taken as examples of the early and late toxæmias; the clinical histories of such cases and the *post-mortem* findings point to a variety of toxins as a cause. In time it may be possible to group the toxæmias of pregnancy into various classes corresponding to the duration of pregnancy. It is also likely that it will be possible to draw a distinction between those cases in which the liver is involved, and others in which there is deficient elimination

by the kidneys. The investigation of the sugars in the urine and blood of pregnant women opens up a wide field for research upon carbohydrate metabolism and toxæmias.

General Principles of Treatment.

The aim of treatment is to neutralize and dilute the toxins in the serum, and to facilitate their elimination by the normal channels of excretion. Rest in bed is essential in the severe cases, as it prevents tissue waste and favours diaphoresis and kidney excretion. A protein-free diet is essential in most cases, and Tweedy and others have found starvation of benefit in severe cases of persistent vomiting and eclampsia. It must be remembered that this method of treatment cannot be unduly prolonged as there is a possibility that acidosis may occur. It is sometimes possible to follow up the treatment by a carbohydrate and protein diet without much interval.

I cannot lay too much stress upon the importance of attention to the teeth. Pyorrhoea should be treated by antiseptic mouth-washes and vaccines, and carious teeth attended to or removed. Experience has shown that the treatment of the teeth gives most satisfactory results in the prevention of the severer forms of toxæmia.

Fluids, alkaline if possible, should be given in all cases of toxæmia. If the condition is severe, all stimuli such as noise and light should be excluded. Purgation must be used with caution so as not to cause irritation of the bowel wall; the days of drastic treatment by croton oil happily are over. Paraffin for more prolonged treatment is of great benefit, as it lubricates the bowel contents, prevents the absorption of toxins, and carries down the bacteria in its substance. The colon, which is the main channel for absorption, should be emptied at frequent intervals by enemata given by means of a long rubber tube at low pressure. Intestinal lavage with saline and sodium bicarbonate (3 ij to the pint) is essential in every case, and the slow method of introduction gives the best results, care having been taken to remove the faecal contents from the lower bowel. It must be remembered that such treatment may in rare cases cause uterine contractions and expulsion of the ovum. The continuous drop method of introducing saline and glucose (2 oz. to the pint) into the rectum is of benefit. In severe cases lavage of the stomach, leaving in a full dose of magnesium sulphate, gives good results. Stimulation of the skin is brought about by baths, radiant heat, and packs. Drugs are of little value. For mild cases intestinal disinfectants, such as thymol, creosote, salol, and small doses of calomel, are of benefit. Potassium chlorate gives good results in cases of repeated abortion (Jardine).

Veratrine for the reduction of blood pressure is advocated, but only one dose should be given. Pilocarpine has been abandoned by most obstetricians as it causes oedema of the lungs. The administration of morphine in eclampsia is still a matter of controversy, although the Dublin school by long experience testify to its good results. It is of great use in diminishing fatigue in cases of prolonged vomiting, and its sedative action undoubtedly outweighs its supposed harmful effects. In some cases of toxæmia with high blood pressure I have had good results from the administration of Dover's powder in 5-grain doses. I have had no experience of decapsulation of the kidneys, nor do I consider this treatment advisable in view of more modern methods. Venesection is advocated in eclampsia, and is of great benefit in cases of full pulse and raised blood pressure. It is contraindicated in cases of anaemia and exhaustion, such as is produced by persistent vomiting. Alkalinized saline transfusion is employed as a means of neutralizing and diluting the toxins in the blood stream. Mild cases of toxæmia respond readily to treatment, but in the experience of most obstetricians in some severe cases, especially if of sudden onset, all treatment has seemed useless.

The Interruption of Pregnancy.

The decision as to the advisability of induction of abortion or premature labour is difficult.

Induction is a confession of failure in treatment, and although the toxins are generated in the placenta and therefore removed in most cases by expulsion of the ovum or placenta, it is not always the case that cure results, and it must also be borne in mind that surgical interference carries with it a degree of risk and possibly the termination of the life of the child when pregnancy is advanced. The process of labour throws an additional amount of toxins into the blood stream. In devitalized conditions the risk of sepsis after any

manipulative interference is not to be ignored. In conditions such as threatened eclampsia with rising blood pressure, persistence of albumin in the urine after treatment, or in those in which the urine is diminished or suppressed, induction is indicated. In persistent vomiting, where there is evidence of exhaustion, with signs of liver and kidney destruction of tissue, as in jaundice and vomiting of blood, the termination of the pregnancy is justifiable. In acute conditions labour sometimes occurs spontaneously at the time when the medical attendant is considering its advisability. The administration of an anaesthetic calls for serious consideration, owing to the action of chloroform upon metabolism and the oedema of the lungs sometimes found after ether anaesthesia. If retinal changes occur or opacity of the lens, as in glycosuria, induction should be considered.

The method employed should be determined in each individual case. In early pregnancy laminaria tents may be employed. Premature labour may be induced by bougies or by the introduction of the soft rubber stomach tube into the uterus. Abdominal and vaginal Caesarean section may be selected for some cases, but these operations are associated with a degree of shock, anaesthesia is deep, and the results in severe cases are not always satisfactory.

Conclusion.

In conclusion, we must bear in mind that the main number of severe cases are preventable if treatment can be given in their early stages. Every pregnant woman should be kept under medical observation, and every case of albuminuria should be investigated. Every premature birth should be notified, no matter at what period of pregnancy, and facilities should be given for examination of the ovum. The public health authorities should take up the question of toxæmia of pregnancy just as they have taken up the question of syphilis. Ante-natal beds should be provided in all maternity hospitals. Financial facilities should be given to research workers, especially in the domain of physiology, for the investigation of the normal function of human pregnancy.

Inaugural Lecture

ON

TUBERCULOSIS IN WALES.

BY

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DELIVERED ON ASSUMING

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THERE are one or two fundamental conceptions referring to the general question of disease that must be comprehended and borne in mind before it is possible to approach the special problems of tuberculosis with any hope of understanding them. Two essential elements must be taken into account whenever the human body is invaded by bacterial disease. The first is the invasive power of the germ—that is to say, the degree to which it can establish itself and multiply in the human host. The other is the power of the human host to resist or react against invasion. Bearing these two essential factors in mind, we reach another fundamental consideration, which is that the number of germs that can enter the body at the time of invasion is limited, and very much inferior to the number that must finally exist in the infected body when the disease is fully established. From this it follows that in resisting invasion, the body has usually to deal with a number of germs that is relatively small in comparison with the number that it has to deal with when it attempts to cure itself from the established disease. These conceptions are of the greatest importance because they imply that during the progress of an illness the body must gradually gain a much greater power of dealing with the germs than it possessed at the beginning. Were it not so recovery would be impossible.

In an acute disease such as typhoid fever the sequence of events is briefly as follows. A relatively small number of typhoid bacilli succeed in establishing themselves in the body. The body, having had no previous experience of typhoid bacilli, has not developed any considerable power of resisting their growth, and consequently they increase and multiply with great rapidity until, after a given time, usually about ten days, they have reached such numbers that they are able to excite the first well-marked symptoms of the disease. By

this time they have gained an ascendancy over the body, and in fatal cases this ascendancy is maintained until the patient dies. But what happens in favourable cases? The ascendancy momentarily gained by the bacilli is soon lost owing to the successful mobilization of the resisting powers of the body. The symptoms take a turn for the better, the patient becomes less toxic, and in an astonishingly short space of time is convalescent and well on his way to recovery. Remember that at first his body was so lacking in resistance that even a relatively small number of germs could successfully invade it. At the height of his disease his blood and internal organs were teeming with myriads of bacilli, and yet, although unable to resist the small initial invasion, this same patient in the course of three or four weeks has reached a position in which his resistance is able to clear his blood and tissues of myriads of invaders that had multiplied unchecked during the first week or so of the disease. This astonishing power of the human body to defend itself against its bacterial foes is so well established that it can be exploited in prevention, and the use of antityphoid vaccine proves to us that even a dose of killed typhoid bacilli is sufficient to evoke an effective mobilization of the resistant powers of the body, with the result that subsequent invasion by the living germ becomes almost impossible while the immunity endures.

This story of invasion of the unresisting body—virgin soil to the germ—with the subsequent acquisition of sufficient resistance to lead to cure, tends to be repeated throughout the whole list of diseases that are caused by bacteria. But while the fundamental factors are the same, there are great variations in their manifestations in different instances. It is unnecessary to remind you how very different the course of tuberculosis usually is to that of typhoid fever. So different are these two diseases that many find it difficult to believe that, apart from the differences in the causative agents, the same kind of pathogenic machinery is operative in both. Yet there is no doubt that such is the case.

It must be admitted at once that while the story of typhoid fever is, in its main events, retold in nearly every case of the disease, the same is not true of tuberculosis. The manifestations of activity by the tubercle bacillus in its human host are of infinite variety. There are, however, certain points that all these manifestations have in common, and I shall now endeavour to formulate a few of the outstanding characters of the process of invasion by this germ.

To begin with, it can reach the human tissues by several different paths of entry, but the commonest is the breathing apparatus. The germ is usually coughed or spat into the air by sufferers from the disease, and is breathed in by the victim along with the dust or cough-spray that gets mixed with the air drawn into his lungs. In typhoid fever there is usually one definite invasion followed by a short period of multiplication or incubation, usually from seven to ten days, before the symptoms appear. In tuberculosis the process is much more gradual. In the first instance a few germs may be breathed in and may pass through the surfaces of the air passages without causing much local reaction, finally reaching the lymphatic glands. But these few will soon be followed by more, sometimes few, sometimes many, because tuberculosis is not usually contracted at one sitting, but through more or less prolonged association with an infected person. The next stage is one of gradual multiplication in the lymphatic glands, or perhaps in the tissues originally invaded; and this multiplication is unaccompanied at first by any considerable degree of general reaction. The body tends rather to devote all its powers to shutting in the invader and holding him down at the place where he has landed. Here there is no question of a few days. A much longer period—months or even years—may elapse before the germs have multiplied sufficiently to cause obvious symptoms and recognizable signs.

Invasion, then, is usually a matter of frequently repeated entries and gradual multiplication in a few sites, the body attempting to shut the germs in by building up defensive walls around them. It is the momentary breaking down of these defensive walls that leads to a sudden invasion of the rest of the body by a much larger number than it can conveniently deal with; and in this lies the explanation of the periods of acute illness that punctuate the history of chronic tuberculous disease. The process of invasion, then, is slow. What of the processes of reaction? These too are slow. Compared to what takes place in typhoid, the action of the germs and the reaction of the body are relatively slight, although both, acting over a long period, may finally lead to far more destructive effects. Where the initial invasions have