Principles in the treatment of inflammation / by T. E. Hammond.

PRINCIPLES IN THE TREATMENT OF INFLAMMATION

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BY

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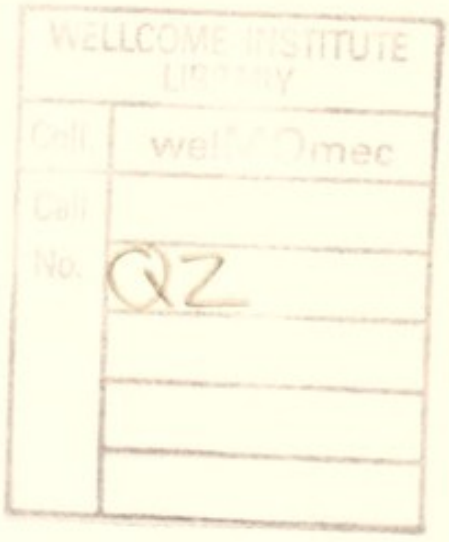
LONDON
H. K. LEWIS & CO. LTD.
1934



Made and Printed in Great Britain

TO

THE BATTALION MEDICAL OFFICERS

OF THE

GREAT WAR

PREFACE

At the bedside of the patient the practitioner is concerned with the following problems :

1. What is wrong with this patient ?
2. What can I do to put him right ?
3. What can I do to prevent this trouble recurring or happening to anyone else ?

But nowadays in our attempt to make of medicine an exact science its practical bearing is at times forgotten and the position is becoming confused. This is seen in the treatment of inflammation. When perusing some books in an endeavour to understand the principles of protein therapy, I was amazed at the knowledge that had been acquired and the work that had been done. Numerous references were made to the views and the work of others ; but the practical bearing was not apparent. In recent years no line of treatment has been evolved that enables us to deal more effectively with an inflammation. Much of what is regarded as an advance is only the giving of names to observed phenomena. It is then assumed that their cause and purpose are known. Expressions such as allergy, hypersensitiveness, etc., are used as if their discovery denoted some great advance. Nothing could be more mistaken, for they are just names given to phenomena that were observed years ago. Even as to their definition few seem to agree.

To come to grips with the problem of inflammation it is necessary to return to the bedside of the patient. This is my standpoint, and I will discuss only points of clinical importance. I am not attempting a complete treatise. To avoid confusion, I will use few terms that have not some clinical significance. I will endeavour to deal with the

underlying principles. But it is easy to talk about principles in the abstract. When put into writing they are very elusive and amount to so little.

It is impossible to write upon inflammation without referring to bacterial infection in general. The term "bacterial disease" as employed in this book covers inflammation and infection in general. There is no sharp line of distinction between them. In inflammation the local manifestation predominates, and treatment is usually directed towards this. But really the principles governing the treatment of both are the same and should be carried out even when the inflammation is well localised. Little consideration is given to operative procedures, for these are adequately dealt with in most of the standard text-books.

To appreciate the problem as it is before us to-day, it is perhaps well to review the course that has been followed during this century. The work of Lord Lister, in pointing out to us the importance of bacteria in the production of inflammation and the necessity of preventing their access to the field of operation, had borne fruit. It was easy to render aseptic the operation field, and wounds healed by first intention. But, when an attempt was made to treat inflammation by application of antiseptics, it soon became obvious that a different principle was involved. It was then attempted to attack bacteria by antitoxic or antibactericidal sera or by vaccines. In 1910 Ehrlich introduced salvarsan in the treatment of syphilis. He then sought some drug that, when injected intravenously, would sterilise the inflamed area, and visualised the production of *therapia sterilisans magna*. Then came the War with its mass of infected wounds, and the controversy as to the value of antiseptics, hypertonic saline, and excision confused the issue and led us nowhere. Few differentiated between the treatment of an infected wound and that of an inflammation. They are totally different. Once an inflammation starts, no direct attack is possible unless the organ can be removed. The first consideration must

now be given to the power of the patient to react. This aspect has received little attention in recent years. It is with the reaction that now sets in that this book mainly deals.

Two main types of inflammation, the sthenic and the asthenic, that are characterised by changes in the local and general reaction, are described. The type that arises depends not only on the bacteria, but also on the constitution and the state of the health, and is possibly more linked up with the central nervous system than is commonly thought.

Chapter II has already appeared in the *Clinical Journal*. My thanks are due to the practitioners with whom the points referred to have been discussed; to Mr. Powell, the librarian to the Royal Society of Medicine, who has brought to my knowledge much that is in the literature; and to Mr. Garrett, who has taken so much trouble with the typing.

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PART I

THE PATHOLOGY OF BACTERIAL DISEASE

CHAPTER I

INTRODUCTION

UNTIL recent years the practitioner when treating an inflammation has endeavoured to remove it or the cause. When this was not possible, as, for instance, in cellulitis, incisions were made up to the margin and at times even into the healthy tissue beyond. The sooner this was done the better the outlook appeared, as it was felt that the toxic products were let out and the harmful effects were overcome. Certain tissues, however, such as the peritoneum and pleura, are able to deal very effectively with an inflammation, if they are not disturbed. Even when pus forms, it can be absorbed. Consequently many have come to realise that certain of the phenomena accompanying an inflammation are really purposeful and are an effort of the body to overcome the infection. In the circumstances they are tending to become more conservative. An inflammation should be looked upon not only as the spread of a disease, but as the resistance of the body to the infection. And what might appear harmful at first sight is really something that is advantageous and the development of which is to be encouraged. Take as an example a cut received in the post-mortem room. If an antiseptic is applied in time, it is hoped that the bacteria will be destroyed and that healing

will take place by first intention, which is of course healing by aseptic inflammation. Compared with this a local inflammation is harmful, for it means that sterilisation has not been accomplished. But this is again to be preferred to a spreading inflammation or a rigor. For if the inflammation is localised, it means that a resistance is being established, whereas a rigor means that the bacteria have gained access to the blood stream. Again, whilst the presence of pus may at one time be regarded as serious, it is a definite indication of an attempt on the part of the body to overcome and to localise the inflammation, for this usually subsides when the pus is let out. It is consequently to be preferred to a spreading inflammation. Hence surgeons used to speak about "laudable pus" and not because it was to be preferred to a wound that healed by first intention. And whilst a rigor is to be regarded as serious, it is desirable if bacteria have entered the blood stream; for it denotes an effort on the part of the body to destroy them and shows that the resistance is good.[1] A rigor is as much an indication of good resistance as of bacterial infection. Only repeated rigors are to be deplored, for they mean that septicæmia has arisen, and that for the time being the infection has not been overcome. So long as bacteria are developing in the blood a rise of temperature is to be desired. A fall of the temperature is desirable only if it is certain that the infection is overcome; for, if it occurs before this takes place, it means that the end is near. A consideration of these phenomena will show that, whilst an inflammatory state may be regarded as unfortunate and even serious, it may be desirable when compared with what might have arisen.

Congestion, stasis, the exudation of serous fluid, the exudation of plastic fluid, the emigration of leucocytes, the formation of pus and the rise of temperature are factors in inflammation that serve a definite purpose and at a certain stage are to be encouraged. It is only when they are

[1] Sir Frederick Andrewes in the *Lancet*, 1926, vol. i, p. 1075.

in excessive amounts or when they persist unduly that they are harmful.

A practitioner, as he faces a case of inflammation in which he is not able to remove the organ or the cause, should put to himself the following questions :

1. Is the reaction just sufficient to control the infection ? Should it therefore be left alone, since the patient is building up his own resistance ?

2. Is the reaction too great and is there a possibility of damage being done to the organ or of its becoming a menace to life ?

3. Is the reaction not sufficiently great ? If so, some stimulant is necessary to bring about those factors which in excess are regarded as harmful.

When these points are being considered it is well to keep in mind that an inflammation in which a good resistance is being put up may begin to extend and become a menace to life. This does not mean that the previous treatment has been wrong, for the possibility of an extension of the inflammation has to be allowed for whatever the treatment. A practitioner can only diminish the risk ; he cannot remove it ; and at times any form of treatment has its dangers. The following case is an illustration :

A surgeon pricked his finger during an operation one afternoon. That evening it became painful and the following morning it was congested. It was obvious that it was infected. Treatment by fomentations and passive congestion was applied. In the afternoon the throbbing became more severe and the question of an incision arose. As the pain was not too severe and as he felt he could put up with it during the night, it was considered advisable to carry on with expectant treatment. It was thought that an incision would not assist as there was no evidence of any great tension and there was no place at which the inflammation tended to point. An incision might bring on septicæmia. He returned home. By 7 o'clock that evening the pain had become more severe and pus was pointing under the skin. There was also a mild lymphangitis extend-

ing up the arm. A small incision was now made and pus was let out. The lymphangitis subsided, and the wound healed in five days.

It is true that there would have been a risk in leaving it until the following morning. On the other hand, there was a definite risk to life in incising before the pus had formed, for at such a time septicæmia might be set up. At the best such a wound would have taken a long time to heal.

Most practitioners have in their lives made one incision in early inflammation and, when septicæmia later developed, have always been a little uncertain whether it might not have been prevented, if nothing had been done. Though in this case there was a time when the pus became a danger, since it apparently predisposed to the spread of the lymphangitis, its presence was desired because it meant the inflammation was coming to a head.

In few diseases has treatment been more irrational than in inflammation. Inflamed fingers are still immersed in antiseptic solutions, though few believe that these have any action and some even think that they do harm. But few are prepared to say so, as it is felt that, where the work of Lister is concerned, this amounts to blasphemy. The practitioner is too often governed by the feeling that he must do something. He is afraid that his reputation is at stake, if the case comes to the post-mortem room without something being done. For someone may suggest that the patient would have lived had an incision been made. It is apt to be forgotten that an incision at the wrong time jeopardises many a life; for it flares up the disease and takes away the patient's only chance. Had Nature been left alone, the life might have been saved.

CHAPTER II

THE WORK OF NATURE

HIPPOCRATES pointed out that in all diseases there was a tendency for the patient to get well; this particularly applied to inflammation. Recovery was attributed to the *vis medicatrix naturæ* or the reaction of the patient. The aim of the physician was to encourage this; it was promoted by healthy surroundings, nursing, rest, and maintaining the functions of the body. Under this form of therapy 90 per cent. of patients recovered. Interference was advisable only when there was a definite indication. If the vital powers flagged, they needed stimulating; if the disease progressed too actively, measures to delay its progress were tried. But expectant treatment and nursing the constitution did not mean that the physician did nothing. He had to be extremely vigilant, for it was necessary to give much thought to each patient. Recovery was attributed to a natural reaction. This was to be expected, for the Greeks had great respect for life and Nature. As little was known about life or disease, little was to be gained by investigating such a case. When the patient died, the physician was told that, had he known how to assist Nature, death might have been prevented. Consequently such a case was carefully investigated. For this reason the Hippocratic writings refer so often to fatal cases. It was thought that if only it were known what happened when the patient passed over, the physician might be able to find out what was the basis of life. Work of this kind, in which there was so much need for thought and careful observation, was particularly suitable to the Greek mind.

Medicine in the Roman Empire was considerably influenced by Asclepiades, a Greek. He had little confidence in the

expectant attitude and ridiculed the Hippocratic method, which he regarded as "a meditation on death." He referred to the frequency with which death was recorded in Hippocratic writing and therefore advocated more active measures. Galen was now the first to lay stress upon Nature. In that age it was essential for treatment to be swift and sure, for the Roman mind was practical and did not brook delay. It was an age of advance. As it was possible to make roads over mountains that were previously impassable, the physician should be able to cure disease. To support their claim this school pointed to the cures that were obtained. Improvement was always attributed to the treatment. Consequently it was not long before it was assumed that, if treatment had not been applied, the patient would have died. That 90 per cent. of patients recovered under expectant treatment was conveniently forgotten. If death took place, this was due to the physician not having been called in sufficiently early or to some other cause. That death might have been accelerated by treatment was never considered.

The Greek outlook on medicine was very different from the Roman. The Greeks thought that disease appeared because the constitution was undermined and that it was a local manifestation of some general disorder.[1] They never

[1] This represented the predominant thought of the Greeks. They were followers of two schools—the Coan and the Cnidian. The Coan dealt with life and gave us the works of Hippocrates. The Cnidian dealt largely with the classification of disease and paid much attention to unessential details As new discoveries were made, their work was proved to be wrong. It is nowadays scarcely worth reading. Much that is taking place in medicine to-day conforms to the work of this school. Because one classification does not meet all cases, another is introduced. There is not the slightest difficulty in doing this. The difficulty comes in making it permanent. For another generation comes along and does to us as we have done to others. But this extensive classification should not be confused with an advance in knowledge. When presenting cases at medical consultations at St. Bartholomew's Hospital before the War, the older physicians would read out the blood count. The younger physicians would slyly ask what it meant. The former did not profess to know. Many of the students were amazed that they had not taken the trouble to keep abreast with

left the bedside of the patient and never forgot that medicine was not concerned with the prolongation of living, but with the restoration of health which was in their opinion just abundant life. As life and Nature are the two things that do not change through the ages, their writings never grow out of date. To them we turn again and again for help and inspiration. Were Hippocrates to come back to earth, he could to-day resume the subject where he left off.

The Romans looked upon disease as something coming from outside the body. In their effort to restore health they did little more than treat symptoms. They rarely attempted to treat the primary cause of disease, some impairment of the constitution. Though they left a wonderful system of sanitation and of hospital organisation, few of their medical writings show any great line of thought. They were too materialistic in their approach to life. Though their system of laws has received admiration through the ages, these laws deal with the control and government of men as a body and not with life.

In the fifteenth century, at the time of the Renaissance, Greek and Latin works were translated. As Latin was the language of men of learning, they were translated into this language and not into English. It is well to remember that the Latin terms in modern medical works often represent Greek, and not Roman, thought. The Hippocratic writings had a considerable influence upon British medicine. Surgery gave us those great thinkers, Sir James Paget and Sir Jonathan Hutchinson, who stressed the power of Nature, and pointed out that, if she were left alone, the patient so often recovered. But they went a step farther than the Greeks

great advances in knowledge. Some of us made up our minds that such indifference would never be shown by us. Yet to-day much of what appears in current medical literature is no longer intelligible to many. The terminology is so confusing. It does not seem worth while to learn these new classifications. For there is nothing to stop another body of young men from attempting the same thing in a few years' time and doing to us as we have done to others. But until some genuine discovery is forthcoming, knowledge really remains the same. But truth like life and Nature never changes. Once discovered it lives for ever.

in showing how essential it was to study each individual patient. The constitution and any idiosyncrasy must be kept in mind. If the reaction was adequate, it was well to leave everything to Nature. The reaction might need to be increased or diminished. But whatever was desired, it was possible only by a response on the part of the patient. If this were not forthcoming, it was harmful to try to produce it. Direct interference on the part of the surgeon was called for only when there was a definite indication. In their hands the practice of surgery was a great art. This is well illustrated in Paget's lecture on "The Treatment of Carbuncle." Though he was treating a severe type of carbuncle that is rarely seen to-day and though he was applying a form of therapy that was commonly referred to as "doing nothing," his mortality was 2 per cent. This lecture shows the consideration he gave to each patient. When he was treating the constitution, he was not bound by any law but was looking out for any individual peculiarity. That 98 per cent. of his patients recovered showed the high level to which he brought the art of healing. Yet never once did he claim more than to have assisted Nature. These figures should be kept in mind nowadays when it is so difficult to keep in contact with any body of patients for a sufficiently long time. Because medical men do not understand what can be attained by leaving things to Nature many wrong claims are made for various forms of therapy. It is well to recall the words of Hutchinson: "This remarkable facility of spontaneous recovery, which is a feature of all catarrhal inflammations, has placed physicians in great difficulty in coming to any satisfactory conclusions as to the relative merits of different plans of treatment." And what applies to catarrhal applies to other forms of inflammation. There is nothing to suggest that there has been any increase in the virulence of bacterial infections since those days.

In infections of the kidney conservative treatment is carried out because the kidney is difficult to expose and is

too valuable to lose. In the majority of cases recovery takes place. The practitioner only assists Nature. Nothing specific is possible, for it is extremely unlikely that bacteria deposited in the mucous membrane are affected by antiseptics excreted in the urine. Of the cases that come into the hands of a consultant, which after all form only a proportion of those seen by a practitioner, not 5 per cent. need any interference, and by this is meant usually the passage of a ureteric catheter. Removal of a kidney is indicated in less than 1 per cent. The mortality is much lower than this.

When certain claims are made for vaunted therapy, it is well to ask, How much does this man grant to the healing powers of Nature ? For 90 per cent. of patients recovered in the time of Hippocrates when nursing was not too efficient ; and in the time of Paget, who paid so much attention to the constitution and who had in addition the help of the skilled nursing introduced by Florence Nightingale, 98 per cent. recovered.[1]

To-day surgery is at the cross-roads. The changed outlook that has taken place in a period of 21 years, like the rapid change that is taking place in all things since the War, is amazing. Yet during this time no discovery with any great bearing has been made in surgery. But whatever our outlook may be and whatever is attributed to the discoveries of science, it should be remembered that life and Nature do not change. They are the same to-day as 2,000 years ago.

[1] Whether a practitioner is optimistic or pessimistic in his views on therapy depends largely upon how much he grants to Nature. If for instance 95 per cent. recover and 5 per cent remain stationary or die, the optimist will say : " The fact that 95 of my patients are cured is sufficient evidence of the value of my therapy." Among such a number it is easy to overlook 5. The pessimist will say : " It is true that 95 of my patients are cured. Though this figure is perhaps better than that given thirty years ago, it must be remembered that to-day there are better facilities for treatment. If nothing had been done, the chances are that the majority would have got well, so great is the power of Nature. I am concerned that 5 have not got well. It is because this number tends to remain stationary that I am dissatisfied with my line of therapy."

When I entered the wards of St. Bartholomew's Hospital in 1910 conservative surgery was practised. It was realised that in inflammatory disease the great chances were that the patient would get well, if the constitution were nursed. Though each surgeon had considerable skill in operating, no operation was performed unless a definite indication arose. The surgery that was practised was worthy of the Greeks.

To-day ability to operate is being confused with the practice of surgery. Advances in technique have been made. To give the patient the benefit of these the surgeon must be extremely vigilant, to find the indication for operating. If this is not seized the moment it arises, the chance of the patient has gone. The great healing powers of Nature are ignored. If the patient recovers, this is to be attributed to the operation. If he dies, this is attributed to the operation not having been carried out sufficiently early or to some other cause. The methods advocated in the time of Rome are being adopted and the practice of surgery will soon cease to be an art, for surgeons are becoming mechanics and are content to cut out. Such a policy is not justified even by the immediate results.

The mortality of appendicectomy for acute appendicitis is still 3 per cent. or more. This is appallingly high for the treatment of an acute inflammation. A practitioner who had to carry out expectant treatment in all cases of appendicitis owing to the absence of operative facilities, and who had little nursing available, told me that his mortality was 3 per cent. Where is the advance ? [1]

The Rise of Operative Surgery

Whatever view posterity may form about the work and thought of this and the preceding generation, the high level

[1] I am not opposed to immediate operation in acute appendicitis. Owing to the fact that it is not possible to visualise the inflammation, and owing to the likelihood of important structures being involved should it extend, it is better to remove the appendix if the diagnosis is made within the first forty-eight hours. But even here the surgeon should exercise some discrimination in his selection of cases.

to which operative surgery has been raised will certainly gain much admiration. From being dangerous and being associated with much pain and suffering, it is now comparatively easy, painless, and safe. But when the application of an art becomes easy, retrogression invariably sets in. For at this time manual and verbal dexterity so often become confused with an advance in its practice. And the power to think languishes and gradually wanes. Some of us are wondering whether this is not now taking place. Posterity will be amused at the claims put forward for operative surgery by many of our leaders and by those who represent research. Such claims so often amount to vaunting their own importance and modesty has become obsolete. In this great age of advance there is no longer any need for this word modesty. Its sound has an old-world ring. Problems have been brought forward to air the views of certain men. When after a few years no solution is forthcoming, they are conveniently laid aside, and something else is taken up. In one generation life and Nature have ceased to be matter for thought and interest. An operation can do so much more.

In these days when such fantastic claims are being made, it is well to realise that a surgeon is always controlled by the pathology of the disease and by the constitution of the patient. Consequently there is bound to be a limit to the achievement of operative surgery. As a result of our advances an obstruction can be efficiently short-circuited and something that is inconvenient to the patient or that is disturbing function can easily be removed. Nothing that has been introduced in recent years can change the constitution of the patient or modify the factor that has allowed the disease to arise. This remains as before. And if the disease is removed, it only breaks out elsewhere. This will always be the case even if a day shall come in which all that is now claimed for operative surgery can take place by a wave of a wand ; that is to say, without any risk to, or disturbance of, the patient.

Ambrose Paré in his writings not infrequently stated : " I dressed his wounds and God cured him." Surgeons in later years never hesitated to state what they owed to Nature. In these irreligious days it is not strange that surgeons no longer attribute anything to God, but it is only ignorance of their art which makes them fail to realise what is due to Nature.

When an inflamed organ cannot be removed, therapy is of little value unless the patient can react. If no response is forthcoming, it is bound to fail. For this reason when treating an inflammation the surgeon puts to himself the following questions :

(*a*) What type of constitution has this patient ?

(*b*) Is it possible to get him to react ?

CHAPTER III

THE REACTION OF THE CONSTITUTION TO THERAPY

When the reaction of drugs was discussed in books upon therapy at the end of the nineteenth century, the importance of the constitution and the state of the health was always stressed. It was not then supposed that they acted so much by a direct attack upon the disease as by some reaction to which they gave rise.

In the subsequent chapters the reaction of the patient is referred to, by which is meant the processes that are set up by the tissues and cells of the body. When no form of therapy has been undertaken it is spoken of as the work of Nature. In the intensive study of disease and of disordered function that has taken place in recent years the power of the patient to react has not always received sufficient consideration. For this reason this chapter is inserted here. It is perhaps best exemplified by a reference to certain principles in surgery and in the treatment of bacterial diseases. Notwithstanding the great advances made in operative technique, the surgeon has always to rely on the power of the tissue to react. For the healing of a wound takes place by the formation of granulation and fibrous tissue, and the union of a fracture by the formation of callus. These are produced by the tissues : they are not something introduced by the surgeon. When a wound is sutured, the surgeon brings the adjacent surfaces into apposition and maintains them there. When a bone is fractured, he reduces the fracture and maintains the ends in apposition. If granulation tissue and callus are not formed by the tissues, union does not take place. Here it is obvious that if the reaction is not forthcoming, the finest operative technique is of little avail.

When bacteria have invaded the tissues and inflammation has started, it is doubtful if a direct attack on the bacteria is possible apart from the removal of the organ. The surgeon has again to rely largely on the power of the tissues to react to overcome the infection.

A comparison of the work in surgical wards to-day with that done in the middle of the last century will always make us realise the great debt we owe to Lord Lister. Not only did he show us that bacteria were the cause of infected wounds and inflammation, but also how these could be prevented by their destruction. The application of his principles by succeeding generations has made modern surgery safe. But our homage to Lister should not blind us to the fact that he taught us little, if anything, about the treatment of inflammation and infectious diseases. For the methods he advocated are of little use when either of these has started. The power of the tissues to react now counts. It is because this is not realised that we have gone so much astray in therapy. For were antiseptics to be present in sufficient strength to destroy the bacteria, they would be more likely to destroy the delicate cells of the tissues. Even before the War it was easy to render aseptic a healthy skin or mucous membrane. Several reliable procedures were available. The only controversy seemed to be as to which gave the better results, the aseptic or the antiseptic method. But neither had much effect on a surface inflammation. Surgeons realised that there was something here with which they were unable to cope. Some other explanation was sought and men were turning to the works of Sir James Paget and Sir Jonathan Hutchinson. Paget, in his Lectures, had stressed the importance of paying attention to the constitution and to the power of the patient to react, and Hutchinson had pointed out how essential it was to study this reaction in therapy.

But the medical profession was dominated by the bacterial conception of disease. As the technique improved it was found that when a man was ill bacteria were present in many

situations where they could not be detected in health. Consequently they were regarded as the cause of ill-health. It was felt that if only they could be destroyed, health would follow. And when, in 1910, Ehrlich introduced salvarsan for the treatment of syphilis, the discovery of some antiseptic that would produce *therapia sterilisans magna* seemed within our reach. For no one doubted that salvarsan acted as a germicide; as Schaudinn, in 1905, had shown that syphilis was due to the treponema pallidum. And Ehrlich had based his work on the supposition that if a dye was capable of staining protoplasm, it could penetrate the bacterial envelope. It might be possible to attach to the molecule of the dye various substances that would make it toxic to bacteria and at the same time non-toxic to the cells of the body. Salvarsan was the 606th substance with which he had experimented. As he had been so successful in this, it did not seem unlikely that some drug would be forthcoming that would have a similar action upon ordinary bacteria and in this way we would be able to make a direct attack upon bacterial diseases.

But during the War our belief in the power of antiseptics was rudely shaken. In the early stages they were applied in concentrated solutions, but these merely led to sloughing and did not prevent infection from arising. Only rarely did wounds heal by first intention. By the end of the War there was a great improvement. At this time the process generally adopted was as follows: As soon as possible after the wound was inflicted, the surrounding skin was washed with soap and water, as much of the damaged tissues as possible was excised, and 1 in 1,000 flavine in normal saline was applied as an antiseptic. Reliance, however, was placed more upon the excision of damaged tissue than upon the application of the antiseptic. For where there was much damage to the tissues, inflammation was liable to arise, no matter how soon the antiseptic was applied. It was difficult to get it to penetrate sufficiently far. Even excision failed if there was much delay.

On the other hand, when inflammation had arisen many wondered whether antiseptics had any action at all, for few, if any, penetrated. In dealing with a surface inflammation, the surgeon was in a favourable position. He could apply antiseptics in any strength desirable and for as long as he wished. He could also watch the progress. Yet their action was problematical and insignificant compared with their great power to render a healthy skin or mucous membrane aseptic where a direct attack on bacteria was possible.

Once an inflammation has arisen it is not bacteria on the surface or pus that are the cause of the trouble, but bacteria that are developing more deeply in the tissues. Even if it were possible to penetrate to these with antiseptics, were these strong enough to destroy the bacteria, the cells of the tissues, which are more delicate than those on the surface, will be damaged. This was well brought home to me a few months ago. I had a patient with a fracture of the patella on which it was advisable to operate. There was a small granulating wound on the front of the knee, which would not heal. Though every antiseptic was available, I was afraid to operate until the wound had been soundly healed for some weeks, as their penetrative power is too uncertain. When an inflammation is present, a surgeon has to rely on the powers of the tissues to react, and can do little to assist. When the writings of Lister are carefully read, it will be found that he never claimed to have revealed to us what these powers were or how to assist them. He advised us to leave Nature alone and that, if a surgeon thought it advisable to interfere, he should make certain that any good that might result is not more than offset by the injury done to the tissues.

As antiseptics had so little action when applied to a surface inflammation, surgeons began to wonder how they could have any when given intravenously. That salvarsan had a definite action in the treatment of syphilis was established, and this was particularly marked when extensive lesions were present. But if arsenic was present in the blood in

sufficient quantities to destroy bacteria, as bacteriologists and biochemists maintained, how did the more delicate and vulnerable cells of the body escape ? And as antiseptics applied to wounds had such difficulty in penetrating into damaged tissues that it was considered better to excise them, how could they penetrate into syphilitic lesions in which the vascular supply was impaired by fibrosis and by endarteritis ? Mercury also has a definite action in syphilis, but the amount in which it is given in my practice (gr. $\frac{1}{2}$ hydrarg. cum crete. t.d.s.), where its action is quite definite, means that it is never in the blood in a strength sufficient to have any antiseptic action. Bismuth also can clear up syphilitic lesions, yet the drug has no action upon the spirochæte when brought in contact with it outside the body. If this is the case, how can it act as an antiseptic when given internally ? Is it not more likely that the action of these substances is due to some reaction that takes place with the cells, producing some change in the constitution ? As a result those factors, that are at times described as the reaction of the patient and at others as the work of Nature, are in some way increased.

Hutchinson foreshadowed this view, for he held that if mercury acted as an antiseptic, some of its action was due to some reaction that took place with the tissues. In his book on Syphilis,[1] he says :

" Small doses of mercury assist the formation of fat and muscle. Everything depends on dose and upon the patient's idiosyncrasy. Whatever the idiosyncrasy, however, if the dose be reduced sufficiently, the drug will be made to agree. Reduce the dose of mercury sufficiently, the drug will be borne, and when it is borne, it will cure. It is not the quantity of the drug that is needed but the effect on the organism ; and, if the specific effect is gained by a minute quantity, it is only not needful, but bad practice to attempt to increase it. The chief difficulties in treatment occur with those who are insusceptible, not in those who respond easily."

[1] Sir Jonathan Hutchinson, *Syphilis* (Cassell & Co., Ltd.).

In his book, *The Pedigree of Disease*,[1] he writes of the action of the iodides :

" Probably there is no drug respecting which the action can be more easily demonstrated, that it is not the dose but its effect which should be regarded. It by no means follows that because a patient has an idiosyncrasy against some drug or an article of diet, that he ought really to abstain from its use. Rather this susceptibility in the majority of cases proves that in him minute doses will effect the cure as efficiently as larger ones in others. I have repeatedly cured tertiary ulceration of the throat and skin in patients in whom I was assured iodide was a poison in all doses, by giving it in quantities of half or even a third of a grain."

Now this teaching of Hutchinson means that it is the reaction of the tissues to the drug that cures the lesion, rather than any direct action it may have upon the bacteria. For by susceptibility is meant that the patient reacts to an extremely small dose. In other words, the beneficial effect of a drug is due to its effect upon the constitution. As a result this is restored to the normal, when it can overcome disease and be indifferent to those factors that lead to it.

Until attention came to be concentrated on the study of bacteria it was felt that as a result of some factor in the constitution some people were predisposed to disease, and the bilious, the scrofulous, the nervous, and the arthritic habits of the body or diatheses were described. Though attention was given to the disease, much was given to the error in the constitution that predisposed to it. For instance, the bilious diathesis included those cases that were later regarded as functional disorders and chronic infections. The local lesion was regarded as secondary to the diathetic factor, to which treatment was largely directed. Mercury was regarded as almost a specific in the bilious diathesis, but the dose was based not so much upon the nature of the disease as upon the type of the constitution and the state of the health. Everything depended upon whether a reaction

[1] Sir Jonathan Hutchinson, *The Pedigree of Disease* (J. & A. Churchill).

occurred. The aim was to produce just sufficient of this. Too big doses were avoided, since over-stimulation could do harm.

This constitutional factor may perhaps be best exemplified by a reference to tuberculosis. Under modern conditions most people inhale or swallow tubercle bacilli during the first few years of life. If any lesions develop, they are usually so small as not to constitute what is regarded as disease. This is because the resistance factor of the constitution is good. If the resistance factor can be maintained throughout life, the disease will not arise. If, however, it breaks down and at this time tubercle bacilli enter the body, disease may start. If the patient is treated by rest, good food, sunlight, etc., he may recover completely. Some are inclined to think they have cured the disease. They have done no such thing. For, apart from rest, none of these has any direct influence upon a tuberculous lesion. All that has been done is to maintain the health, as a result of which the resistance factor in the constitution has been restored and the patient enabled to control or to overcome the disease. It is true this amounts to the same thing, but the method by which it is produced is different. At times a tuberculous patient goes down-hill in spite of every care. In other words, he is being consumed by the disease. When his condition is regarded as hopeless, for some reason that is not apparent, he will suddenly begin to recover and his disease become quiescent, though there has been no change in the treatment. Some think that the disease improved first, but this is not so; for often it is obvious that in the earliest stage there is no change in its amount or in its activity. Rather something happens to the constitution as a result of which the resistance factor is brought back into its normal state. The tissues are now indifferent to the tubercle bacillus.

This also happens at times in an ordinary inflammation. In 1929 a patient with a cellulitis of the arm, due to a streptococcus, was admitted to hospital under my care. No

improvement followed administration of sera. The question of the intravenous injection of mercurochrome arose. As at that time I had had little experience of it and the writings indicated dangers in its use, I decided not to give it unless the patient was worse that evening. That night her condition appeared hopeless, but, as no mercurochrome was available or procurable, none was given. The following morning there was a definite improvement in the general condition though not in the cellulitis. After this, improvement was rapid in both. Had the mercurochrome been given, I should have regarded this case as a wonderful result. All that took place was some reaction on the part of the patient which was due to something inherent in the constitution or to the nursing.

Cases such as this occur in the practice of all. What takes place we do not understand. All that can be said is that at one time the constitution is such that streptococci can develop in the tissues, and at the other it has been brought back to the normal in which the tissues are indifferent to bacteria. This is well seen in pneumonia where the condition is serious until the crisis suddenly supervenes. Even then there is at first no change in the nature or in the amount of the pulmonary inflammation. Somehow the resistance factor in the constitution has been brought back into the condition in which it was before the onset of the pneumonia. As a result the tissues can again be indifferent to the pneumococci that enter them. The difficulty with which we are faced is that we have no means of estimating the constitution scientifically. Rather we have to estimate it by the way the body reacts in health and disease.

We are inclined to ignore this reaction and to look upon it as a side issue, since it is difficult to fit in with our outlook on medicine. It is, however, something of fundamental importance that must be considered in the treatment of all inflammations. Probably when we know what it means we shall be able to deal as effectively with an inflammation as we can with a field to be prepared for operation.

The mistake is widespread that disease arises because the body has been brought in contact with its cause for the first time. Probably this has been going on from childhood upwards, and disease can develop only if the constitution has first been undermined. So, in therapy, not only must attention be given to the impairment of the health that is secondary to the disease, but also to that state of the constitution that has allowed it to develop. When it is overcome the disease becomes quiescent.

These principles are illustrated by the following cases.

A. The Reaction of the Constitution and its Bearing on the Acid State

A. C., aged 43, a labourer, was admitted to the Cardiff Royal Infirmary in 1933. He had a stricture of the urethra which was dilated by an internal urethrotomy and a stone in the bladder which was removed by suprapubic cystostomy. On his discharge there was no residual urine and no pyuria. He was given hexamine and acid sodium phosphate and told to drink plenty of fluids. His general condition was not too good, but it was expected that this would improve after he returned to work. In 1934 he was readmitted with a large phosphatic stone in the bladder which was again removed by cystostomy. The urine cleared up quickly and there was neither residual nor great infection that might predispose to a stone. This was due to something in his constitution, for he was hyposthenic with a low blood pressure (115) and a persistently alkaline urine. Unless this could be overcome it was likely that the stone would recur. The carbohydrates in his food were lowered and the fat increased. Excessive fluids were not advised. He was given small doses of mercury, hexamine, acid hydrochlor. dil., insulin, and artificial sunlight. His weight improved, his blood pressure rose to 125 and his urine became acid. His condition was totally different from that on his first discharge. At that time it was thought that as the operation had been successful his general condition would improve. The urine was to be kept acid by giving less alkalis and by increasing the amounts of acid by the mouth. The recurrence showed how this had failed.

Now an attempt is being made to improve his health by trying to create some reaction and so change his constitution. As mercury, hexamine, acid hydrochlor. dil., and artificial sunlight do not put anything directly into the body and act only if some reaction takes place, the dose that is given at first is very small. That the treatment is successful is shown by his good condition and by the urine becoming acid. This change is also the basis of the ketogenic diet. At the first operation all that was done was to remove the cause of the symptoms. Now an attempt is made to overcome the cause giving rise to the stone. The modification of the constitution has taken place when he is at rest in hospital. Whether it can be maintained when he returns to his work is problematical, for he will then have to face the stress of living and under the prevalent economic conditions good food may not be available. His constitution may again be impaired.

B. Chemical Shock

A boy, aged 15, was admitted to the Cardiff Royal Infirmary complaining of pain in the right iliac fossa, vomiting, and a temperature of 100°. The appendix was removed, but the symptoms persisted. As there was some rigidity below the twelfth rib the perinephric region was explored, but no pus could be found. His general condition became so serious that the anæsthetist would not consent to the operation being prolonged to permit exploration of the kidney. After the operation he became worse and the pyrexia persisted. The leucocyte count was 26,000. As this might possibly be due to a carbuncle of the kidney, uroselectan was injected. After 8 c.c. had been given he collapsed. For some days he was so ill that it was thought he would die and during this time all the lymphatic glands throughout the body became enlarged and tender. Rapid improvement in health then set in and in a few weeks he was discharged convalescent. The pyelogram showed a normal pelvis to both kidneys.

This was an example of chemical shock, though why it occurred I do not know ; for I must have given close upon

a thousand injections of uroselectan and have seen it only once before. He nearly died at the time of the injection and for some days was very ill. When salvarsan was first used, it was not uncommon for it to produce a rigor and severe collapse. If not fatal, such cases did well. I have seen this result only once with neo-salvarsan, when a gumma cleared up as if by magic. This type of shock seems to be an extreme form of the vasomotor disorder that is sometimes seen when drugs are injected intravenously. It must be differentiated from poisoning by the drug. Some claim to use it in therapy. But it is not something that can be produced at will. It is due to some abnormal response on the part of the cells. It is not dependent on the nature of the drug or on the amount. The few cases I have seen have occurred most unexpectedly, and I cannot think of anyone attempting to produce it. For it is one of the most terrible things to watch. The patient's condition is desperate and, apart from the injection of adrenalin, little can be done to control it. Few patients who have experienced it will ever consent to the continuance of the treatment. They prefer the disease. A doctor who was at death's door with phthisis and who recovered after an injection of sanocrysin that led to severe shock told me that while it was preferable to owning six feet of earth, he was doubtful if he would submit to an injection again. If at times shock cures, it sometimes makes the condition worse. It is not possible to foretell its course, and once it begins it cannot be controlled. An elderly practitioner told me that it conformed to a form of therapy carried out many years ago and which was described as " shaking up the system." It was abandoned because of the uncertainty of the results. Shock therapy really amounts to this.

C. Change of Air

A woman, aged 25, was examined by me at Glanely for genito-urinary tuberculosis. Her temperature rose to 104° and she was at times delirious. It seemed that miliary

tuberculosis had developed. It could not be accounted for by anything in the urinary tract. We were aware that the right kidney was extensively diseased. No operation was possible. She was taken home by her relatives to die. A few months later she returned with the remark, " Here comes the corpse." As no quack remedies had been tried, she still had confidence in us. Since then her right kidney has been removed. Here was a woman with tuberculosis who was rapidly losing ground though she was being treated under the best conditions. Yet when she was taken home she recovered. There was no question of any change in the amount of the disease or of an abscess bursting. One could only assume that the change of air in some way modified the constitution, as a result of which the disease could be controlled.

A surgeon, who was wounded in the lung, developed a cough, and tubercle bacilli were found in the sputum on one occasion. After the War he went to Switzerland and visited many health resorts. His condition became worse and at the end of six months he felt that there was no alternative but to return home to die. As a last resort he went to Davos. From the day he arrived his cough disappeared, his condition improved, and his health soon returned. There was no question of faith, as this had disappeared long ago. He attributed the improvement at first to some balm-like action of the air upon the mucous membrane of the lung. But he has now come to the conclusion that it must have been due to some action upon the constitution. For in later years when his health was impaired and there was no cough he felt much better immediately he went to Davos. This was out of proportion to the benefit he derived from other Alpine resorts.

Change of air may at times work wonders. It was for many years believed that in phthisis it had some direct action upon the tuberculous lesion by penetrating into the alveoli. But consideration of the pathology of this disease shows that it can have none in this way. On the other hand, a change of air may be disastrous. At Davos some patients become worse soon after arrival. The change seems to modify the constitution and create a state that is favourable

or unfavourable to the progress of the disease. For the constitution is something very delicate that is affected by slight causes—sometimes even by a change in the direction of the wind. A change of air may bring the constitution into its normal state, when disease can be overcome ; or it may increase that factor which allows the disease to go ahead. This of course amounts to saying that it aggravates or cures a disease, but it gives a plausible cause for its action.

D. The Empirical Action of Drugs

A. W. was seen by me in consultation with Dr. R. K. Shepherd. He was demobilised from the army with a cough and in 1920 had hæmoptysis due to phthisis. In April, 1925, the left knee was involved, and healed by ankylosis. In July tuberculous disease broke out in the sternum ; in Sept. in the right testis ; in Oct., 1927, in the left testis. In March, 1928, both testes were removed. Artificial sunlight was given for the disease in the sternum, but that in the lung flared up. In Jan., 1932, urinary symptoms arose and both kidneys were found to be involved. This was confirmed by an intravenous pyelography. It was looked upon as a terminal event. He was treated by tuberculin and rest ; there was no improvement in the urinary symptoms nor had opium any action upon them. In Aug., 1932, he was given methylene blue. On the following day the symptoms began to subside. He has since remained fairly well.

In August, 1932, on looking through some old notes on genito-urinary tuberculosis, I found that some years previously I had given methylene blue. At times it had a marked action. But in a series of cases it did so little good that it was abandoned. As it was then given upon the supposition that it had some antiseptic action, it was probably discontinued because it was thought it could have no direct action upon the disease. Since August, 1932, I have continued to use it with definite benefit in some cases. It does little good where the disease is active and there is much pus or a rise of temperature. It seems to act best where the

patient is holding his own and, though frequency and pain are present, the disease is not progressing. At such a time methylene blue seems to modify the constitution and raise the resistance factor, just as a change of air does now and again. As a result the disease can now be overcome. A. W. is a case in point. There was no difference in the amount of disease present at the beginning and the end of August, and there was no suggestion of an abscess bursting. He was literally riddled with tuberculosis. For him methylene blue was just the thing needed to put his constitution into that condition in which it could overcome the disease. It does not follow that it would have a similar effect in another case of genito-urinary tuberculosis; for we now know that it can have no local action upon the disease. But it would if given to a person with a similar type of constitution. Probably because this was not appreciated, it was abandoned in past years, when the mistake was made of directing all attention to the disease.

E. The Bilious Diathesis

A surgeon, A., aged 45, had suffered since boyhood from colds and abdominal disorders. Some focus of infection to account for his lack of stamina was sought. In 1913 a fibrosed appendix was removed. He then suffered from sore throats. In 1914 his tonsils were found to be full of pus and were enucleated, after which he developed bronchitis. He served in Gallipoli, where he had both types of dysentery and jaundice and was wounded in the lung and spine. On returning to England he suffered from alternating colitis, bronchitis, gingivitis, and pain in the right side of the epigastrium. After a couple of years the pain became localised there. Whenever the health became impaired, this pain always occurred. It was particularly marked after mental or physical fatigue or when the east wind blew. In Dec., 1929, an infected gall-bladder, containing forty stones, was removed. When convalescing, the gums started to bleed. On taking a trip out East he had sunstroke and whilst getting over this in Switzerland he suffered from streptococcal septicæmia and

later from nephritis and uræmia. The teeth were regarded as the focus and were removed. The colon now gave rise to trouble. One infection just followed another. Life was now going to be difficult, for long periods of rest would have to be taken and no great work could be done. After reading an article on the constitution he felt that his state conformed to the bilious diathesis for which mercury was regarded as almost a specific. Profiting by the teaching of Hutchinson that it was the reaction of the patient that counted and not the amount of the drug that was taken, he began with $\frac{1}{20}$ grain of hydrarg. cum crete twice a day, which was slowly increased to $\frac{1}{8}$ grain three times a day. The improvement in his health has been marvellous and the sense of well-being is one that he could not recall. The colitis has almost disappeared. His recovery has now lasted for two years. Looking back on life he feels that much of his ill health was due to a desire to excel in games and to harden himself to meet all weathers. Being of the bilious diathesis, when the health became impaired the resistance of his mucous membranes was lowered. A low-grade type of inflammation developed in what probably was his weakest organ, the purpose of which seemed to be to raise his resistance. For when the appendix was removed the tonsil was picked out and after this the gall-bladder. And rather than regarding this as the focus of infection from which his ill health came, it should have been looked upon as a barometer which indicated to him the state of his health. Now that the weak link in his constitution is overcome by taking mercury, there seems no necessity for this inflammation to arise.

A., the medical superintendent of a hospital, had suffered from a coli infection of the urinary tract for years, that was liable to come on after fatigue or when the east wind blew. When he discussed his case with me I pointed out that nowadays I was more inclined, when no gross pathological lesion of the urinary tract could be detected, to treat the constitution. In my experience a coli infection appeared in one of the bilious diathesis. He promptly told me that not only was he of this diathesis himself, but so were other members of his family. For four months he has taken small doses of mercury. There has been an increase in weight and a marked

improvement in the general health and in the sense of well-being. So far there has been no recurrence of the infection. He writes to me and says, " The east wind has now lost its terrors."

Now the mercury here had no direct action upon the mucous membranes. It acted rather as an alterative, as a result of which some error in the constitution was overcome and the health was improved. But it must be remembered that, as this is possible only by a response on the part of the cells, the more ill a patient is the smaller the dose that should be given. The bilious diathesis is seen rather in those of the hyposthenic type of Hurst and is more common in women than in men. Any mucous membrane may be picked out.

F. The Neuralgic Diathesis

J., aged 51, a colliery surveyor, consulted me in 1929 for pain in the left lumbar region that passed down into the gluteal region, and had been present for three years. It was sometimes worse after exercise and sometimes more marked at the end of micturition. He had had continuous treatment from his practitioner with no improvement. He was cystoscoped and X-rayed but nothing could be detected to account for the pain, which was attributed to some form of neuralgia. Treatment was directed to the relief of this, but, as he derived no benefit, he discontinued it. He came to consult me in Jan. 1934 for a hydrocele. He then told me that after leaving me in 1929 he had taken some herbs for a couple of weeks, when his pain disappeared. Whenever they recurred, he found these acted like a charm. There was no question of a neurosis. Some might say it is a coincidence. I was inclined to think that the herbs had in some way modified his constitution and brought it back to normal. This was probably an example of the neuralgic diathesis which is more prevalent in the hypersthenic.

In certain types of irritable bladder where no cause can be found to account for the symptoms, much relief will follow the administration of small doses of opium or of liquor arsenicalis, minim 1 of the tincture or liquor three

times a day being enough. In some cases it is also advisable to refrain from anything containing caffeine. Since some hot drink is necessary and milk is so insipid, one of the tisanes is prescribed. At times a condition previously resistant to treatment clears up. This type of bladder seems to be part of the neuralgic diathesis, in which there is some irritable state of the nervous system that becomes localised in one organ. Just as in the bilious diathesis mercury may modify the constitution, so may opium, arsenic, or some herb do so here and the state that has led to the symptoms disappears. It must be borne in mind that it is some reaction on the part of the body that is induced and small rather than large doses should be given. This effect must be differentiated from the sedative action of opium which is dependent upon the size of the dose.

Though these cases do not reveal anything about the nature of the constitution, they do show that it can be modified and disease and ill-health overcome, and indicate the possible action of therapy in cases which in the past we have been inclined to regard as examples of suggestion. There is a type of case in which no headway is made or in which the symptoms become worse. Though numerous remedies are tried, none gives any relief. Then some drug that has no direct action is given and leads to an immediate improvement and cure. Though faith and hope cannot be definitely excluded, they are not likely to be the cause, since they have so often been tried out. The improvement is due rather to some modification of the constitution that is set up. This is all that should be aimed at in the conservative treatment of bacterial disease. For this will subside, if the reaction can be produced. This line of therapy just amounts to assisting Nature.

CHAPTER IV

THE STAGES OF AN INFLAMMATION

The Stage of Congestion

AFTER a preliminary constriction there is dilatation of the arterioles, capillaries, and venules ; as a result the flow of blood is increased, serous fluid is exuded and diapedesis of leucocytes takes place. The object is to bring the body fluids and the leucocytes into contact with the bacteria so as to destroy them and to neutralise and remove any toxins that are being formed. These agents normally have great antibactericidal powers which seem to be increased immediately an inflammation arises. For in the early stages of peritonitis, whilst bacteria can be detected in a stained film, so often none can be grown on culture. This is particularly noticeable if there is any delay in plating out. In certain cases of hydrothorax due to tuberculosis, the fluid may be swarming with tubercle bacilli yet none may be grown on culture. They have been destroyed by the body fluids produced in response to their activity.

The Stage of Stasis

Here the blood flow in the arterioles, capillaries, and venules becomes slowed and at times ceases altogether. It seems as if there is an attempt of the tissues to shut off the inflamed area to limit the absorption of toxins, and to allow the antibactericidal fluids to remain in contact with the bacteria for a longer time. This serves some definite purpose, for passive hyperæmia by the method of Bier, which increases stasis, has a definite value in the treatment of inflammation ; and in intra-abdominal inflammation the prognosis seems better when fibrinous deposits take place.

They mean an attempt to shut off the general peritoneal cavity. The stasis and the output of fibrin place a limitation on the activity of the bacteria and give time for the antibactericidal properties of the body fluids to increase ; for during this stage a general reaction occurs, as is shown clinically by a rise of temperature and leucocytosis. The antibodies are also increasing. Generally speaking, their presence means that the resistance is increasing and that the disease is being overcome. For instance, the positive Widal test in typhoid is generally associated with disappearance of the bacilli from the blood and the development of antibodies in pneumonia with the onset of the crisis. But even though the antibodies are being increased, it by no means follows that the local lesions clear up or that the patient survives.

Many excellent books have already been published on the subject ; and as this one deals mainly with the clinical aspects of inflammation, little reference will be made to the action of antibodies. It is well, however, to realise that most of the work dealing with these is based on experiments on animals and not on observations at the bedside.

The Stage of Formation of Pus

Here the fluid and cells are increased. If at the same time the tissues are being destroyed, an abscess is formed and comes to be surrounded by granulation tissue. This limits the activity of the bacteria and the absorption of toxins. The value of a layer of granulation tissue is realised by all surgeons, for when it is well formed the prognosis is better.

Until more is known about the pathology of inflammation there will be much controversy about the significance to be attached to the presence of pus and the purpose it serves. When pus forms, healing by first intention can no longer take place and convalescence is prolonged. Hence the surgeon is apt to regard its presence with dismay. Yet the presence of pus sometimes means that the inflammation is subsiding. It is certainly preferable to a spreading

inflammation or to septicæmia. Hence, in pre-antiseptic days when so many wounds went septic, surgeons spoke of laudable pus ; for if a wound became inflamed and yellow pus was formed in appreciable amount septicæmia did not supervene and the inflammation subsided. Consequently the presence of pus was desired. As sepsis became less common after operation, surgeons were inclined to ridicule the term. They failed to realise that it was appreciated as the alternative to something worse—a spreading inflammation. There are still surgeons to-day who realise that once it is obvious an inflammation cannot be aborted, the sooner the pus appears and the more yellow it is the better that patient will eventually do ; but as to what purpose it serves few are certain. Pus contains many degenerated cells from which a tryptic ferment is formed that helps to dissolve the sloughs. On the other hand, at times it serves as an admirable medium for the growth of micro-organisms and so aggravates the inflammation. Though at one time harmful, at another pus is beneficial, for when it forms the inflammation subsides. In some way it builds up the resistance.

That pus may be harmful is certain, for if at a stage of an inflammation it is let out there is an immediate improvement. This is so often demonstrated in the surgery of appendicitis that no further examples need be given. Hence pus was described as putrid by Lord Lister, and as corrupt by Sir Almroth Wright. And the practically universal teaching is that whenever pus is forming an incision should be made to drain it away. For it may lead to the destruction of vital structures ; it may track and involve other organs ; bacteria may be absorbed giving rise to septicæmia ; or toxin may be absorbed that would impair the functions of some vital organ. This policy has dominated the practice of surgery. It has become the teaching that the surgeon should go farther and that his aim in the treatment of an inflammation should be to prevent the formation of pus.

On the other hand, the operation to let out pus may be more dangerous than to leave it to be absorbed or to find its way to the surface. It is surprising at such a time to find how well the patient tolerates pus in large amounts and occasionally seems better for its presence. In former years when an empyema was diagnosed, the practice was immediately to make an incision and let out the pus. To prevent its reaccumulation a drainage tube was inserted. But during 1917–18 the mortality in the American Army of this treatment was on the average 30 per cent. and in one camp reached 70 per cent. It was found that these results were due to some extent to the rush of air into the pleural cavity, which, owing to the collapse of the lung and the displacement of the heart, threw a great strain upon the circulation. To prevent this, aspiration was recommended until frank pus was present and adhesions had formed. Aspiration was repeated if the pus reaccumulated. Though many of the cases were due to a streptococcal infection, the mortality was soon lowered to 5 per cent., the general conditions of the patients improved, and, if at some later date an incision was necessary to drain the pleura, there was less shock and the wounds healed more quickly. Also complications such as pericarditis, involvement of the other lung, and septicæmia were less common. Though this treatment is totally opposed to the prevalent teaching that pus must be let out immediately it is detected, it is now followed by most surgeons in empyema.

Many are coming round to the view that in the early stages not only is the incising of inflamed tissues dangerous, since it may lead to septicæmia, but that it encourages rather than prevents the formation of pus, and causes wounds to take much longer to heal. Whereas if conservative methods, such as the application of warmth and treatment by rest, are adopted the mass becomes smaller and an area of softening appears from which the pus can be let out by a small incision. The inflammation now subsides and the wound soon heals.

Metastatic complications are much less common and there seems little tendency for the inflammation to recur. In osteomyelitis some surgeons now make only a small incision to relieve tension. Better results follow than after the guttering of the bone that was the practice a few years ago. Many practitioners have told me that, since adopting this procedure generally in the treatment of inflammation, they have obtained much better results. Some have noted that in the case of septic fingers where the patient has not at first sought medical advice, the end results are better than when an incision is made straightaway. It does seem, therefore, as if at times the formation and retention of pus help to build up the resistance. As so much depends upon the significance that is to be attached to it, its bearing on certain states will now be investigated.

A. The Relation of Pus to Septicæmia

When a collection of deep-lying pus has to be opened up and healthy tissues have to be incised, there is always the danger of them becoming infected and of septicæmia arising. When this takes place, healthy granulations do not form and the amount of pus diminishes.

When a wound is discharging freely and septicæmia supervenes, the pus becomes more serous or dries up and the granulations lose their healthy appearance and become somewhat like raw ham. When good thick pus re-forms, it is often the first clinical sign that recovery is taking place and may appear long before there is an improvement in the general condition.

When in septicæmia a local abscess arises often at the site of a previous infection, the general condition will be found improved. Consequently, French surgeons introduced the practice of producing a " fixation abscess " by injection of turpentine. It was held that this in some way fixed the bacteria or that certain products were absorbed from the abscess which raised the resistance and lead to a cure of the septicæmia.

It is my impression that when an abscess forms in a patient who is recovering from septicæmia, it is not the cause of the improvement but is incidental to it. It often forms at the site of some previous injection. When a patient with true septicæmia is losing ground, it seems impossible for him to produce pus.

B. The Relation of Pus to the Peritoneum

When a patient is brought to hospital with general peritonitis and his condition is poor, my practice in recent years has been to carry out expectant treatment. It is somewhat strange to see an inflammation, that had previously progressed until the general health was impaired, now subside. At times a local abscess may form. Even when it is one of considerable size, it is often surprising how well the patient looks. The question arises, Has this abscess formed because the patient is recovering and his resistance is increasing or vice versa ?

In most cases of cholecystitis and in cases of appendicitis seen after the forty-eighth hour, it is my practice not to operate, if the inflammation shows no sign of spreading. Experience has shown that a large mass containing pus quietens down and can be completely absorbed. During this time the patient looks and feels extremely well. In other cases a residual abscess is left, which when opened later heals in a few days.

It does not seem that absorption of the inflammatory mass necessarily has a detrimental effect. Often the debility is less than when an operation is performed, and during the convalescence the patient seems stronger. Such sequelæ as bronchitis and thrombosis, that are not infrequent even when the appendix or gall-bladder is removed, are rarely seen under the expectant method. Possibly when an inflammation is allowed to run its cycle undisturbed the powers of resistance are increasingly raised.

Certain types of patients do badly. In those previously of robust health often little pus is formed and the inflam-

mation tends to extend and lead to septicæmia. Even when an operation is performed at the earliest stage, septicæmia still occurs. This also holds for young children. When the general health is poor, though there is little local reaction, much pus may be formed, but this is rarely yellow and laudable. Generally it is serous and unhealthy. Even when the abscess is drained, it will go on discharging profusely ; and it sometimes seems as if opening it up has done harm. Only as the general health improves does the discharge show any tendency to subside. It is often difficult to decide which occurs first. Often it seems to be the former.

C. The Relation of Pus to Granulations

When a varicose ulcer fails to heal by ordinary applications, if the leg is encased in Unna's paste or in an elastoplast bandage for some weeks it may heal at once. Though this keeps the part at rest, it also retains in contact with the granulations discharges that were previously washed away. These in some way stimulate the healing process.

When an operation is performed in children for osteomyelitis the dressing of the wound causes much pain which may undermine the health. This is not prevented even if a general anæsthetic is given. Therefore my practice for years has been to cover the walls of the incision with bip and then to plug with gauze which is not removed for ten days. At the end of this time the granulations are found to be healthy and to bleed freely, showing that contact with pus does no harm.

During the War the dressings of the guillotine amputations caused so much pain that an anæsthetic had to be given. To avoid this the wounds were not dressed for some days. Not only was the general health much better, but the granulations were healthier and the wounds healed more quickly than when the dressings were changed each day.

Orr's treatment of compound fractures also shows that the retention of the discharge in contact with the wound promotes healing and prevents the spread of sepsis.

D. The Relation of Pus in Tuberculosis

A tuberculous lesion in a person whose resistance is good becomes fibrosed or calcified. If the resistance is poor, pus tends to form. As this so often corresponds with some impairment of the health, it is therefore assumed that the ill-health is due to the absorption of toxins from the pus. Hence pus in tuberculosis has been regarded as harmful and in past years every effort has been made to remove it by aspiration. But if the diseased part is placed at rest and the general health improved by fresh air, sunlight, etc., the pus becomes absorbed. It is now realised that pus in itself is not harmful, for if it becomes absorbed the case does as well as if no pus is formed. This is well shown when a psoas abscess arises in Pott's disease. Probably pus is formed because the disease is not being overcome and its presence means that the resistance is low. Hence its harmful significance. When it disappears by absorption, probably the resistance has been raised, though it is possible that the pus itself may set up some form of protein therapy and lead to this.

The Stage of Formation of Fibrous and of Granulation Tissue

From the early stages there is a tendency for granulation tissue to form and for fibrosis to occur. These denote that a good resistance is being put up and that an attempt is being made to shut off the inflamed area. They may be absorbed as the inflammation subsides. When it becomes chronic, this fibrosis and granulation tissue may be the very things that stop healing, if the organ cannot collapse. At such a time they should be looked upon not merely as the disease, but as the evidence of a good resistance to the spread of the inflammation earlier on.

It does seem as if each stage of an inflammation serves some purpose. This applies to congestion and the exudation of serous fluid, to stasis and the formation of fibrin, the exudation of leucocytes and the formation of pus and of fibrous and granulation tissue. It

is only an excessive degree or undue persistence of a reaction that is harmful.[1] For instance, congestion may lead to tension and to necrosis of the tissues. Stasis, by impairing the blood supply, may also lead to this. Though sometimes pus is harmful, because it aggravates the inflammation and undermines the general health, at other times it seems to localise the inflammation and in some way to increase the powers of resistance. For if after it is formed the mass is absorbed, there does seem to be less asthenia; and recurrence of the infection is less common.

This may be due to the absorption of pus setting up a form of protein therapy. When we are certain as to what purpose pus serves and why its presence at one time undermines the health and aggravates the inflammatory process, and at another improves the health and causes the inflammation to subside, some light may be thrown upon protein therapy.

[1] This is best illustrated by a reference to tuberculosis, where the lesion may be looked upon as the advance of the disease or as the resistance of the body to an infection. When tubercle bacilli are deposited in an organ, the miliary tubercle is the primary lesion. The tuberculous lesion is composed of an agglomeration of these, and results from the activity of bacilli and the resisting powers of tissues. If resistance is poor, disease may go ahead and develop into acute miliary tuberculosis or extensive local infiltration with the formation of pus. If resistance is good, fibrosis is set up. The tuberculous nodule is due to this, and its development means that the disease is being resisted locally. But later, when the resistance factor is restored, this fibrosis may prevent the cavity collapsing and be the cause of persistence of ill-health. Injurious as it may then appear, it is well to keep in mind that there was a time when its presence was desirable, since it meant that the progress of the disease was being resisted. In the same way, when faced with a case of inflammation the practitioner should put to himself this question : Harmful as the signs may appear, may not the state of this patient be much worse if no resistance were being established ?

CHAPTER V

THE CLINICAL CONTROL OF AN INFLAMMATION

WHEN an inflammation is being investigated the signs that are of value clinically are the following :

1. Redness.
2. Heat.
3. Pain.
4. Swelling.
5. A rise of temperature.
6. The leucocyte count.

Redness is dependent first of all upon congestion and later upon stasis, and must be differentiated from the infiltration with hæmoglobin that is sometimes seen. It is present from the start with surface inflammation and with deep inflammation only as this approaches the surface. As a certain amount of congestion is desirable, redness is a favourable sign, for it denotes that a reaction is taking place locally. It is undesirable only if it is excessive or tends to spread. Then the part may have an angry blush. This means that the inflammation is progressing.

Increased heat generally goes with congestion, though in a deep-seated inflammation such as that of a knee-joint, there may be a definite increase of heat even when there is no surface hyperæmia. It generally means that the inflammation is still active, though not necessarily that it is progressive.

Pain is a variable symptom. It is greater in those who are strong than in those who are weak. It varies with the sensitivity of the part affected. An inflammation under the finger nail can be extremely painful. But pain seems to be more dependent upon the amount of the exudation

and the ease with which distensibility can take place. For instance, in osteomyelitis due to a staphylococcal infection, pain is often severe from the start, whereas in a perirenal infection, where the exudation can occur without much tension, there may be little or no pain.

But something more than sensitivity and tension comes into play. For peritonitis due to the pneumococcus causes less pain than that due to the streptococcus or the B. coli. This is also seen in the case of joint infections with these organisms. It is not, I think, entirely due to the fact that the pneumococcal effusion appears sooner and is greater than the other effusions. For the most painful joint affection is that of acute rheumatic fever, and though there is an effusion this is very transitory and the pain is not proportionate to its amount. Equally painful may be the arthritis due to the gonococcus, where there may be no effusion at all. There is some factor in the production of pain that is at present beyond our knowledge. A throbbing pain means that an inflammation has begun. It serves a definite purpose, for it is increased by activity and the part is therefore kept at rest. But when pain becomes boring or more intense, this means that the effusion is increasing and often denotes that it is under tension. One of the most definite indications for an incision into an inflammatory mass is this change in the nature of a pain, particularly if at the same time it increases in intensity.

Swelling is due to congestion, to exudation of serum or fibrin, to the formation of pus, and of granulation and fibrous tissue. Sometimes as pus forms, an area of softening appears, the skin becomes wrinkled, and the swelling smaller. This is because the inflammation is subsiding.

Temperature. When bacteria or their toxins have invaded the blood stream, there is usually a rise of temperature. This is to be desired, for resistance is now good and antibodies are being produced. It is only an unfavourable sign if it is prolonged, for this means that the

infection is persisting; or if it is excessive, for this means that too great a reaction is being called for on the part of the body. A fall in temperature, particularly if associated with a steadying of the pulse rate, generally means that the infection is being overcome and that the inflammation will subside. With raised temperature the pulse, though increased in rate, may be full and bounding and the blood pressure raised. Such a reaction is said to be sthenic. In other cases the pulse rate is rapid and of low tension and the blood pressure is low. The reaction is now asthenic.

The leucocyte count. If toxins are being absorbed, and particularly if suppuration has taken place, an increase in the leucocytes is to be expected. Though, as will be seen later, this may take place with one organism and not with another.

Now when these signs are considered, it will be found that the only two that can be estimated with any scientific exactness are the temperature and the leucocyte count. But we are by no means certain what these exactly indicate. All that can be said is that when in inflammations of a certain type both are raised the resistance is generally good. But a high temperature and a high leucocyte count do not always mean that a good resistance is being established. At certain times in septicæmia when it is clinically obvious that the patient is losing ground and is soon to die, both may be raised. And in sunstroke, where the temperature may be raised, and in leukæmia when the leucocyte count is very high, the resistance to infection is low. Possibly a raised temperature or leucocyte count have themselves nothing to do with resistance. But they often coincide with the presence of something of which so far we have no exact knowledge.

The rise of temperature and the leucocytosis may have the same significance as the rise of urea in the blood in uræmia. If this increases, the prognosis is worse. But of one thing we feel fairly certain, that urea itself is not the

cause of uræmia. Probably its presence synchronises with that of some other substance of the nature of which we are as yet uncertain.

When these signs are estimated in relation to the general condition of a patient, the reaction to an infection is ascertained.

CHAPTER VI

THE INFLAMMATORY STATES

ONLY five will be considered : the acute sthenic, the acute asthenic, the chronic sthenic, the chronic asthenic, and the septicæmic.

Acute sthenic inflammation is seen in a carbuncle, in pneumococcal pneumonia, or in staphylococcal infection of the bones or of a kidney. It is characterised by local congestion and by much pain. The general reaction is considerable and the temperature is high. The pulse is full and bounding, the blood pressure is usually raised, and, though the patient may feel ill, there is not at the start marked depression. If there is delirium it is of the violent type. In many cases the inflammation subsides without suppuration. If pus forms and can be discharged, resolution of the inflammation follows, leaving little impairment of the general health. When the inflammation is very acute, if the inflamed organ can be completely removed the patient will soon feel quite well.

Acute asthenic inflammation is seen in gas gangrene, influenzal pneumonia, and acute pyelitis due to B. coli. The local congestion and pain are not so marked as in the former type. The pulse is fast and the blood pressure somewhat low, but the temperature may be even higher. Delirium is of the low muttering type. The characteristic feature is that the patient feels depressed, and there is marked physical and mental prostration, often out of proportion to the local and general signs. In the acute sthenic type, though the temperature is high and the patient feels ill, there is not any marked depression. On the other hand, in the acute asthenic inflammation this appears very early in the disease. Whether the toxins pro-

duce immediate changes in the nervous system, which is most probable, or whether some impaired bodily state has preceded the inflammation, is not certain, but marked improvement does not follow the removal of the disease.

Chronic sthenic inflammation, such as is seen when a carbuncle or boil becomes chronic, is characterised by little impairment of the general health and by definite yellow pus, corresponding to the " laudable pus " of pre-antiseptic days. There are some congestion and a definite swelling, and a tendency to the formation of healthy granulations and of fibrous tissue. If the inflammation persists for some time, there is much destruction of tissue. Some definite pathological lesion of an organ can usually be found to account for its persistence, or a cavity has formed which cannot contract or the walls of which cannot fall together.

Chronic asthenic inflammation is characterised by marked impairment of the general health associated with slight local changes. There is little congestion and little tendency to the formation of healthy granulations or fibrous tissue. As a rule, there is not much swelling. When present, this is due to the exudation of serum rather than of fibrin. Little or no pus may be formed, or it may be present in considerable amounts and is then thin and of the nature of sero-pus. Laudable pus is extremely rare. One of the features is that no matter how long the inflammation persists there is little destruction of tissue provided there is free drainage. For instance, when the urinary tract is infected with the B. coli, and when this persists for years, if there is no stasis no serious surgical pathological lesion is, as a rule, to be found even when the urinary tract is most carefully examined by cystoscopy and pyelography. Though the urine contains only a trace of pus it may be swarming with bacteria. At times the bacteria may increase to an enormous extent without any corresponding reaction in the urinary tract. The malaise, weakness, and wasting are out of proportion to the local findings, and instability of the nervous system is a prominent feature.

With this type associated disorders of the stomach, intestine, heart, and genital organs are commonly found, though a pathological lesion is hardly ever to be detected in them. This type of inflammation is also frequently associated with that peculiar condition known as visceroptosis.

It is not suggested that many more clinical types of inflammation might not be described or that any type is ever clear-cut, for one so often passes into another. But this classification will serve as a basis for approaching inflammation from the clinical standpoint. The essential feature of the sthenic inflammation is that the patient reacts both locally and generally as if trying to overcome the infection. There is usually much congestion, much exudation, much pain, a high temperature, and a high leucocyte count. The tendency is for the reaction to be too great. With the asthenic type the depression is both general and local as if the patient is unable or unwilling to overcome the infection. The temperature may be very high, but there is little congestion, little exudation, little pain, and generally no leucocytosis.

It is important to differentiate between the general and the local reaction to an infection and the rate of progress. For the rate of progress may be very rapid when these reactions are very slight. This is well seen in the pneumonia of the aged. Here the progress may be marked and death may take place in a few days. Yet both the local and the general reaction, shown by the pain and the temperature, may be slight. Death is due to the action of the toxin upon some vital organ whose tissues were previously degenerated and whose function was already impaired.

Bacteriæmia and Septicæmia. In former years bacteria from the blood could be cultivated only when the patient was seriously ill. In an infectious disease the prognosis then became worse, for death was likely to follow. To this state the term "septicæmia" was given. As the methods for growing bacteria have improved, it is found that bacteria can frequently be found in the blood during

the course of an infectious fever. For instance, in the early stage of pneumonia and in typhoid fever this is the rule. As the disease progresses they disappear. Their presence is of little significance and is just incidental to the disease. To this state the term "bacillæmia" or "bacteriæmia" has been applied. After death bacteria are to be found in all the tissues of the body. It is probable that as death approaches bacteria pass into the blood stream. This also takes place during many severe illnesses. But here the presence of bacteria in the blood is secondary to and is not the cause of the general state. Though the patient is extremely ill and the bacteria are developing in the blood, the term " bacteriæmia " should still be employed. The term " septicæmia " should be retained for those conditions in which bacteria are responsible for the serious state of the patient.

The inflammatory reaction that follows a bacterial infection will depend upon the type of bacteria and its virulence, the site of the lesion, the constitution of the patient, and the state of his general health.

CHAPTER VII

THE INFLUENCE OF THE TYPE OF BACTERIA

THE reaction that is set up varies with the type of bacterium.

The anthrax bacillus gives rise to an intense congestion and much œdema locally and rapidly develops into a septicæmia. Only little pus is formed. There is an acute sthenic reaction.

The streptococcus gives rise to a congestion that is less marked than in the case of the staphylococcus. It tends to spread and not to be localised. Lymphangitis and lymphadenitis are generally present. The pus is not so thick as that due to the staphylococcus, though it generally cannot be described as sero-purulent unless the infection is very virulent. Leucocytosis is generally marked. The reaction is sthenic but less so than that due to the staphylococcus. The streptococcus affects the skin, some serous membrane, or some mucous membrane. It is very apt to lead to septicæmia, and to endocarditis, when an asthenic state is likely to supervene.

The staphylococcus gives rise to an intense local congestion and the formation of thick pus. The inflammation tends to be localised. It is not common for spreading lymphangitis or any adenitis to be set up. The inflammation is usually associated with much destruction of tissues and is followed by much fibrosis. Leucocytosis is generally marked. The staphylococcus tends to affect the parenchyma of an organ.

The pneumococcus gives rise to an intense local congestion and the formation of much pus of a creamy yellow colour and the exudation of much fibrin. It is associated with a high temperature and a marked leucocytosis. The reaction is essentially of the sthenic kind. Leucocytosis is

generally marked. The pneumococcus tends to affect a serous membrane or the parenchyma of the lung.

The gonococcus gives rise to a local reaction and the formation of pus. The congestion is not very acute. As a rule there is no general reaction nor is a septicæmia or toxæmic state likely to arise. An arthritis or any blood-borne infection is relatively rare. There is no leucocytosis. Generally the inflammation clears up without the patient feeling any the worse apart from the local discomfort. The inflammation may lead to fibrosis, but not as a rule to destruction of tissue.

The B. coli gives rise to a local reaction which is not generally characterised by the intensity of the inflammation. Pus that is formed is sero-purulent. Very rarely does laudable pus arise. A leucocytosis may be present, but generally it is not marked. It usually leads to little destruction of tissue and, even if it persists for years, may be followed by little fibrosis. A chronic infection tends to persist. The general reaction may be very great, but this is definitely of the asthenic type. It can be said of the coli infections that the general malaise is out of proportion to the local reaction. It tends to affect mucous membranes, particularly those of the gall-bladder and the pelvis of the kidney.

The diphtheria bacillus. The local reaction is quite definite but tends to remain localised and not to spread. Little pus but much fibrin is formed. There is a severe general reaction characterised by depression and weakness and at times by involvement of the nervous system. From the start the reaction is asthenic.

The typhoid bacillus produces local ulceration of the intestine ; little fibrin is formed. There is also little tendency to the formation of pus. The toxæmic state, with its marked depression and asthenia, is the characteristic feature. The reaction in both the general state and the local lesion is asthenic. The former is out of all proportion to the latter.

The B. Welchii. Apart from the formation of gas, any local reaction is slight. It is the tension of the gas that

gives rise to the pain. Though there is much exudation, little pus is formed unless other bacteria are present. There is no leucocytosis. The characteristic feature is the marked toxæmia leading to mental and physical prostration, an increase in the pulse rate, and a fall in the blood pressure.

Influenza. It is uncertain whether influenza is due to a bacillus or to some ultra-microscopic virus, and whether the organism gives rise to some local reaction or merely prepares the soil for the development of other bacteria. It seems that the organism itself does not give rise to any local reaction, for so often none can be detected when the disease is severe. The characteristic feature is the marked mental and physical prostration.

Just the usual features have been given that are to be anticipated when infection with the organism takes place. Others frequently occur. For, as will be shown in later chapters, the reaction is considerably modified by the constitution and the state of the health. The staphylococcus may give rise to a spreading cellulitis similar to that seen with the streptococcus, the gonococcus may give rise to a septicæmia, and the bacillus typhosus to yellow pus. Though the discharge from a urethritis due to the bacillus coli is generally sero-purulent, I have seen a case where it was as thick and creamy as that due to gonorrhœa. But such phenomena are exceptional. For practical purposes bacteria may be tabulated in the following order :

B. anthracis Streptococcus Pneumococcus Staphylococcus Gonococcus	Sthenic state most likely. Gram positive.
B. coli B. diphtheriæ B. typhosus B. Welchii B. of influenza	Asthenic state most likely. Gram negative except B. diphtheriæ and B. Welchii.

The gonococcus gives rise to a local reaction with the formation of pus. As a rule there is no general reaction. As the table is ascended, the local reaction becomes more marked, the congestion more intense, and the tendency to the deposit of fibrin greater and to the formation of pus less. The general reaction is now more marked and the bacteria tend to invade the blood stream and to give rise to the septicæmic state. The reaction also becomes more sthenic both in its local and general aspect. As the scale is descended the local reaction becomes less marked, there is little congestion and less tendency to the formation of pus or to the development of leucocytosis. On the other hand, the general reaction is characterised by mental prostration and weakness is more marked. The reaction in its local and general aspect is definitely asthenic. When invasion of the blood takes place with the typhoid and coli bacilli it is of the nature of a bacillæmia and not of a septicæmia, and this is not nearly so serious or so fatal as that due to the gram-positive cocci. So far as is known the B. Welchii and the bacillus of influenza do not tend to invade the blood stream. The general reaction, though severe, is more of a toxæmia probably from the action of some toxin upon the central nervous system, for the mental and physical prostration and the fall in blood pressure in the early stages are marked; though, strangely enough, at times the mental state may still be most acute.

Generally speaking, the gram-positive organisms give rise to the sthenic inflammation, and the gram-negative to the asthenic. This suggests that the type of inflammation set up is related in some way to their chemical composition. It might be thought that a local reaction depends upon the power to retain Gram's stain were it not that at the head of the scale might have been put the bacillus tetanus, which is gram-positive. Here, however, there is no local reaction and no tendency for the bacilli to enter into and to develop in the blood stream. It is only the toxins that act

upon the nervous system. But their action is definitely sthenic. The twitchings and convulsions are an indication of this. The B. diphtheriæ is gram-positive. It gives rise to an asthenic inflammation if estimated by the general reaction and the local congestion. On the other hand, it is definitely sthenic if estimated by the production of fibrin.

CHAPTER VIII

THE REACTION TO INFECTION IN HEALTH AND DISEASE

THOUGH the reaction to an infection varies with the type of bacteria, much depends on their virulence; for this is known to modify the inflammation that may follow their injection into animals. But an alteration in the virulence is hardly sufficient to account for the varying reactions seen in man, which differ not only from age to age, but between one man and another. This depends upon many factors—the anatomical site, the constitution, and the state of the health.

A. The Bearing of the Anatomical Site upon an Inflammation

Bacteria will grow on one site and not on another. For instance, the gonococcus shows a preference for the mucous membrane of the urethra and of the eye, and, when it is absorbed into the blood, picks out certain joints and certain fibrous structures. But the inflammations that arise when the same organism affects two parts may be dissimilar. A staphylococcal infection of a long bone is generally followed by an intense reaction leading to massive necrosis; that of the skin by a less severe reaction that may lead to sloughing of the tissues; that of the perinephric tissues by a mild reaction that may lead to the formation of much pus. It is often assumed that the result depends upon the products being able to accumulate without any tension arising. Though this undoubtedly plays a part, something inherent in the organ itself also comes into play. For when the streptococcus infects the skin it rarely gives rise to the formation of pus, though this is to be expected in a synovial

membrane or in the peritoneum. The difference does not depend on a change in the type of organism, for Sir Lenthal Cheatle[1] records two cases of streptococcal cutaneous erysipelas which spread and yet the only part in which there was suppuration was in an underlying bursa. This change in the reaction is well seen with the gonococcus. When the anterior urethra is involved there is a profuse discharge with little or no absorption. Hardly ever is there any rise of temperature and arthritis is almost unknown. When the posterior urethra becomes involved, the discharge becomes less, there is often a rise in temperature and it is not uncommon for arthritis to develop. It is thought that this is due to the external sphincter preventing the discharge from escaping and that consequently absorption is more probable. But a difference in the reaction is evident if the disease becomes chronic. For in the anterior urethra there is a tendency to fibrosis and stricture formation; whereas in the posterior this rarely takes place even if the disease persists for years. A papillomatosis is more common. The fact that the posterior urethra is developed from the allantois and is of hypoblastic origin, whereas the anterior urethra comes from the genital tubercle and is of epiblastic origin, offers an explanation. But a difference is noted in the reaction to the gonococcus between the mucous membrane of the bladder and that of the posterior urethra which are derived from the same embryonic layer. In the case of the peritoneum the reaction that follows an infection of the pelvic portion is quite different from that underlying the diaphragm. So far it is not possible to account for this.

B. The Bearing of the Constitution upon an Inflammation

Long before the introduction of salvarsan and the improved results of the treatment of syphilis that followed, it was found that the disease was becoming much milder.

[1] Choyce, *A System of Surgery*, vol. i, p. 146.

The severe lesions shown in the Hunterian Museum were becoming rare. Surgeons then in practice were quite definite that a change had taken place during their lifetime. On the other hand, when syphilis developed in a virgin soil such as Uganda, its ravages seemed to be just as severe as ever. It was therefore thought that many people had acquired some immunity; for, as syphilis was so common, it was unlikely that a man could go back through three or four generations without someone in his family tree having contracted the disease. This explanation was not satisfactory; for other diseases such as gout, that were not due to bacteria, were changing and becoming less severe. This could only be due to some alteration that was taking place in the constitution. For people were taking more exercise and were paying more attention to their food than in former years. Owing to the introduction of cold storage, etc., a better and more even diet was available throughout the year. This may account for the modification so frequently seen in bacterial disease; for if the constitution changes so will the power to react. When the bearing of the constitution and the general health upon an inflammation is considered, it is extremely difficult to form even impressions, for in times like these nothing is stationary for even a few years.

For instance, owing to the attention that is now given to exercise, the physique of the people has improved in the last twenty years, and this particularly applies to women, who are much more muscular. As a result, the muscular type of constitution predominates. On the other hand, in certain areas where the industrial depression prevails, malnutrition is becoming evident and is having a serious effect on the physique and the resistance to disease. Owing to the depression in the heavy industries, South Wales has become converted from a place of great prosperity into a place of great poverty, with 30 per cent. of its population unemployed. Already in the course of a few years, tuberculous disease of the genito-urinary tract seems to have become modified. Up to 1929 it was unilateral in the majority of cases and those affected were of fine physique.

Only rarely was nephrectomy not performed because of the poor general condition. But in recent years the number of bilateral cases in my practice has increased, and frequently I now refuse to operate because the general condition is not sufficiently good. It is felt that even if the patient recovers from the nephrectomy, tuberculous disease will only break out elsewhere. Whilst fibrous adhesions formerly added to the difficulty of the operation, in recent years these do not seem to be so common and are replaced by pus. This means that the resistance is becoming less good.

The dangers of forming wrong impressions are consequently very great. It is well to keep in mind the words of Sir James Paget [1]:

"The questions involved in trying to estimate these risks are very difficult, even in their simplest form; and the difficulties are subject to manifold increase when, as commonly happens, varieties of habit, constitution and general disease are variously intermingled. . . . I refer to all these difficulties, not to magnify the value of anything that I can tell you, but to justify my speaking doubtfully on many points, and talking of belief rather than of knowledge. I must thus speak, especially when referring in this lecture to the influence of local disease on the risks of operation; of these no man's life can be long enough, busy enough and thoughtful enough to enable him to gather such experience as can justify positive assertion. I cannot pretend to have attained to more than such belief as being vague, we vaguely express by speaking of impressions more or less strong. I might doubt whether such beliefs should be promulgated, if it were not certain that much of our most useful practice is founded on similar beliefs. We may be very ready to call them knowledge, but they do not deserve the name; and yet we must practice in accordance with them, just as in all the affairs of ordinary life, when certainty is not attainable, we are bound to act, if at all, upon the highest probability that we can discern."

Now Paget was one of the greatest thinkers that surgery has known, and he lived in days when it was possible for a

[1] Sir James Paget, *Clinical Lectures and Essays* (Longmans, Green & Co.).

surgeon to keep in touch with his patients; and if one with such ability found it so difficult to form conclusions, how much shall we of lesser ability who live in these days when, owing to the mobilisation of the population which took place during and after the War, it has not been possible to keep continuously in touch with any body of people, so that they can be observed from time to time both in health and disease over a number of years.

On the other hand, we are favoured in that we are much more certain of the causes of disease and are able to differentiate between certain types of bacteria. For instance, we know that gonorrhœa is due to the gonococcus and we can be certain when this disease is present. We can also distinguish between a tuberculous and a non-tuberculous organ. This does make the work easier, for when Paget wrote his classical work on *The Various Risks of Operation* he had had no help from the science of bacteriology, and the clinical thermometer was only just being used. He had to rely on his powers of observation for his conclusions.

It is to be regretted that practitioners, and particularly those who live in country towns, do not help us with this work on the constitution and its reaction in disease. For they have an opportunity of observing their patients over a number of years. In addition they sometimes have the added advantage that they can see the progress of disease through two or more generations and often in collateral branches of the same family.

The impressions that have been reached by me are put forward with much diffidence. I realise too well that many will eventually be found to be erroneous, for the grounds on which they are formed are so flimsy. It is at such a time as this when long observation is so essential that the effect of the War on our work is felt, for it divided it into two. And some of us are only now beginning to take up the thread where it was cut.

Race. Years ago it was recognised that peculiarities of the constitution predisposed to certain infections and modified

them when they developed. The scrofulous diathesis was spoken of. It was often seen in one who was rather weak and ill-nourished and who did not respond vigorously and effectively to tuberculosis, though it seemed that the resistance was diminished to infections in general. Though this predisposition to tuberculosis existed, it was strange that the disease often tended to run a peculiarly sluggish course. If it extended, this was usually locally, for there was little tendency to dissemination. Though the tubercle bacillus had little difficulty in gaining and maintaining a hold, it had considerable difficulty in making headway. The scrofulous diathesis showed itself in two quite different types, the sanguine or pretty, and the phlegmatic or ugly. The former had a delicate complexion, fine fair hair, large blue eyes with long lashes, and generally a slight build. They were often intellectual and inclined to be artistic. Temperamentally they were highly strung. In the latter the skin was thick, the hair coarse and dark, the features ill-modelled, and the build clumsy and thick. In the former the disease might run an acute course ; it was in them that the spes phthisica was so likely to arise. In the latter progress was much slower and a general reaction was unlikely.

Whatever the factors are that modify the reaction to tuberculosis, race undoubtedly plays a part, for the reaction of the Nordic race is different from that of the Celtic and Latin races. This has been brought home to me in Cardiff, where I have had the opportunity of coming across much genito-urinary tuberculosis which generally runs a chronic course and is not so likely as phthisis to be influenced by atmospheric conditions. Though Cardiff is the capital of Wales, only 30 per cent. of its population are pure Welsh. In addition, many of my private patients come from the neighbouring counties of Gloucester, Somerset, and Devon, which have not been much affected by the rapid changes that followed the industrial development of the nineteenth century ; and, as the Bristol Channel had prevented any active communication with the Welsh people,

intermarrying has not taken place to any appreciable extent. Consequently they still contain typical English people of yeomen stock; and as up to 1925 Cardiff was a flourishing port with a large overseas trade where boats came from all parts of the world, an opportunity was given to me to study patients from many countries. Patients can be divided into two classes: the phlegmatic Nordic race consisting of those of Teutonic, Scandinavian, and Anglo-Saxon descent, and the Latin and Celtic races, who are highly strung. In the Nordic people the reaction is generally more chronic, the progress of tuberculosis seems slower, the disease tends to be less extensive, and the immediate and remote results after operation are better. After nephrectomy there is little shock and the symptoms quickly disappear even though signs of the disease are still present. In the Celtic and Latin races the diseases seem to run a more acute course, and an evening rise of temperature, which is unusual in genito-urinary tuberculosis, is sometimes found. On the other hand, the symptoms persist long after the signs of the disease have passed away. Whilst they are good patients when they are ill, as soon as they begin to feel well they are inclined to neglect advice. It is my firm impression that quite apart from this the person of Nordic descent is a more favourable subject for the treatment of tuberculosis than the Latin or Celt. His resistance seems to be greater.[1]

It does seem as if the reaction to tuberculosis is more acute among the Celtic and Latin races. For a sthenic reaction with a rise of temperature is more common among them. This may to some extent depend upon temperament, which gives a patient a different outlook upon disease.[2]

[1] This probably accounts for the varied statistics that at times come from different countries. E. G. Bowen (see *Journal of the Royal Anthropological Institute*, vol. lviii, 1928) noted that so far as the inhabitants of Wales were concerned, the short, dark, long-headed person of Celtic origin differed from the fair, blue-eyed person of Nordic origin in his resistance to tuberculosis.

[2] This different outlook is inborn. It was noticeable during the War, and particularly when heavy shelling was on. Though Celtic troops were inclined to be apprehensive, they did not seem surprised when a shell landed and killed some of the men. English troops were so unconcerned. But if a shell landed and killed some men, they seemed surprised. In my opinion the best troops were those from the Welsh, English, and Scottish

Some such difference is seen in ordinary inflammation. But it is not possible to form anything but vague impressions, for the difficulties are almost insurmountable. Not only is one uncertain from what race a man really comes, but the reaction to an inflammation will vary with the type of bacteria and the state of health for the time being.

In the Celtic and Latin races inflammations seem to start more acutely and there is a sharper reaction than in the Anglo-Saxon and Teutonic.[1] This is a question of race and not of environment or upbringing, for it is my impression that it was evident among the colonial troops during the War. But the reaction at the start must not be confused with that which takes place if the inflammation progresses. It is at such a time that the vitality of the Celt seems to go to pieces and the stamina of the Anglo-Saxon begins to count: for the latter undoubtedly put up a greater resistance. When the individuals in a race are considered it will be found that those who are highly strung have a more acute reaction than those who are phlegmatic, but this is only for a short time. For if the inflammation persists an asthenic state is likely to supervene when the latter are still putting up a good resistance. Those who are tall and blond with delicate skins seem less liable to inflammation and do not react so acutely as those who are dark and vivacious. But once an inflammation begins to go ahead in the former, it at times astounds one by its rapid progress when a good resistance should be expected.

Hypersthenic and Hyposthenic Types. When the

borders. Whatever happened they never seemed surprised. They were never known to be rattled. It was as if the spirit of their ancestors, who had watched one another across the borders through the centuries, had been handed on. It is my impression that this is also seen in their outlook on disease.

[1] When a soft gum-elastic catheter is tied in the urethra, urethritis sometimes develops even if it has been boiled and the urethra carefully irrigated. This undoubtedly occurred more frequently in Cardiff than in London. The explanation was only forthcoming when this difference between Celtic and Anglo-Saxon people became evident, for it was in the former that it was more likely to appear.

constitution is considered it is advisable to limit oneself to two types, the one where there is excess and one where there is a want of energy. The excess of energy may be predominant in the nervous system, leading to the hypersthenic constitution, when it may be associated with much activity. If the nervous system is normal, it leads to the development of firm fat and the presence of the sanguine temperament. If the nervous system is over-sensitive, it leads to the artistic and highly-strung temperament. The excess may be predominant in the muscular system when it leads to good muscular development : in the blood when it leads to plethora : in the cardio-vascular system when it leads to hyperpiesia. When an inflammation arises in one with the hypersthenic constitution a sthenic reaction is to be expected, and the cause is more likely to be the staphylococcus or streptococcus than the bacillus coli. When the energy is deficient the hyposthenic constitution is present. The blood pressure is low, the circulation is poor, and the hands and feet are cold. Such a person may be fat or wasted. But the fat, like all the tissues, feels soft and flabby and is not firm as in the hypersthenic. There is a tendency to visceroptosis and to a low-grade inflammation of the mucous membranes. There is no clear line of demarcation between the hyposthenic, who is liable to a chronic bacterial disease, and the chronic invalid, in whom it is liable to be persistent. When an inflammation arises in one of hyposthenic constitution, an asthenic reaction is to be expected. B. coli infections are common. A staphylococcal infection is not so common. If it arises, there is rarely a severe reaction.

It was probably to this hyposthenic type that Sir James Paget referred to when he wrote as follows :

" You often hear me speak of patients as ' cold-blooded.' I do not know that the whole of their blood is less warm than that of ordinary persons, but some of it is, for their hands and feet are seldom or never naturally warm ; and some of them feel, when you touch them, as cold as reptiles

in the same climate. . . . And with these signs you find small pulses and general indications of slowness in all vital processes. They digest slowly and are very prone to constipation. . . . They are not bad subjects for operation; rather I should reckon them amongst the good ones; for they have always seemed to me singularly little liable to fall into the troubles of erysipelas or pyæmia or any other disorders of the blood, and the healing of their wounds is not apt to be interrupted."

As few operations upon the abdomen were done in his day, the infections that arose in wounds were probably due to the staphylococcus or streptococcus.

Health. When the general health is good a sthenic type of inflammation is more likely to arise. With a staphylococcal infection an intense congestion and much pain are usually found, for a good resistance is being put up. Yet it is surprising how, when once an inflammation begins in a person of robust health, and particularly if he is good at those games that test the wind, he is liable to go under from septicæmia. He seems to have great power to prevent an inflammation from arising; but so little to stop it once it starts to get a hold. Strong sthenic people seem particularly liable to acute staphylococcal diseases.

Though osteomyelitis, a staphylococcal infection, is seen more frequently among the poor than among the well-to-do, it does not just pick out those whose health is undermined. My experience is that those who are physically fit are more often affected. It is probably more frequent among the poor because the children play about the streets, and as a result suffer from so many accidents and are not able to lie up to the same extent.

In those whose health is not too good, the inflammation is more likely to be of the asthenic type. This also applies to those who play few games and who are inclined to live a sedentary life. They are more liable to B. coli infection. When pneumonia arises in them it is surprising how mild

a course it runs, for neither the local nor the general reaction is great. It always seems to me that at times the prognosis is better than in the very fit.

Age. Both the young and the old have not a great resistance to infection. In the young there is a marked local and general reaction and the inflammation is at first definitely of the sthenic type and pus tends to form. Convulsions with a high temperature are not uncommon, but septicæmia supervenes at an early stage. When pneumonia occurs before the age of 2, empyemata are very common, and such complications as pericarditis and meningitis are more frequent. Though an inflammation runs a rapid course in the aged, the local reaction is not marked and there is little pain. The asthenic type of inflammation is usually seen. An asthenic state soon develops. There is not the same tendency to form pus and empyemata are not common. The patient may die in the early stages, but death is usually due to the action of the toxin upon organs previously degenerated. Though bacteria are to be found in the blood, this is rather of the nature of a terminal bacteriæmia and not a true septicæmia.

C. The Bearing of Disease upon an Inflammation

The difficulties here are even greater than those that arise in connection with the constitution. For the same disease may in a short time modify the state of the health, and a constitution that is at one time able to respond to the demands made upon it and if need be set up a sthenic type of inflammation may, as a result of a disease of even a few days' duration, be unable to do so, in which case a more asthenic type would result. Consequently when the bearing of disease upon the course of an inflammation is discussed, it must be realised that the impressions that are formed are even more vague than those in the case of the constitution.

Whilst any impairment of the general health is liable to lead to some bacterial disease, the cause is particularly likely to arise if there is loss of sleep, mental anxiety, or over-

work. An inflammation that then arises tends to run an acute sthenic course and is liable to end up in septicæmia. Malnutrition undoubtedly predisposes to the inflammatory states, but when it is prolonged these tend to be rather of the asthenic than the sthenic type. They tend to run a rapid course because the organs, having so little reserve power, are quickly affected by the toxæmia.

Bright's Disease and Diabetes. Both of these in some way predispose to boils and carbuncles, though not in my experience to coli infection. These may occur long before there is any impairment of the health. If erysipelas or some other infectious disease occurs the prognosis is much worse. When in former years an operation was performed upon a diabetic, an acute sthenic inflammation was apt to arise which spread rapidly and led to death from coma. If the patient survived, a chronic asthenic inflammation developed around the wound which took a long time to heal. But the introduction of insulin has revolutionised the outlook in diabetes, and sepsis is now quite rare.

When the prostate is enlarged or a stricture is present and there is back-pressure on the kidneys, septic infection of the bladder is liable to arise and to spread to the kidneys. But unless there has been much destruction of the latter, it clears up when the back-pressure is overcome. Though the majority of infections are due to the B. coli, the more serious are due, in my experience, to streptococci. There seems little tendency for an infection to spring up elsewhere in the body, as is stated to be the case in Bright's disease. I have had little experience of the bearing of Bright's disease upon an inflammation apart from a few cases of carbuncles and boils.

Pregnancy. Though pregnancy is a physiological state its effect will be considered here. At this time the resistance to the B. coli is lowered. Hence infections from it are liable to arise in the urinary tract. The resistance to other organisms seems, if anything, to be raised. There is less tendency to pneumonia, boils, carbuncles, and to strepto-

coccal infections, and a pre-existing tuberculous lesion will show little tendency to flare up.

Once labour has begun, the position is altered. For the next few weeks resistance to certain types of bacteria is lowered, but it is a streptococcal infection that is likely to arise. It is now that fatal streptococcal septicæmia is seen. Though bacillus coli infections are still common, they are rarely acute unless associated with some other organism; and, when there has been a pyelitis due to this organism during pregnancy, it is rare for it to remain very active during the puerperium. At this time a tuberculous lesion, previously quiescent, is likely to flare up. This is attributed to the shock incidental to labour. But it is not seen during pregnancy after operations that give rise to shock unless an abortion takes place at the same time. It can be accounted for only by some great change that has taken place in the constitution. During pregnancy the state that prevails is definitely hyposthenic. The relaxation of the smooth muscle, that is so obvious in the uterus and that is probably due to an internal secretion from some endocrine gland, is seen throughout the body. For from the early months some dilatation of the uterus and the intestine takes place. If no toxæmia is present, the blood pressure falls. The breasts become engorged but do not secrete. Once labour begins there is a tendency for the smooth muscle to contract, and this persists for some time after it is over. It is a time of great functional activity. The breasts now actively secrete, and once the shock of labour is overcome the hypersthenic state prevails. There is really a tremendous change in the constitution, which is responsible for the altered resistance to infection noted between the pregnant and puerperal states. For, as has been pointed out, the inflammation that arises in the hyposthenic constitution is usually of the asthenic type, and often due to the bacillus coli, while that which arises with the hypersthenic constitution is of the sthenic type and often due to the staphylococcus or streptococcus.

Lesions of the Nervous System. During the War

lesions of the peripheral nerves were extremely common and many hundreds passed through my hands, but I cannot recall one in which an acute inflammation arose in the area supplied by the damaged nerve, though injuries to this part were not uncommon. This was somewhat singular, because they were treated in the same wards as septic compound fractures and frequent opportunities for infection arose. Though I expected an acute inflammation to arise in these, it rarely occurred. Trophic lesions of the skin were common and so were chronic ulcers, but the inflammation associated with these was always of a chronic asthenic type that showed little tendency to clear up, no matter how carefully treated. Yet after the nerve was sutured the improvement in the condition of the skin and the healing of the ulcers were often the first evidence that regeneration was taking place.

In gunshot wounds of the spine, with a lesion of the cord, massive sloughing of the tissues and bedsores were not uncommon. Whilst this gave rise to sepsis that tended to persist and to extend, it was rare for an acute spreading inflammation to arise. In the bladder severe sepsis followed the passage of a catheter and this was liable to extend to the kidneys. But the reaction in the former was generally of an asthenic type. I noticed in cystoscopies that whilst the bladder wall tended to slough, and to be covered with phosphates, there was little congestion ; and though when both kidneys were involved the patient was severely ill with a big rise in the temperature, there was little pain or tenderness over the renal area. This absence of any marked reaction with an inflammation is seen in nervous diseases in general, for a sthenic reaction is now rare and there is also little tendency for the inflammation to extend or for pus to form. B. coli infections of the urinary tract are frequent even when no catheter has been passed. But there is no severe reaction and little pus is present in the urine. A perforating ulcer in tabes may extend deeply and may gives rise to chronic and persistent sepsis. But it is rare for an

acute inflammation to occur or for much pus to form. When pneumonia arises in such diseases as general paralysis of the insane or in tabes, it usually runs a mild course. The pain is not severe, empyema is very uncommon, and the comfort of the patient is extraordinary when compared with the familiar picture. The ease with which one who is mentally afflicted gets over an infection that would be likely to kill a normal person seems definitely established.

Acute Specific Fevers. It sometimes happens that an acute fever arises during the presence of some inflammation. At one time it seems to lead to an improvement, at another it may make it much worse. The former may occur with fevers of the sthenic type, where the pulse is full and bounding and the blood pressure raised; the latter, with fevers of the asthenic type, where the pulse is rapid and of low tension. Those of the sthenic type, such as scarlet fever or erysipelas, may lead to the clearing up of some chronic infection. I can recall only one case of gonorrhœa in which erysipelas developed, and it had a most favourable influence on its course. But the difficulty of assessing this action in both scarlet fever and in erysipelas is that, whilst in the early stages the sthenic type is usually present, as the disease progresses it undermines the constitution and gives rise to the asthenic state in which the vital functions become impaired. If this occurs some pre-existing inflammation tends to light up or to become unduly chronic. Fevers of the asthenic type, such as typhoid and influenza, generally aggravate a preceding infection or inflammation. I cannot recall one case where their onset led to any improvement. Once they have occurred it is often some time before laudable pus can again be formed. Not only may the disease go ahead rapidly, but if it subsides some chronic bacterial disease is liable to persist. In some way an asthenic fever lowers the resistance. For if some quiescent tuberculous lesion is present, or one that has been active is doing well, an attack of influenza is very likely to

flare it up. This is also seen in gonorrhœa. In the 1918 epidemic some cases that were progressing favourably had serious relapses. Since then I have noticed how a case that is going on well becomes much worse and is likely to become chronic and extremely difficult to cure after an attack of influenza.

The difficulty of reaching any conclusion in the work outlined in this and the preceding chapters is brought home immediately the subject is discussed with other medical men. For instance, with B. coli infections of the urinary tract, a sthenic reaction both locally and generally may be seen. Urologists in London tell me that it occurs more frequently than I think. But a general talk on the cases we see reveals that theirs are different from mine. For they are called in consultation when surgical measures are anticipated, whereas I am often called in to clear up a diagnosis in the semi-medical case. Practitioners also hold different views. So much depends on their skill as clinicians and the care with which they examine the urine. Those who examine it systematically under the microscope when any malaise is present will discover coli infections that are missed by others. The percentage of asthenic reactions will be much higher in their practice.

CHAPTER IX

THE CAUSES OF BACTERIAL DISEASE

WHILST disease is produced by bacteria, these do not necessarily set it up. Some other factor is essential. In pre-antiseptic days only a proportion of the wounds suppurated and, with the dirty instruments that were used and the soiled coats that were worn, it is unlikely that bacteria were not introduced at each operation. When it was discovered that bacteria were the cause of the sepsis, it was felt that this absence of suppuration in certain wounds might be due to some alteration in the virulence. For in new wards or when old wards that had been closed down were reopened, sepsis was less common. Experiments on animals supported the view that the passage of bacteria through a series of patients increased their virulence. This did not give a complete explanation; for in France during the War all the large wounds must have been infected. Yet not all went septic, though this generally took place when there was much destruction of tissue. When the health was poor, and particularly if this was associated with mental strain and fatigue, sepsis was more likely. A relation to a want of food was not so noticeable, though possibly this rarely came into play, as the catering for the troops was excellent.

By the end of 1918 the conclusion to which surgeons were coming was that whilst obviously sepsis must be due to bacteria, it was favoured by certain local conditions and certain factors that modified the state of health. This applies to infectious diseases in general, but there are other forces at work the meaning of which is still very uncertain.

For instance, gonorrhœa is due to the implantation of the

gonococcus upon a mucous membrane. Whilst the eye and urethra are so vulnerable, the nose and mouth are rarely attacked. No difference between these mucous membranes which gives a satisfactory explanation has been detected. There is little doubt that the liability of the individual to become infected also plays an important part. For some, who are most promiscuous in intercourse and who take few if any precautions, never pick up the disease, whilst others who are most careful do so almost every time they take any risk. It is consequently said that some have a natural immunity.

This is also seen with the B. typhosus. For when the source of an epidemic can be ascertained many hundreds will be found to have drunk the infected milk or water or otherwise to have come in contact with the source of infection. Yet only a small proportion suffer from the disease. It is now realised that if a moderate dose of bacilli of moderate virulence were injected into a hundred men, the disease would arise in only a few. For many have a natural immunity to it. But this after all is just a phrase, for if the blood from two men were sent to a skilled bacteriologist he would not be able to differentiate between them. Nor are we certain what are the factors that cause this natural immunity to disappear. For in districts where typhoid is prevalent a man may pass through two or three epidemics untouched without taking any precautions. During this time he must have swallowed the bacillus on many occasions, but the disease has not arisen because his immunity is effective. Yet during a subsequent epidemic he may contract the disease and die. Often no reason can be found for this, for there may have been no impairment of the health.

The blood normally has great antibactericidal powers. As the technique for blood culture is being improved, it is found that invasion of the blood stream by bacteria is much commoner than was realised. But for clinical research the difficulty is to be able to investigate the cases at a sufficiently early stage.

It is known that fevers and rigors may follow the passage of urethral catheters and bougies. They are frequent after operations upon the urethra even when all aseptic precautions have been observed and contamination from an outside source is impossible. They have always been attributed to the absorption of bacteria. Barrington and Wright [1] investigated such cases and found that bacteria could be detected in the blood within a few minutes after operation upon the urethra in a large proportion of cases, where the urine in the bladder was previously infected. They disappeared quickly from the circulation, and although positive cultures were obtained from the blood immediately after the operation, blood drawn off half an hour later was sterile. But invasion of the blood was likely to occur again when the urine was first passed. In most cases there was no rise of temperature. In only one case was there a rigor. Though in this case bacteria in fairly large numbers were detected in the blood after the urine was passed, blood examined immediately after the rigor was found sterile. This is of great interest, for it denotes that a rigor is not merely the sign of an infection. It may be the reaction of the body to an infection which it overcomes. Barrington and Wright showed that a bacteriæmia is relatively frequent, but is rendered harmless by the antibactericidal properties of the blood and tissues. So long as these can be maintained it is of little significance. As in these cases it was due to absorption of bacteria previously lying latent in the urinary tract, it may be said that the body has already acquired a certain degree of immunity to these organisms, and would have little difficulty in destroying them when they enter the blood stream. But experiments on animals show conclusively that when large quantities of bacteria are introduced into the blood stream they disappear with great rapidity and no lesion need appear in any organ, proving how effectively the blood and the tissues can deal with bacteria.

[1] F. J. F. Barrington and H. D. Wright, *The Journal of Pathology and Bacteriology*, vol. xxxiii, 1930.

But when the local or general condition is favourable to the growth of bacteria their absorption may be disastrous and fatal. For instance, when there is back-pressure upon the kidneys and the patient is bordering upon uræmia, the dangers of the passage of a catheter under the most rigid aseptic precautions is known to all surgeons. The absorption of bacteria into the blood can now be disastrous, which shows that there is no effective immunity.

This work of Barrington and Wright shows that once a laceration occurs in certain areas the absorption of bacteria into the blood frequently takes place. It is of little importance if the resistance is good, as the blood can easily overcome bacteria without even an apparent reaction, such as a rise of temperature or a rigor. These are called for only if the number is very large.

Though the skin and most mucous membranes are covered with bacteria, no infection takes place. Even should they enter, it is not likely that anything would happen, for the undamaged tissues have normally a great resistance to bacteria. This is well shown in the case of the bladder. Experimentally quite virulent bacteria can be introduced into it in animals without giving rise to cystitis. This takes place only if the wall of the bladder is injured, if its nerve supply is damaged, or if its function is interfered with by obstructing the urethra. This is borne out clinically, for at times the lack of care in the sterilisation of instruments to be passed up the urethra is deplorable. Yet it is only rarely that an inflammation is set up. One surgeon to whom I acted as house-surgeon had a large out-patient clinic, but had very little confidence in asepsis. When starting his work he would put on an old morning coat that was much the worse for wear. On the table by his side was 5 per cent. boric lotion in a jar in which were placed metal and gum-elastic bougies. Olive oil was used as a lubricant. He would pass from one patient to another without washing his hands and no attempt was made to clean the meatus. After a bougie was passed it was replaced in the lotion with-

out being cleansed or boiled. The first day I worked with him, thinking he had done this in error, I promptly seized the bougie and inserted it in the steriliser. To his question as to what I was doing, I stated that it was being sterilised. He replied, " Haven't you yet learned to give the germs a chance ? " I watched his cases for many months, as according to my previous teachers these patients would be certain to develop an urethritis or a cystitis. Nothing ever happened.

The power of the tissues to overcome bacteria may be considerably impaired. This was revealed during the War in the treatment of injuries of the spine. When retention of urine followed and a catheter was passed, cystitis almost invariably supervened. Death often followed unless a cystostomy was performed, as the infection ascended to the kidney. This was not due merely to the injury itself. For if reflex micturition was established or nothing was done and overflow incontinence followed, death only rarely took place. There was much controversy at the time as to the mode of infection, and it seemed to me that it could only be due to the introduction of bacteria from without. Three cases were taken in hand in which no catheter had previously been passed. This was now done under aseptic and antiseptic precautions which were most rigid and which would have guaranteed the safety of any operation. All three cases became seriously infected, two with B. coli and one with streptococcus. It is the experience of most surgeons in civil practice that, where there is a complete lesion of the cord, the passage of a catheter, no matter how carefully it is performed, sooner or later leads to an infection of the bladder that ascends to the kidneys. Cases occur where this does not take place, but these are few and far between. The infection comes from bacteria previously lying latent in the urethra. No satisfactory explanation is forthcoming as to why the bacteria remain inactive in the urethra, for the conditions are those regarded as favourable, namely, a mucous membrane deprived of its nerve supply and kept constantly moist with urine. It is true that there

is constant flow from the bladder to the external meatus, but this is not a stream of urine that washes the mucous membrane clean. It is just a dribble, and the flow that normally takes place from the kidneys to the bladder does not prevent bacteria ascending to them.

At the time the infection of the upper urinary tract was supposed to be due to the introduction of bacteria into the bladder and the urine becoming an excellent culture medium owing to its stagnation. On the other hand, when a suprapubic cystostomy was done early, this serious state could be avoided, whether the urine was allowed to flow out continuously or if the tube was clipped and it was let out every two to four hours. It was not that the urine did not become infected, for this took place quite early. The success of the method was attributed to its no longer being possible for the urine to stagnate, but this could equally well be prevented by the passage of a catheter every four hours, and no matter how carefully this was done a serious state of sepsis was only too likely. The only difference between the two is that with a cystostomy urine no longer passes over the prostatic urethra, whereas with a catheter constant trauma to this is going on. This region has great absorptive powers, particularly if any laceration is present ; and when a catheter is passed it leads to the absorption of bacteria into the blood. The antibactericidal properties of the blood first come into play. These are probably depressed, like the vitality of the tissues in general after a spinal injury. Consequently there comes a time when the bacteria starts to develop in the blood, and as a result the virulence of bacteria that the urethral mucous membrane is normally indifferent to is in some way increased. There comes a time when a bacillæmia or even a mild form of septicæmia is set up. To counteract this there is a tendency to localise the infection. This takes place in the most vulnerable parts, namely, the upper urinary organs.

A. The Relation of a Bacteriæmia to a Bacterial Disease

It is no longer believed that in typhoid fever the disease begins in the intestine by an ulceration limited to Peyer's

patches, from which bacilli later enter the blood. Whereas they can be cultivated from the blood from the earliest stages, they can be found in the fæces only about the seventh day. Probably they are absorbed into the blood stream from the stomach. In those who will manifest the disease they are able to multiply, giving rise to a bacillæmia. About the seventh day ulceration begins in the intestine, and the signs and symptoms of the disease are more evident. The object of this localisation seems to be to enable the resistance to be built up. For it coincides with the Widal becoming positive and the disappearance of the bacilli from the blood.

Acute pneumonia was thought to be due to the direct spread of pneumococci from the throat to the bronchial mucous membrane. But on this theory it was difficult to account for the clinical findings and for the morbid anatomy. There is rarely any evidence of any preceding affection of the throat and severe tonsillitis is very infrequently followed by pneumonia. On the other hand, in the early stages pneumococci can be grown from the blood, but as the disease progresses they disappear. It is only if the patient becomes worse and goes down-hill that the bacteriæmia persists and the condition conforms to what in previous years was clinically regarded as septicæmia. The early bacteriæmia is stated to be found in 30 to 50 per cent. of cases of pneumonia. But few cases of pneumonia are seen until a rigor has occurred or the disease is established, and it is then that the blood culture is first made. It is rarely that the patient can be investigated in that prodromal stage where there is just malaise. A rigor means that a severe reaction has been set up by the body, which may have destroyed the bacteria in the blood. But in the prodromal stage it is not possible to differentiate between a person who is about to be seriously ill from pneumonia and one who is merely unwell. To carry out blood cultures as a routine would necessitate a colossal amount of work. In addition, owing to the large number of cells present, it is difficult to

detect bacteria in stained specimens of blood; and as it has powerful antibactericidal powers, unless cultures are made straightaway, it will destroy any bacteria it contains. A delay of half an hour may enable this to take place. Were it possible to examine the case at the onset probably positive cultures would always be obtained. For it seems that pneumonia, like many bacterial diseases, begins by the growth of the bacteria in the blood. The rigor is an indication of the effort of the tissues to overcome them. The appearance of the inflammation in the lung means that this has failed and is an attempt to localise the infection and to build up the resistance.

B. The Bacterial Conception of Disease

At first attention was given to the bacteria giving rise to the infection and an attempt was made to link up the various manifestations. But as time went on more attention came to be given to the study of the reaction as displayed in the various organs, especially since medicine has become more specialised. We have come to speak of osteomyelitis, boils, otitis media as separate diseases and not just as a local manifestation of a lowered resistance factor to the staphylococcus.

In recent years we have gone farther and attempts have been made to identify different types of bacteria to account for variations in the character of the same disease in different individuals. For instance, four types of pneumococci have been identified. Not only is the reaction said to vary with each, but it is claimed that in therapy each type should be treated by its own particular serum. Though this is the limit to which the bacterial conception of disease has so far been carried, it by no means completes the aim of its adherents, who believe that only by the further differentiation of bacteria is any advance likely to be made.

The second or clinical school, to which I belong, think that little help is to be expected from the laboratory, particularly so far as therapy is concerned. For it is over

50 years since the tubercle bacillus was discovered by Koch, and even now bacteriologists are uncertain as to what is a human, a bovine, and an avian tubercle bacillus. Whilst their work has given much help in the diagnosis of tuberculosis and in the elucidation of its pathology, it has helped us little in the treatment. The mistake of recent years is that we have concentrated too much on the study of bacteria and have too long ignored the response of the patient. For even if virulent bacteria are deposited on a mucous membrane, nothing is likely to happen if it is intact and if the resistance factor of the constitution is unimpaired. At the most a local inflammation would arise. Even if they pass through into the blood they would be destroyed by its antibactericidal powers.

(1) *Can Bacteria pass through a Healthy Intact Mucous Membrane?*

It is not possible to give a definite answer to this question. The chances are that they do not as a rule. In acute or chronic intestinal obstruction, where the lumen of the intestine is swarming with bacteria and the surface is highly absorptive, it is only towards the end that they can be grown from the blood or from the urine. But here so often right up to the onset of the attack the health has been good and the mucous membrane healthy. But the examination of lymphatic glands at necropsies at various stages of life suggests that infection of these is repeatedly going on. This probably takes place when the health is impaired, and clinical investigations lead us to believe that in certain states of health the passage of bacteria through an intact mucous membrane is not uncommon. For in certain anæmias streptococci can be grown from the blood, and in nervous diseases the B. coli can be found in the urine in a large number of cases, without any lesion of the intestine being present. The organisms can come from the throat or bowel; for in these diseases the mucous membranes throughout the body are lax and toneless. Such a

condition is also seen after influenza and in many forms of ill-health.

(2) *Is the Introduction of some Virulent Bacteria from an Outside Source Essential?*

The typhoid carrier is immune to the bacteria he carries so long as they are confined to the mucous membrane, whilst they may be very dangerous to those with whom he comes in contact. From this and from our knowledge of the prevalence of bacteria, it seems that the individual is immune to those normally present in his skin or mucous membrane so long as this is not injured. We have no means of ascertaining what are and what are not virulent bacteria, and it is often not easy and sometimes impossible to differentiate between those from a healthy mucous membrane and those from an inflamed organ. But, when a coli infection or pneumonia arises, it is only rarely that the patient has been found to have been in contact with anyone suffering from the disease. The chances are that the bacteria causing the infection were there before. Bacterial diseases at times show a peculiar seasonal variation and there is little doubt that they are influenced by certain atmospheric conditions. For instance, some people get erysipelas each year, and often in the same month or season. This might result from some modification of the constitution; for there is now little doubt that the health varies with the seasons and atmospheric changes affect certain mucous membranes, which is shown by the onset of congestion.

On the other hand, it is possible that the vitality of bacteria is modified by similar conditions. For that of man, animals, and plants varies not only with the season but with the weather and the time of day. This also applies to the smallest forms of life. As one sits on the bank of a river it is possible to muse on this question of vitality. For one sees the Rough Olive, the March Brown, the Iron Blue, the Mayfly, the Red Palmer, the Olive Dun, the July

Dun becoming active at certain hours of the day and in certain months. Those who have a great knowledge of Nature are able to tell almost to a day when they will appear. Though the vitality of bacteria seems to us to be negligible, it is more than probable that had we some method of recording a variation, it would be found like that of life in general to vary with the seasons of the year and with certain climatic conditions. This would account for the prevalence of certain epidemics in certain types of weather and at certain seasons, and for those that arise spasmodically even where great care has been taken and where contact with some outside source has never occurred.

Though it is not possible to say that bacteria cannot pass into a healthy mucous membrane, it seems unlikely. Even if they do they will be destroyed by its antibactericidal powers. If these fail, those of the blood will come into play. If these also fail and the bacteria are deposited in some internal organ, the antibactericidal powers of the latter will have to be overcome. Consequently, before bacterial disease of an internal organ, such as the testis, can arise, the following would have to be present:

1. Some increase in the virulence of the bacteria.
2. The power to pass through the mucous membrane without being destroyed.
3. Some diminution in the antibactericidal powers of the blood.
4. Some diminution in the power inherent in the tissues of all internal organs to deal with bacteria deposited in them.

The chances of all four existing at the same time without some general cause is unlikely.

C. The Resistance Factor of the Constitution

The Hippocratic school regarded ill-health as a modification of the temperament, and this word was used where we now speak of constitution. The sanguine, the phlegmatic, the melancholic, and the lymphatic temperaments were described. It was thought that ill-health was due to too

much or too little of one of the four humours, yellow bile, black bile, blood, and phlegm. The physicians of a later period believed that the planets exercised some influence over each person. This view was held up to the time of the Middle Ages and gave rise to the astrological theory. It was said that a man came under the influence of Jupiter, Saturn, Mercury, Mars, or Venus. This affected his mental make-up and gave rise to the jovial, saturnine, mercurial, martial, and venereal temperaments. It was believed that the influence of the planet was exercised through the humours, the amount of which would vary with its position. And as a result people were at times predisposed to a disease. Though this theory was later abandoned, it was felt that there was a predisposition to diseases which was dependent on some factor in the constitution, due either to inheritance or the way of life. This predisposition came to be known as a habit of the body or diathesis, and the bilious, the scrofulous or lymphatic, the nervous, and the arthritic diatheses were referred to. Though attention was given to the disease, much was given to the error in the constitution that predisposed to it. It was felt that if this could be overcome the patient would get well. If it could be prevented, disease would not arise.

As medical research became concentrated on the study of bacteria, less and less attention came to be given to any constitutional factor that predisposed to it. Disease and ill-health were assumed to be due entirely to the activity of bacteria to which any changes in the constitution were secondary.

Now that the ease with which bacteria can get into the blood and the great powers of this and of the tissues to destroy them are realised, our outlook on bacterial infection has been considerably modified. Soon after birth bacteria are present in the skin and eventually reach many of the cavities. So long as the skin and mucous membranes are intact and the health is good the body is indifferent to their presence. The mistake of past years was the assumption that

disease arises the first time the individual is brought into contact with the cause. The chances are that this happens with each individual every month in his passage from the cradle to the grave. Yet in only a few does it arise, even though the state of the health may become much impaired or great risks are taken that are supposed to predispose to the onset of bacterial disease. It will be found that this occurs thousands of times for the one where disease arises. Even when virulent bacteria are introduced from outside sources nothing often happens. This is seen with the tubercle bacillus. For under the conditions of civilisation few people go a month without swallowing some germs. Yet in only a very few does tuberculosis develop, and in these there is some impairment of the constitution at the time bacteria enter the body.

This resistance to bacteria, whilst indirectly and to some extent influenced by race, inheritance, and mode of life, is personal to each individual. But there is no method of estimating it, and it can be assessed only as he passes through life. If, however, a careful history is kept of the state of his health and any illnesses he has passed through, with the life-history of his immediate relatives, by the time he reaches 21 a fair indication is obtained of what might be described as the resistance factor of the constitution.[1] Now so long as this can be maintained he can be indifferent to bacterial infections. When it becomes impaired there is a predisposition to bacterial disease. But it is only when active bacteria can enter the tissues that disease arises. If this happens occasionally the patient is said to suffer from a certain disease. But if the resistance factor is very vulnerable and is impaired by slight causes, such as overwork or fatigue, a diathesis is said to be present. The only difference between this and disease is the frequency with which the bacteria become active; for both are due

[1] The expression "resistance factor of the constitution" is used in this book in preference to immunity in that it implies some reaction on the part of the patient.

to the same cause—an impairment of the resistance factor. But when bacterial disease has developed, should the resistance factor be again restored to the normal disease is overcome. For the blood and tissues can now deal with bacteria that enter. This has been proved clinically and experimentally. It is to the production of this state that Nature works. It is for this purpose that the tissues react. Now that it is realised that a direct attack on bacteria is scarcely possible once an inflammation has developed, attention is being given to attempts to restore this resistance factor of the constitution. As a rule it is only gradually restored by good nursing, etc. Occasionally it is suddenly restored, as was illustrated in certain cases referred to in Chapter III. These account for some of the spectacular cures in medicine. Because we have looked upon therapy as acting directly upon disease and not indirectly by the restoration of the resistance factor in the constitution, we have failed to grasp certain phenomena in therapy. Yet only when we know what this resistance factor is, and how to increase it directly without any reaction on the part of the body being necessary, can we hope to make a direct attack upon bacterial disease.

D. The Nature of Bacterial Disease

This will be illustrated by a reference to pneumonia and to B. coli infections. If the resistance factor were unchanged and either the virulence of the pneumococci normally present were increased or some of great virulence introduced from outside, it is probable that they would be overcome by the antibactericidal properties possessed by a healthy mucous membrane. If this is not sufficient, a local inflammation would arise. Should the bacteria pass into the blood or the lymphatic stream they would be destroyed by the antibactericidal properties of the body fluids. This is shown by the work of Barrington and Wright, and by experiments on animals. If the resistance factor is impaired and the destruction does not take place,

they would multiply rapidly to counteract the hostile medium in which they are placed ; this in some way adds to their virulence. Their continued presence in the blood is likely to be associated with malaise and possibly mild shivering. This does not constitute disease as we know it, nor is it certain to follow. The bacteriæmia just denotes that the resistance factor of the constitution is impaired. If the bacteria continue to multiply, the condition is slowly becoming serious for the host. For there is now not only the impairment of the resistance factor that allowed them to develop, but also the impairment of the health that is secondary to their presence. During this time the bacteria are trying to create that state in which they can develop whilst the host is trying to produce that state in which he can survive with the health unimpaired. The mild attack of shivering, seen sometimes without a rise of temperature and popularly known as a chill, is the effort of Nature to overcome the infection. Preceding the onset of pneumonia a history of one or more of these is not uncommon. At times it is sufficient to raise the resistance factor and bring the constitution back to the normal. If it fails, then there comes the severe rigor, so often the precursor to pneumonia. Not only does the rigor frighten a man, but it makes him feel ill and causes him to lie up. Possibly the rigor by itself can restore the resistance factor to the normal, in which case the blood and tissues can overcome any pneumococci that enter. Some practitioners tell me that, when pneumonia is endemic, it is not unusual to come across cases where rigors suggestive of the onset of pneumonia occur, but where definite signs in the lung never appear. If the resistance factor is not restored by the rigor, then an inflammation arises in the lung and pneumonia sets in. All the powers of the body are devoted to overcoming the infection. As the inflammation is established, the infection becomes localised and antibodies begin to accumulate in the blood. The resistance factor is now being raised. When it is restored to normal, the host can again be in-

different to pneumococci in the blood or in the tissues. At such a time the crisis occurs.

In a B. coli infection of the urinary tract a history of malaise, headaches, gastro-intestinal disorder, and mild shivering for many days is not uncommon. Then there comes a rigor, pain in the side, and disorder of micturition. Kidd found the B. coli in the blood when cultures were made at the time of the rigor. There seems little doubt from the history of these cases that a bacillæmia preceded by many days the onset of urinary symptoms. To be certain of this it would be necessary to investigate these cases before the rigor, for the B. coli is a very delicate organism and is easily destroyed by the blood. Probably the bacilli are those normally in the body. Possibly on account of some seasonal or climatic variations, their virulence is increased. In ordinary circumstances they can be dealt with by the antibactericidal properties normally present in the mucous membrane. If these fail a local inflammation will be set up. If they enter the blood stream they can survive only if the resistance factor is impaired. Attempts are made to raise this by attacks of shivering or a severe rigor. If these fail a septicæmic state is imminent when the life of the host will be seriously threatened. To overcome this a localised inflammation is set up, usually in the gall-bladder or the pelvis of the kidney. According to this theory, the inflammation is secondary to the bacillæmia and is an attempt on the part of the body to localise the disease and to prevent the onset of septicæmia. The formation of pus at its first appearance is to be regarded as an extension of the local reaction that is being called for to overcome the infection.

It was formerly believed that an inflammatory state was due to a few bacteria entering the blood stream and becoming deposited in an organ whose resistance was temporarily lowered—the so-called *locus minoris resistentiæ*. For instance, in osteomyelitis it was believed that as a result of trauma the metaphysis of the bone was damaged and the

circulation impaired. If at that time a few bacteria entered the blood stream the bone would become infected. But it is now realised that so long as the resistance factor of the constitution is maintained the blood and tissues are indifferent to bacteria. In osteomyelitis a period of ill-health precedes the onset of the symptoms in the limbs. During this time pain is present in many parts of the body. Were the blood to be examined at this time, positive cultures would no doubt be obtained, for probably, like many of the acute inflammatory states, osteomyelitis begins as bacteriæmia. Once a rigor has failed to overcome this, a localised inflammation is set up.

Why in B. coli infection the pelvis of the kidney and the gall-bladder should be picked out, in a pneumococcal infection the lung or a synovial membrane, in a staphylococcal infection the bones of children and the kidney and prostate of adults and the skin in both, and in a streptococcal infection the skin or a synovial or tendon sheath, is not known. This local inflammation seems to be a means by which the resistance factor of the constitution can be re-established and the infection in the blood and tissues overcome. When a septicæmia arises in association with an inflammation, it should not always be regarded as the extension of this, but rather that the inflammation has failed in its object, namely, the raising of the resistance factor.

The view put forward in this chapter is based on the following clinical findings:

(*a*) In established septicæmia the development of a definite local inflammation is a favourable sign. It is often associated with the disappearance of bacteria from the blood. If it can be maintained and is not incised, there is a chance that the patient will recover.

(*b*) When with an inflammation the general symptoms persist but the local condition tends to clear, the outlook is bad, for it so often means that septicæmia is developing.

(*c*) When during a severe illness the question of septicæmia arises, it is less likely if some active inflammation is

present and particularly if one has recently appeared. It is more likely if none can be found.

(*d*) In gonococcal arthritis, which is an evidence of gonococcal septicæmia, the development of an epididymitis or an abscess often means that the arthritis will clear up.

(*e*) When in B. coli infections of the urinary tract the kidney becomes enlarged and tender and there is much rigidity over it, or where there is a severe inflammation of the testis, the outlook is much more favourable than when a pure bacilluria is present. For the local changes means that a definite reaction has taken place.

The points previously discussed deal with certain phenomena that are known to occur and for which a certain amount of evidence is forthcoming. The possibility of the inflammation being a favourable localising symptom is an assumption based upon certain clinical findings. So far nothing has been said about the cause of the lowering of the resistance factor which allows the bacteriæmia to develop. This precedes the entry of bacteria into the blood and is responsible for it. Only when we discover the nature of this resistance factor shall we be able to prevent the onset of an infection and to cut it short when it develops. At present we know nothing about the resistance factor. In experiments on animals these are so often healthy, or the health is artificially impaired by withholding certain food-stuffs and is regained as soon as they are administered. The impairment of the resistance factor that plays the chief part in man does not come into play in experiments on animals. So often these are just simple infections, not diseases.

Now bacterial diseases are liable to arise when an illness has been present for some time or towards the end of life, when they are just a terminal event. They are very common when there has been prolonged malnutrition, or when the health has been impaired by alcohol or some such poison. Chronic forms are also common in diseases of the nervous system. But these factors are not the cause. For they may be present to a marked degree and yet bacterial diseases

do not arise. It is only in a proportion of those affected that there has been any prolonged impairment of the health, and in a large number none is present. And the impairment only predisposed to them ; all that can be said is that at such a time the resistance factor is more likely to be affected.

When the bacterial diseases are investigated, it is advisable to eliminate cases where there has been some predisposing factor of long standing or where it is obvious that the infection is just a terminal event. For in such cases the course is modified and the issue clouded. It is better to concentrate on cases where, until a short time previously, the health seemed good ; for fewer secondary factors have then to be considered. There is sometimes a recent attack of influenza or measles, but a history of exposure to cold, some mental shock, worry, or undue mental strain is not infrequent. These are not in themselves the cause ; for most of the patients have in the past been subjected to them again and again and nothing happened. It does seem, however, that with a constitution of a certain type, and with the health in a certain state, they are likely to lead to a lowering of the resistance factor. If at this time bacteria of a certain type gain admission or if those normally present become more virulent, disease is likely to arise. What this resistance factor is we do not know. It is not the same as an acquired immunity, for the antibodies that are then present are not detected in those whose resistance to disease is good. It is not possible by just examining the blood to say that the natural resistance of one person is good and another poor. For we have no test by which the resistance can be estimated even in a comparative sense. It is to some extent dependent on all the organs of the body working properly. For instance, if those forming the blood are impaired and lead to anæmia, the resistance is generally low. It is also no doubt dependent upon the efficient working of the reticulo-endothelial system throughout the body. But it is also in some way intimately linked up with the central nervous system.

E. The Bearing of the Central Nervous System upon the Resistance Factor

There is a definite relationship between mental strain and fatigue and the onset of bacterial disease. For the two occur together more frequently than mere coincidence would lead one to expect. There is little doubt that lesions of the nervous system predispose to the development of bacterial disease. This is shown by the study of diseases of the nervous system. For instance, in tabes an infection of the urinary tract is very common, even if no catheter is passed. It runs a chronic course from the start and is very difficult to overcome. It is, however, rare to have an acute infection.

It is strange that bacterial diseases run a less acute course when any nervous disease is present. So often the characteristic feature is the absence of any severe reaction. Pneumonia, for instance, runs a particularly benign course ; and, though the temperature may be high, the patient looks and feels well and suffers little discomfort. In complete lesions of the spinal cord, chronic infections and ulceration are common, but only rarely does an acute spreading inflammation arise. When a nerve is completely divided chronic ulceration is common, but an acute inflammation in its area of supply is rare. Now, in all these nerve injuries the blood supply is normal, so are the internal secretions, and the reticulo-endothelial system throughout the body is able to function. The one thing that is wanting is nerve energy from the nerve centres. When this is absent a sthenic inflammation is unlikely ; on the other hand, an asthenic inflammation is common and tends to persist. But it seems that no severe reaction is possible. This absence of a reaction may also be responsible for the failure of therapy. For when chronic sepsis arises in a patient with a complete lesion of the spinal cord, little can be done. No matter what care is taken, harm rather than good seems to follow most lines of treatment. The surgeon is now so powerless, because the tissues can no longer

respond. A similar condition is seen in the ulceration that may arise in an area deprived of its nerve supply. Yet immediately the nerve regenerates it clears up. All that has happened is that nerve impulses can now pass down.

Bowlby and Andrewes[1] say:

"The nervous system plays in inflammation a less striking share than might have been anticipated. The influences which govern the behaviour of the leucocytes seem purely of a chemical nature. All the phenomena of acute inflammation can go on quite well in regions bereft of their nerve supply; for instance, in a rabbit's ear, all the nerves to which have been divided. The only part which the nervous system seems to play in inflammation is to be found in vasomotor mechanism. Anything which impairs vaso-dilatation hinders the promptness and efficacy of the inflammatory reaction."

This, after all, applies only to the physiological aspect of inflammation, for there is no question that the processes giving rise to this can occur in a part deprived of its nerve energy, for ulceration which is so common is just a variety of inflammation. There is, however, a big difference between the way in which wounds heal in normal tissues and in those deprived of their nerve supply, and healing of a wound is really an aseptic inflammation. Spiess[2] has shown that when the pain of an inflammation is removed by orthoform or novocain, all sorts of wounds heal remarkably quickly. He says:

"Inflammation will not occur if it is possible by means of anæsthesia to suppress the reflexes in the centripetal nerves coming from the inflammatory focus. Inflammation which already exists heals rapidly when the inflammatory focus is anæsthetised. Anæsthesis must affect only the sensory

[1] *Surgical Pathology*, 6th edition, p. 33 (J. & A. Churchill).

[2] Spiess, G., *Münch. med. Wochenschr.*, 1906, vol. liii, pp. 345–51.

nerves and must not affect the normal behaviour of the sympathetic nerves."[1]

The nervous system certainly plays an important part in a sthenic inflammation. For if in the treatment of an acutely inflamed boil or carbuncle ½ per cent. novocain or 1 in 1,000 percaine is injected into the surrounding nerves twice a day, not only is there less pain but the inflammation tends to subside.

It does seem from the examples given that the central nervous system plays some fundamental part in the maintenance of those factors by which the skin and mucous membranes can be indifferent to the bacteria and also by which the tissues can generally overcome an inflammation that has arisen. When the nervous system is functioning normally a good resistance is possible and a sthenic reaction can be set up. When the nerve impulses are cut off, chronic asthenic inflammation is very common, but a sthenic reaction is very rare. The question arises: Is this due to something inherent in the nerve cell or does it depend upon some impulse from a special centre in the brain?

A school is arising which believes that the central nervous system is the basis of the constitution and towards its maintenance all the energy produced by metabolism, the internal secretions, the blood pressure, etc., is directed.[2]

[1] In tetanus it is known that the bacilli do not invade the blood or spread for any distance from the site of the inoculation. Although the tissues in the immediate neighbourhood are rich in toxin, not much is absorbed into the blood. In order to reach the motor cells the toxin must be taken up by the plates of the motor nerves and conveyed by the axis cylinders to the cells. Toxin injected into a sensory nerve or into a posterior nerve root does not set up tetanus. If the bacteria are injected and the motor nerve divided, the disease does not arise. There is no question of the importance of the nervous system here.

[2] No further reference is made to the bearing of other factors, such as the endocrine glands and the vitamins. I originally intended to include this, but early on came to the conclusion that the subject would become too complicated. In my practice I have so rarely found any good follow the administration of vitamins or any endocrine preparations, and I therefore assume that in the majority of bacterial diseases they play

From its cells pass impulses that influence all the functions of the body, including those governing the resistance. These are probably of two kinds, the eusthenic and the dysthenic. When they are equally mixed the constitution is normal and health is good. When the eusthenic are in excess there is the hypersthenic constitution with its excess of nerve energy and a tendency to too much vitality. When the dysthenic are in excess, there is the hyposthenic constitution with its want of nerve energy and a tendency to too little vitality. When the eusthenic are in excess any modification of the resistance factor usually predisposes to bacterial infections giving rise to a sthenic inflammation. When the dysthenic are in excess, those giving rise to an asthenic inflammation.[1]

little part. It is true that in myxœdema some infection is likely. This also applies to avitaminosis, particularly when due to the absence of vitamin A. I would suggest that in both myxœdema and avitaminosis the infection results from the impaired state of the nerve cells. The difference between bacterial disease as seen in myxœdema and exophthalmic goitre might have some practical bearing. But my experience of these diseases is very limited, and those from whom I sought advice could give little help.

[1] This bearing of the central nervous system upon the resistance factor and its relationship to the constitution is unfortunately no more than a supposition that receives a certain amount of support from clinical observation. It cannot be proved or disproved. But there is a big difference in the reaction that takes place when inflammation arises in a part with a normal nerve supply and in a part which is deprived of its connection with the central nervous system. After all, each has the same supply of blood, endocrines, and antibodies. The only difference is in the nerve supply. One can only assume that when the nerve supply is intact impulses come down that modify the inflammation. It is my impression that eventually some nucleus will be found among the basal ganglia of the base of the brain that has some controlling influence upon inflammation. No scientific proof is forthcoming. Its presence is assumed from certain clinical observations. From this nucleus two types of impulses are believed to pass, the eusthenic and the dysthenic. Until more is known about this supposed function of the nervous system, it is doubtful whether a sthenic reaction is due to stimulation of eusthenic or to paralysis of the dysthenic impulses. The mode of action of therapeutic measures is therefore problematical. The terms " eusthenic " and " dysthenic " have a very broad application and conform to " stimulant " and " depressant " as used by some writers. They have no exact scientific value, but are used in preference to others since some reaction on the part of the tissues is implied.

F. The Bearing of Vitality upon Bacterial Disease

A comparison between the bacteria giving rise to the sthenic and those giving rise to the asthenic inflammations reveals that they are apt to affect different types of people and to occur at different seasons. Pneumococcal, staphylococcal, and streptococcal infections seem to prefer those with a tendency to muscularity and to an acid urine, and these are often found with the hypersthenic constitution and with robust health; that is to say, where the eusthenic impulses are in the ascendant. Until recent years this is the constitution to which men rather than women tended. For this reason these infections are found more often in men. Boils and carbuncles are examples. For every case of staphylococcal infections of the kidneys I have seen in a woman, there have been five in men. They often arise after a holiday when the health is better than it has been for some time. Like diseases in general, they are common during the winter when impairment of the health is likely to occur, but they are very prevalent in the early spring and at the close of the summer. During this season years ago something to tone down the system, such as the old brimstone and treacle, was given to children and young adults. As a result pimples and eruptions of the skin were less common.

B. coli and typhoid diseases are more likely to arise in those whose musculature is not too great and who are somewhat wanting in energy. This is the condition that prevails in the hyposthenic, where dysthenic impulses are in the ascendant. Hence these diseases are more common in women. This applies even when cases secondary to pregnancy are excluded. When strong healthy people are affected, it will be found that previous to the onset the health has been impaired by mental strain or some disease, such as influenza; that is to say, the hyposthenic state has temporarily developed. When the vitality is great, asthenic bacterial diseases are uncommon and quickly clear up. For instance, though B. coli infections occur in children,

they do not become chronic unless there is stasis of urine; and typhoid fever is uncommon in infancy and childhood and runs a very benign course. Such infections are more common when the health becomes impaired in winter and autumn.

It thus seems that bacteria giving rise to a sthenic reaction prefer the type of constitution where the eusthenic impulses are predominant and are more prevalent in seasons that increase vitality; whilst the bacteria giving rise to an asthenic reaction prefer one where the dysthenic impulses are predominant and are more common in seasons that lower vitality.

The view put forward in this chapter may offer an explanation for the following observations:

During pregnancy there is a deviation of the constitution to the hyposthenic type. Once the shock of labour is over, there is a sudden reversal to the hypersthenic. As the hypersthenic and hyposthenic constitutions predispose to certain infections, different types would be expected in pregnancy and the puerperium. This is found to be the case. It has been stated in Chapter VIII that during pregnancy a B. coli infection is liable to arise, whereas in the puerperium a staphylococcal or streptococcal is more common.

Certain epidemics are more prevalent in certain seasons and in certain weather. Is this dependent on the variation of the vitality with the time of the year? Vitality is lowest at the solstice of Dec. 21st and highest at that of June 21st. This is marked in Nature, but also occurs to some extent in man. As a result, during the first half of the year the eusthenic impulses will be in the ascendant; during the second half of the year the dysthenic. As the pneumococcus and streptococcus seem to prefer a constitution with eusthenic impulses in the ascendant and the B. typhosus one with the dysthenic, the former would be more likely to be prevalent in the first part of the year, the latter in the second part. This seems to be the case, for pneumonia is

more common from January to April ; scarlet fever in the spring or late summer ; and typhoid in Sept., Oct., and Nov. But other factors, such as some seasonal variation in the vitality of bacteria, cannot be excluded.[1]

[1] This bearing of vitality on the question of infection is of practical importance. The relationship of fatigue is definitely established. When the common cold or influenza seem imminent, if rest in bed is possible straightaway and a good night's sleep is forthcoming, they are at times aborted. Puerperal sepsis is on the increase though considerable attention is being given and skilled nursing is now available. This is particularly noticeable among the upper classes. May it not in part be due to the indiscriminate way in which drugs are given to relieve pain at childbirth ? For if given in too big doses or for too long a time, they undoubtedly impair vitality and may in this way lower the resistance to infection. It is at times difficult to explain the onset among medical men of some infection such as tonsillitis on the return from a holiday when the health seems improved. It is suggested that it results from the disappearance of an immunity acquired by the passage of bacteria into the body. But from what is known of immunity in general, this is not likely in so short a time. The onset is rather to be attributed to the development of that state of health in which eusthenic impulses are in the ascendant. As a result, there arises a state favourable to the growth of certain types of bacteria.

CHAPTER X

CHRONIC BACTERIAL DISEASES

WHENEVER the health becomes impaired or when there is a sudden change in the weather, some people are liable to an inflammation of a mucous membrane. This is not unlikely to follow influenza, typhoid, or some severe mental strain. Even when this inflammation has persisted for years and the organ can be examined at operation or necropsy, no gross pathological change may be found. To such a state the term " chronic infection " has been applied, but, in accordance with the nomenclature here adopted, it will be referred to as chronic bacterial disease. It is found in two types. In one, the hypersthenic, where the health is often robust and there is a tendency to staphylococcal or streptococcal infections and particularly to boils. In the other, the hyposthenic, where the health is somewhat poor, there is a tendency to gastro-intestinal disorders and to an infection of some mucous membrane, often due to B. coli. This was formerly referred to as the bilious diathesis. When the etiology is discussed, medical opinion falls into two camps. One asserts that the infected organ is the cause of the ill-health ; the other, that the ill-health is part of some constitutional defect which becomes obvious after any mental or physical strain and to which the chronic infection is just incidental.

A. Focus of Infection

The development of bacteria in the body may undoubtedly lead to ill-health, for an active tuberculous lesion gives rise to wasting and lassitude. These are seen during and after an attack of typhoid. They may be associated with an empyema or an appendix abscess and disappear when it is

drained. Consequently when ill-health is present it is not surprising that every effort is made to find some inflamed area in the body from which toxins may be absorbed into the blood. Some have gone a stage farther and believe that, if bacteria can be detected on a surface that is normally sterile and ill-health is present, then they are the cause; though there may not be the slightest evidence that there is or ever has been any inflammation and similar bacteria are known to be normally present in the body and do not lead to any trouble. Again, when disordered function in an organ that normally contains bacteria is associated with ill-health, the absorption of bacteria or their toxins is immediately regarded as the cause. Any one of these is at times referred to as a focus of infection and attempts are made to clear it up either by removal of the organ, by drainage, or by applying antiseptics to the surface.

The cures that have been claimed are legion, and numerous specialists have striven to point out how a mild infection of the mucous membrane of the tract in which they are interested must be the cause of ill-health which is cured when it is cleared up. Amongst them throat specialists, abdominal surgeons, and gynæcologists are conspicuous. All sorts of operations are brought forward to substantiate their claims. If success is not obtained by others, it is attributed to an error of technique and some modification is introduced. It is not realised that the results are poor because treatment is based upon a wrong pathology, and good results will at times follow any line of treatment provided the patient lives. For Nature is always trying to assert herself to get the patient well. The rationale of some of these operative procedures is difficult to comprehend. For instance, if ill-health is associated with some disorder of menstruation and if there is a discharge that contains abnormal cells or bacteria, the uterus is regarded as the focus of infection and dilatation and curettage are performed. But the uterus is really a very insensitive structure from which normally

little if any absorption takes place, and owing to the thickness of the walls none is likely to follow a mild infection. Whilst there may be something to be said for dilatation if it allows a discharge to escape, curettage violates all the principles of surgery. For it amounts to nothing more than the scraping of an inflamed surface, and this opens up fresh channels to infection and absorption. And as it removes only a part of the disease, this is certain to recur. A surgeon should regard the layer of granulation tissue, whether on the surface or on an internal organ, as the patient's greatest safeguard.

Abdominal surgeons are by no means blameless. At one time the appendix was regarded as the cause of ill-health, then the colon, and nowadays the gall-bladder. Lately it has been asserted that if the last is infected, it will lead to disease of the heart or of the kidneys, and this clears up if it is removed. To put patients through a major operation with a mortality of 2 per cent. is a sheer abuse of surgery, for the constitutional factor that has led to the chronic infection of the gall-bladder has not been touched. When an inflammation arises in an organ, complete recovery is the rule if the health is good and if no pathological condition has developed that prevents the discharge from being excreted or a cavity from collapsing. When the expectant treatment of acute cholecystitis and acute appendicitis has been carried out and an operation is performed at some later date, it is not uncommon to find healthy-looking organs. Generally an operation is performed to remove the appendix because of the possibility of the recurrence of an acute attack and not because of the persistence of ill-health. If an acute inflammation can clear up in this way, surely this should also be expected in chronic bacterial disease. The reason it does not take place is that the impairment of the resistance factor that allowed the latter to develop has not been remedied. If the infected organ is now removed the ill-health persists and the infection is likely to break out elsewhere. This is found to take place.

Some years ago, when convalescing from an illness, I was surprised to find the large number of invalids at spas who were under treatment for arthritis or some gastro-intestinal disorder who had some focus of infection removed and who were quite definite that, apart from some temporary improvement, they had derived no real benefit. This is the experience of most medical men. When cases are investigated over a number of years the improvement in health that follows the removal of some supposed focus will be found rarely to persist. In my practice I recognise that iritis, arthritis, and fibrositis can follow a gonococcal lesion in the prostate or a stricture of the urethra and clear up completely when this is treated. Occasionally ill-health may be associated with a gross pathological condition in some organ and may clear up when this is removed. But the cases where it is definitely established that ill-health is due to a chronically inflamed organ and is cured by its removal can almost be counted on the fingers of one hand.

I have discussed this question with general practitioners, and particularly those who live in country towns and have the advantage of being able to maintain contact with their patients for many years. The majority are quite definite that, whilst improvement may follow if the inflammation is active or the organ is seriously diseased, any improvement is just temporary when there is only a mild inflammation. When their patients have gone elsewhere for such treatment it is not rare for them to come back improved, and consequently they are often claimed as cures. But when the ordinary routine of living has again to be followed with its stresses, the ill-health too often recurs. They point out that the treatment is often combined with other measures, such as fresh air, rest, and good food, which all play some part. To these must be added faith and hope that therapy inspires. In such circumstances it is so often difficult to know to what a temporary improvement is due. They point out that pyorrhœa is constant amongst many people of the poorer classes who never suffer from the slightest

inconvenience or any ill-health until towards the end of life. During prolonged ill-health they have noticed that sponginess of the gums and gingivitis arise which may pass on into definite pyorrhœa. When, however, the health is regained these so often clear up.

There is nothing to suggest that the mere presence of bacteria on a mucous membrane will in itself impair the health. The typhoid carrier is generally a very healthy person, and these bacilli, which are so dangerous to others, do not do him any harm. A man with a tuberculous kidney may for years be excreting tubercle bacilli over the prostatic urethra, which is known to be highly absorptive, without suffering any ill effect. The amount of chronic sepsis that can exist without any impairment of the health is sometimes amazing. It was conspicuous when recruits were examined during the War.

On the other hand, bacteria may develop in any region and lead to an inflammation when the health becomes impaired. When it is regained they disappear.

This was brought home to me when I acted as medical officer to that great battalion, the 4th South Wales Borderers in Gallipoli. Practically all the men had suffered from both types of dysentery and jaundice, which disappeared when the cold weather came. At the time of the evacuation of Suvla Bay the health was poor. Most had colitis and gingivitis and many had a chronic ulceration of the skin which showed little tendency to heal. But after a week's rest at Lemnos the muscles became firmer and of better tone, the eye became clearer, and the general health improved in every way. In many the colitis and gingivitis were disappearing and the ulcers of the skin had already healed. When they paraded for the evacuation of Cape Helles, they were a different body of men. Had I not witnessed this, I could not have believed that so marked a change could occur in so short a time. There was no difference in the food and I am doubtful if the air at Lemnos was better than that of Gallipoli, which in ordinary circumstances would be quite bracing and healthy. But it was the first time for many months that the men got away from

the constant anxiety and the strain of trench fighting and consequently were able to have proper rest and relaxation. Though during the next two weeks at Helles the strain was great, the good health persisted and there was little tendency for gingivitis to return.

This episode showed me very clearly that a chronic infection could be the result of ill-health, particularly if at the same time there was any mental strain. I always keep it in mind when this subject is discussed.

When the possibility of a focus of infection being the cause of ill-health is under consideration, it is well to keep in mind that when the constitution is normal, the tissues are indifferent to bacteria. They can develop only if the resistance factor is impaired. If this is restored the infection usually disappears. It will persist only if there is some gross pathological lesion that prevents a cavity from contracting or a discharge from being excreted.

B. The Bilious Diathesis

Years ago it was realised that a certain type of constitution predisposed to certain diseases, and the bilious diathesis, in which disordered function was common in the gastro-intestinal tract and there was a special liability for an infection to arise in some mucous membrane, was often mentioned. In one person it was the nose, in another the lung, the gall-bladder, the uterus, the appendix, or the urinary tract. The condition is more common among the Celtic and Southern European races and among women. The majority are of spare build and of the hyposthenic type in whom generally the health has never been robust. Whilst they are very keen on sport, at which they are often expert, they are prevented by an absence of stamina from reaching the front rank. This becomes obvious if they are called upon to make an excessive or sustained effort. Intellectually they are often above the average but are inclined to be emotional. Some instability of the cardio-vascular system, tremors of the hands, and a tendency to pigmentation are

often present; the hands and feet are cold, and the blood pressure is low. A want of tone in the muscles and ptosis of the viscera are common. If the organ giving rise to the trouble is removed upon the supposition that the infection here is the cause of ill-health, the condition is certain to recur in some other. This was very apparent a few years ago when surgeons thought it possible to restore health by removing such an organ. Though many successes were claimed, the tragedies were only too frequent, and after a short experience the practice was abandoned. The following is by no means an extreme example of what took place.

In 1911 there was demonstrated at the out-patient department at the National Hospital for Nervous Diseases a woman aged 32, who was complaining of a want of physical and mental energy. Her health had never been good since her marriage at 23. It had become worse after the birth of a child at 26. To overcome malaise that persisted, the uterus had been dilated and curetted on at least three occasions. The appendix and gall-bladder and tonsils had been removed for some supposed infection and a normal kidney sewn up. Some of the nasal sinuses had been drained. In 6 years she had been put through 10 operations for each of which a fee had been obtained. At last she was driven to seek advice in this famous hospital. The physician did not hesitate to make an attack upon surgery. He could have desired no better case. He then demonstrated how the impairment of health was due rather to wrong living, and this was borne out by the history. He pointed out that the disorder of the various organs that had been operated upon was largely functional and imaginary.

This case was so well demonstrated that the moral was not missed by some who were there. Since that day I have always kept it in mind when approaching a patient with ill-health supposed to be due to a chronic infection. But later experience makes me feel that the physician was wrong when he attributed the disorder of the various organs entirely to the imagination. For a careful study of such cases reveals that a mild inflammation does really arise

whenever the health becomes impaired, particularly if there has been any mental or physical strain or a sudden change of weather. Some impairment of the resistance factor occurs at this time. It is produced so easily. In some way the inflammation seems to restore it. Whilst relief of the discomfort follows removal of the inflamed organ, any improvement in the sense of well-being is temporary and after a time the inflammation breaks out elsewhere.

Really it may be an advantage to a patient to have such an organ, if he will but realise that it acts as a barometer to reveal to him the state of his health, and an inflammation arising in it is the result and not the cause of the impairment. The latter is sometimes due to some mental strain that cannot be avoided, but more often to some breaking of the rules of living. The disordered function, so often seen at the time, is secondary to some vulnerability in the constitution. When this is remedied, the trouble clears up.

In past years there has been much controversy as to the site from which bacteria came and the route that was followed. Much of the controversy was due to the belief that their entrance into the blood stream was a certain prelude to septicæmia. Nowadays we believe that when the resistance factor is impaired, a bacillæmia occurs frequently and is of little significance. The infection in the bilious diathesis no doubt takes place in this way and comes from the throat or intestine. For if this can take place from the urethra, it can do so here. It is uncertain whether with each attack there is a fresh bacillæmia or merely that at times those already in the infected organ become more active. This can be ascertained only by long and careful observation. All that can be said is that the resistance factor in these patients is extremely vulnerable and becomes impaired after some slight strain.

After all, where the bacteria come from and the route that is followed is of little practical importance. The point of interest is why they are not destroyed by the blood and why they can persist in an organ in which they are deposited,

even when no obvious pathological lesion exists. Could we but grasp the principle at issue here we should be able to proceed to a direct attack upon chronic bacterial disease.

It is not known to what this bilious diathesis is due. It seems to be inherited rather than acquired, for in many the gastro-intestinal disorder begins in childhood though it becomes more obvious around puberty. It possibly has something to do with an idiosyncrasy to some form of protein. For when gastro-intestinal disorders appear in infancy, those due to faulty fat or carbohydrate metabolism are easily cured, but not those due to faulty protein metabolism; children so affected never seem to have robust health. Possibly in them the bilious diathesis will be found to develop.

This is perhaps well illustrated in the case of the surgeon A. (see page 26). At the age of 3 he had scarlet fever which his mother also contracted. The other two children were not affected. Four more children were born. His mother for years had some gastric trouble and at the age of 75 had cholecystectomy performed for an empyema of the gall-bladder and gall-stones. Since that time she has had colitis. Both A. and his mother suffer from egg-poisoning. Though the other children, now grown up, had measles, chicken pox, etc., none had scarlet fever though they passed through several epidemics; none has had any gastro-intestinal trouble; none suffers from egg-poisoning. Is the coincidence between A. and his mother to be attributed to their having had scarlet fever, or are the scarlet fever, the cholecystitis, and the colitis due to some constitutional factor bound up with the bilious diathesis associated in their case with an idiosyncrasy to the protein of egg? Might their troubles have been avoided had this been discovered early in life and eggs omitted from the diet?

But to whatever it is due, this diathetic factor can to some extent be controlled by careful attention to the manner of living. It can be overcome by administration of small doses of mercury. At times the effect is so marked that it seems almost specific for this type of constitution.

CHAPTER XI

TERMINAL BACTERIAL DISEASES

Soon after death bacteria can be found in most of the tissues, and, as life is coming to an end, they are entering and growing in the blood. This may be so marked as to constitute definite diseases. For instance, in anæmia a terminal septicæmia is the rule rather than the exception. At other times a definite inflammation may arise. Such bacterial diseases are very evident as an illness progresses or as age advances. They should be regarded as incidental to this and as terminal events, and not as a complication or as a separate disease. Sometimes their appearance may be the first indication that life is on the wane, though it may be many years before decay becomes evident. Nowadays we pride ourselves on our wonderful constitutions. We claim almost everything except immortality, and some writers seem inclined to suggest that even this is imminent. There is little doubt that men now live longer than they did fifty years ago, but this is largely because the food supply and housing conditions are better and travelling is not so big a strain. Though some take much pride in the years that are gained, longevity must not be confused with vitality. For nothing has been discovered in recent years that adds anything to man's vitality or that enables him to recuperate more quickly from an illness. This still depends on the reactive powers of the tissues and varies with the age. If Nature is not able to assert herself, there is practically nothing that can be put into the body that directly helps.

This bearing of age upon an infection is perhaps best illustrated by a reference to pneumonia. When this arises under 40 the immediate and remote prognosis is good.

After 50 the reactive powers are not so great and bronchitis may follow. This recurs with a change of weather or when the health becomes impaired. This liability for inflammation not to clear up completely is seen in other organs as well as in the lung. Again as age advances or as an illness progresses chronic bacterial diseases are likely to arise. The cause now is something incidental to age or the illness as a result of which the resistance factor is very vulnerable. Though with good nursing and attention to the mode of living the bacterial disease clears up, it is certain to recur with any mental or physical strain or even with a change in the weather. Permanent good health would be possible only if the illness could be overcome or the clock put back. Treatment is difficult because the tissues cannot react. In consequence a line of therapy that was very efficacious at an earlier age may now be of little avail. The illness will recur because the predisposing cause is not overcome. No drug adds directly to the vitality of a man. Until we realise that with advancing years or with impaired health the resistance factor becomes easily upset and also it is more difficult to restore, we shall go astray in the treatment of bacterial diseases. The following case illustrates this point :

A., a highly-strung Celt, aged 50, was seen by me in April 1930 for frequent and painful micturition of 2 years' duration. He had 12 stones in his bladder and there was a residual of 8 ounces. An operation was advised, but he preferred to put up with his symptoms. In Sept. he suddenly decided to undergo this. As I was going away on holiday a colleague removed the stones through a suprapubic incision. He was an extremely difficult patient to manage and persistently refused to allow the surgeon to carry out treatment. As a result his wound took a long time to heal. I saw him again in Jan. 1932 in consultation with Dr. Owen Parry. His symptoms were still present, he had a residual urine of 8 ounces and his urine was full of B. coli, but contained hardly any pus. His blood urea was 40 mgm. and the urea concentration 2·5 per cent. There was some enlargement of the prostate. Transurethral resection of

the prostate was not advised as the first operation showed he would not tolerate the presence of a catheter, nor would he have put up with a cystostomy. In addition he was the type of patient who, though walking about and looking fairly fit, was hanging on to life by a fine thread. He was really cracking up. The slightest thing going wrong would prove fatal. As his condition became somewhat worse, it was decided to wash out the bladder each day. There was a slight improvement at first, but the suprapubic wound became inflamed and a fistula formed. He was admitted to the Cardiff Royal Infirmary, where the B. coli was grown on one occasion from the blood. It was considered kinder to withhold active treatment and he died in three weeks.

Drainage is the ideal treatment for an infected bladder, but death would have taken place whatever had been done because he had reached the stage when his tissues could no longer react. Even if the prostate could have been removed with a wave of the wand, he would not have had long to live. For though a comparatively young man, from the time I saw him in Jan. 1932 it was evident that he was dying with and not from a chronic bacterial disease. Even if the disease had cleared in the bladder it would have broken out elsewhere.

Terminal bacterial diseases should be viewed in the same light as tuberculosis that occurs towards the end of an illness. When the latter is incurable its onset is often a blessing in disguise, for it cuts short the suffering. It is extremely important to spot these cases. For with them therapy gives rise to only a temporary improvement and more often fails. It is not fair to put such patients through a long course of treatment with its cost and suffering, when it is so obvious that life is hardly worth living and vitality can never be regained. For them the art of medicine should be to make the passing out from life as quiet and peaceful as possible. When a man has reached a certain age or an illness has reached a certain stage, terminal infections cannot be avoided. It is well for many that they do arise, for they

shorten the end. How many really want, as some suggest is going to be the case when the hey-day of medicine comes, to sit quietly waiting for life to end, joining "the company of weary old men who sit on the sunny side of the workhouse wall and wait for the tender mercies of God," fearful lest the faculties may first fail and leave a dotard to be beheld by all. Such years do not add anything to life: they only prolong the act of dying. Few people really want to linger on in senility when their interest in life has gone. For many the tragedy in life is not that the end is in sight, but that its coming can be so long.

Some of these unfortunate people are still put through operations when they are content and would prefer to die. This is just an abuse of surgery. A medical man who can speak with the experience of eight operations tells me that he would not go through one unless he were certain of having a year of *active* life. For not only is there much mental and physical suffering, but asthenia persists for some months afterwards. A surgeon before performing an operation should make certain—

1. That the patient will live.
2. That life will be worth living.
3. That the expectation of life will justify the suffering which the operation entails.

The last two are apt to be forgotten now that operating is easy and safe. The success so often claimed is that life has been prolonged, but too often lingering in decay is mistaken for living.

In all bacterial diseases it is well to consider whether they may not be terminal events. Even if there is an acute flare-up, it may now be kinder for the surgeon to hold his hand to allow Nature to run her course. It is no good hoping that the focus that has been undermining the health is at last revealed and that vitality will return after it is removed. Experience shows that this rarely follows. No faith can now be placed in Nature, for if she could she would have asserted herself long ago. In no circumstances should

any promise be given to the patient that the health is likely to be better if the operation is performed ; for if anything, the vitality will be a little lower than it was before.

The duty of the surgeon is to the particular patient and he should try to put himself in his position. He should ask himself : If I were in this patient's position, would I consent to undergo the suffering of an operation just to prolong my life ? For the success of an operation is dependent not so much upon life being prolonged as upon that life being worth living. Life should be reverenced so long as the patient wants to go on living and there is sufficient vitality or at any rate an expectation of it to make living worth while. But reverence for life must not be confused with mere sentiment.

PART II

THE TREATMENT OF BACTERIAL DISEASE

CHAPTER XII

THE NATURAL COURSE OF BACTERIAL DISEASE

When treatment of bacterial disease is discussed, people often speak as if it were possible to foretell the course it will run, and hence many wrong claims are made. Not only will the course vary from one individual to another, but also from time to time. For much depends upon the virulence of the bacteria and upon the resisting power of the patient. The latter in turn depends not only upon his original constitution, but upon his state of health. It may be considerably modified by the onset of some disease. There is no method of ascertaining with any degree of exactness the virulence of bacteria or the power of the body to resist their invasion. Consequently there will always be some uncertainty as to how much improvement is to be attributed to treatment.

A bacterial disease is generally self-limiting. This is perhaps best seen in pneumonia. For even if no specific therapy is attempted, in the majority of cases the disease comes to an end by crisis about the eighth day. The hope of many practitioners is to see this occur before the toxæmia has undermined the vital organs. If so, the patient is almost certain to recover. Now the crisis is not something that is produced by good nursing or medical treatment. It means that the reaction that is started by the inflammation in the lung has been accomplished, that the resistance factor is restored, and once again the body fluids and the tissues can be indifferent to any bacteria that enter. So far as we know, only some reaction by the patient can produce this result. Many bacterial diseases are self-limiting, though the

termination is not so certain or so spectacular as is the case with pneumonia. But nevertheless it can occur in a case that looks almost hopeless. For instance, in erysipelas or cellulitis when the condition may appear to be so hopeless that all active treatment is stopped, the inflammation clears up in a remarkable manner and the patient recovers. All that can be said is that something comparable to a crisis has occurred. How or when it is going to occur cannot be foretold. It is because its possibility is so rarely taken into account that so many wrong claims are put forward for therapy. When scientists carry out experiments on animals and apply certain forms of specific therapy, they always seem to predict with accuracy what would have taken place were it not applied. This may be possible in animals. In man it is not possible to foretell with any accuracy the future course of bacterial disease.

For teaching purposes diseases are described as running a certain course, but the description is always on very broad lines. A case that is true to type excites comment, for this is so rare. In almost every case there is some deviation from what is regarded as the normal, whether treatment is carried out or not. The difficulty of forecasting with any accuracy the course bacterial disease would run was brought home to me before the War when trying to ascertain the value of various forms of therapy in gonorrhœa. Even if nothing were done, few cases ran the same course ; and, if with treatment a case did well or some complication ensued, it was a little uncertain whether to attribute this to therapy or to regard it as the natural reaction of the tissues or something peculiar to that patient. If this applies to gonorrhœa, which is due to the direct implantation of the gonococcus on the urethral mucus membrane, how much more does it apply to diseases such as pneumonia and erysipelas, where not only is it uncertain whether the organism existed previously in the body or has come from outside, but before the disease could have developed there was some lowering of the resistance factor ?

The more that the reactions which take place in the body when disease is present are studied, the more does the purposive work of Nature become revealed. But the tendency is rather to attribute great purposive powers to those factors that lead to the preservation of man and to assume that other forms of life have so little. Few consider that fish have brains. A year or so of angling will modify their views ; for it brings home the great intelligence of trout when they work along lines in which they are interested. A study of the life-history of eels and salmon must make anyone realise that, if they are guided only by instinct that serves no definite purpose, luck plays with them an extraordinary part. Those who have studied the way of bees and ants are amazed at their routine and almost eulogise their intelligence. Because we cannot visualise the mechanism underlying the activity of bacteria, we are too apt to assume that it is purposeless. But from what we know of life in general it is unwise to assume that they are insensate and that their sole function is merely to divide and form toxins. It is said that they are the enemies of mankind, and that their aim is to lead to his destruction. But what end does this serve?[1] When the host is dead their

[1] Disease does not seem to be to the advantage of the host or of the bacteria. It doesn't necessarily follow that it indicates that there is not purposive design in Nature. For where life is concerned, Nature has only a directing influence—she cannot control. Civilised man has within reason the will to do as he wishes. Yet he insists on going to war, which as history shows is rarely to the advantage of the victor or the vanquished. Take the case of the Great War. The British and German peoples had been on fairly friendly terms since the time the Angles invaded Britain in the fifth century. Though the rivalry was keen, there had been no war. When their empires were at the height of their glory and greater than anything that had been seen since the days of Greece and Rome, they proceeded to destroy one another. Their leaders had always the power to prevent or to stop the War. It is useless to blame Nature for their want of ability and of foresight. In 1914 the leaders in the world were the British and German peoples, who had much the same ideals. In their place to-day are nations that in 1914 were second-rate powers and civilisation is definitely on the decline. Who is to be blamed for this : Nature or the stupidity of man ? Disease must be viewed in the same way as war. It is not possible to make it appear rational.

means of subsistence comes to an end. When he is buried or cremated, they die or cease to be active by forming spores. Is it not rather that so long as they find the medium satisfactory they are perfectly content to go on living at peace with the host? That should be their aim if their life is purposive. For the longer the host lives the longer will be their life. This is seen so well with the typhoid carrier, for here the host and the organism are content not to harm one another. This also applies to the pneumococci in the throat. For they are present in this region before an attack of pneumonia. Though the power of the blood to destroy them is increased after the crisis, this does not mean that they disappear from their normal habitations; for long afterwards they are present there in great numbers.

When an inflammation arises the surgeon should put to himself the following questions:

1. How much of this is due to the reaction of the patient in his effort to overcome the infection? This is to be regarded as beneficial.

2. How much is due to the effect of the toxins in this effort of the bacteria to produce a medium in which they can survive? An excessive reaction is dangerous to the patient. I look upon it as the reaction of a particular type of constitution to bacterial toxins which under stress are produced to make conditions more suitable for the bacteria.

Three types of infection should be kept in mind when this problem is studied. Only the main points need be outlined:

1. Gonorrhœa, where the inflammation is quite local at the start and as a rule there is no general reaction. The invasion of the blood stream is a rare late sequela. To this type many inflammations of surface wounds conform.

2. Pneumonia, where the reaction, local and general, is essentially sthenic.

3. Typhoid fever, where the reaction, local and general, is essentially asthenic.

In the last two, invasion of the blood stream takes place

early. Gonorrhœa, pneumonia, and typhoid have been chosen because they run a certain course and tend to recovery whether treatment is instituted or not ; they are considerably influenced by the constitution and the state of health. It is better to consider only cases where the health was previously good and there is no disease of any organ. Otherwise much confusion will be added to what is already a difficult problem.

A. Gonorrhœa

The inflammation extends backwards by contiguity of tissue, but is held up for a time by the compressor urethræ. If the urethra is irrigated immediately after coitus, it is often possible to prevent the onset of gonorrhœa. But, whilst its course may be modified by treatment, it is not possible to abort it. Whenever a patient has any semblance of a urethritis after exposure I advise the injection of potassium permanganate if he is hypersthenic ; of zinc permanganate if he is hyposthenic. If the patient has not got gonorrhœa, this will do no harm ; if he is developing it, it may do good. In past years when there was slight congestion of the meatus and the smear showed gram-negative diplococci and gonorrhœa did not arise, I felt it had been aborted ; but in such cases the diagnosis was always in doubt. There never was a case where this happened where the diagnosis was certain. After all, gram-negative diplococci are often present in a healthy urethra and can easily be confused with the gonococci, and this is very likely in the early stages. Before it can be claimed that an attack is aborted, a positive culture should be obtained. It seems that once an attack starts it is never overcome until the whole of the anterior urethra has been affected by direct extension. But, when the disease is limited to the anterior urethra, there is inflammation of only a surface mucous membrane, the involvement of the urethral glands being usually a minor affair. When the inflammation extends to the posterior urethra, invasion of the prostate is likely to occur and the

inflammation can no longer be regarded as one of a mucous membrane but rather of a deep-lying parenchymatous gland.

So long as the disease affects the anterior urethra only, no general reaction takes place, there is no rise of temperature, no leucocytosis, and the complement fixation test remains negative. Once the posterior urethra is involved a rise of temperature and a moderate leucocytosis may occur, and direct invasion of the blood stream leading to arthritis and septicæmia occasionally follow. How much of this is due to the mucous membrane here having a high absorptive power and how much to the prostate being involved is uncertain. If the disease is limited to the anterior urethra, it tends to clear up after three to six weeks and may often leave no after-effects. Examination with the urethroscope shows no changes. At times a stricture may form, but this is composed of fibrous tissue and is nothing more than too great an effort on the part of Nature to make a cure certain. If it is prevented from contracting and a secondary infection is avoided, such cases do well. At other times a relaxed condition of the mucous membrane, that leads to a persistent mucous discharge which contains no pus cells or gonococci, persists. This must be differentiated from a continuance of the disease. It merely means that though the infection has been overcome, the reaction has not been sufficiently great to restore the mucous membrane to the normal; it still remains toneless. When a parenchymatous gland such as the prostate is involved, the course cannot be foretold with any degree of accuracy; for much will depend on whether the products formed by the inflammation have a free exit. If they have, though the disease is likely to be more persistent, the greater number will clear up if treatment is not too active. If there is not a free exit, or if an abscess cavity is formed that cannot contract, the inflammation becomes chronic and the disease goes on indefinitely. The persistence of infection will depend upon whether there is any fibrosis obstructing the outlet of a gland or whether a cavity is present that cannot contract. This will depend

not upon its size, but upon the size of the aperture and whether the walls can collapse.

Should, however, some sthenic fever arise during the course of the disease or should a severe epididymitis occur, the attack is cut short and a cure seems more certain. Either seems to raise the antibactericidal powers of the blood. It therefore seems that even in a local inflammation it is an advantage to bring into play the antibactericidal powers of the tissues generally. Clinical observations suggest that, where there is a certain amount of congestion and pain and thick creamy pus is formed, i.e. a definite local reaction is taking place, the outlook is good. But because a certain amount of congestion is desirable it must not be thought that a great amount is more advantageous. For when this occurs invasion of the blood stream and the development of arthritis are more likely. On the other hand, when the reaction is not sufficient and the pus tends to be sero-purulent and is formed in greater amounts and there is little pain, the disease runs a more prolonged course and tends to become chronic. The reaction has been attributed to the virulence of the bacteria. But if it is severe and the patient is treated by rest, local and general blood letting, big doses of magnesium sulphate by the mouth, and morphia, definite improvement usually occurs. None of these has any immediate effect upon the virulence of the bacteria. They can only modify the reacting powers of the patient. The severe reactions generally occur in the healthy, particularly if the constitution is hypersthenic and there is a tendency to plethora or muscularity. Years ago it was recognised that those of the gouty diathesis were extremely vulnerable to the gonococcus. The reaction is less severe in the hyposthenic, particularly if there has been a tendency to some chronic infection or constipation. It seems, therefore, that if the eusthenic impulses are in the ascendant the reaction tends to be too severe; if the dysthenic, it is too mild. The remote sequelæ also depend on the constitution. For a stricture is more common in the hyper-

sthenic and a relaxed condition of the mucous membrane in the hyposthenic.

Once gonorrhœa has started it is difficult to reduce the attack to less than three weeks, no matter what treatment is given. Why this period has to be run no one knows. It is said that it is necessary to create immunity, but this after all is no more than a phrase. It is in most cases essentially a local disease that tends to clear up without treatment. This was more conspicuous years ago when fewer facilities were available.

I am convinced that a reaction is an advantage in gonorrhœa and that if this is maintained the patient is more likely to be cured. The mistake in the past has been to look upon this reaction as harmful and to direct efforts to overcome it. This makes things easier for the patient as the symptoms become less severe. I am sure that if carried out too far it prolongs the course of the disease. In patients who had gonorrhœa in the past and who now show no sign of the disease, though no treatment was ever carried out, it is often found that the discharge was quite definite, there was much pain, or an attack of epididymitis developed. On the other hand, gonorrhœa that begins without a reaction and with little or no pain tends to persist. I prefer to see a local reaction, and if it is not present am inclined to encourage it by local or general measures. After it has persisted for some days, measures may be taken to diminish its severity. If the reaction is too severe, it should not be regarded as merely due to greater virulence of the bacteria. Rather it is to be looked upon as due to a constitution where the eusthenic impulses are in the ascendant. It is necessary to take measures to decrease these locally and generally by the action of dysthenic drugs and measures. As cases do better if the antibactericidal powers of the body are mobilised, some form of protein therapy should be given from the start. Really I find myself coming back to the therapy that was practised when attention was given to the constitution and to the power of the tissues to react. This is

borne out if for eusthenic is substituted something that stimulates and for dysthenic something that soothes or depresses.

B. Pneumonia

Though the onset is usually very abrupt with a rigor, there is often a prodromal period lasting for two to three days in which there is some malaise. Once the attack commences, the skin becomes hot and dry, and the breathing rapid even when there are no signs in the lungs. The temperature remains continuously high, the pulse is full and bounding, a leucocytosis is to be expected and is of good import. Eventually there is a massive inflammation of the lung. But at times the general signs may be present for some days before local changes in the chest can be detected. The termination is usually sudden and by crisis, and within a few hours the patient may be at ease.

At the time of the crisis percussion and auscultation do not show any immediate change in the lung, though the temperature and respiration rate are normal and the pain has disappeared. The amount of tissue involved is the same for some days. If no vital organ has been damaged by the toxæmia convalescence is rapid. It is surprising to see a man who was so acutely ill just a few days previously ready to get up and walk about. As a rule health is completely restored and any degree of asthenia and a persistent infection are uncommon. After a short time no changes in the lung are to be detected, but a relaxed condition of the bronchial mucous membrane may persist for some months. Very rarely there is some tendency to fibrosis, but this involves either the pleura or the parenchyma of the lung and leads to bronchiectasis rather than to a stricture of the bronchi.

Here from the first there is a general reaction, as if all the forces of the body are being brought into play. When there is a sudden onset, a good sthenic reaction, and the attack ends by crisis the case does well and complications

are rare. There is less tendency to ill-health afterwards. When marked herpes facialis develops during the attack the prognosis seems better. When the reaction is excessive, as shown by hyperpyrexia, severe pain, etc., complications such as pericarditis and syn-pneumonic empyema are more common. It is in such cases that the pneumococci do not disappear from the blood and septicæmia supervenes. White hepatisation should be regarded as a purulent infiltration of the lung. It clears up after the crisis. The pus that is formed in the pleura at this time, giving rise to the syn-pneumonic empyema, should be looked upon as an extension of the white hepatisation and an indication that the inflammation in the lung is failing to set up the resistance to prevent septicæmia. It should be regarded as an attempt to increase the local reaction, so as to prevent the septicæmia from progressing. The pericarditis should be viewed in the same way. The syn-pneumonic empyema must be differentiated from the meta-pneumonic. The former is characterised by an intense local and general reaction and is likely to be associated with septicæmia; the latter is characterised by a mild reaction and leads to toxæmia and only rarely to septicæmia.

This excessive reaction is difficult to understand. It can hardly depend on some change in the virulence of the bacteria, for even during the same epidemic it may affect some and not others. As in the case of gonorrhœa, it probably depends upon some factor in the constitution or in the health. It is more common in those in good health, particularly if the constitution is hypersthenic and there is a tendency to muscularity or to plethora. For pneumonia at times picks out the sensitive and the strong. It is strange that at such a time strength and vitality can be a danger to a patient. An excessive reaction is rarely if ever seen in those of the hyposthenic constitution, particularly if they have been liable to chronic bacterial diseases. It is not seen when there is some nervous disease such as tabes or G.P.I. In the old and infirm pneumonia runs a

rapid and fatal course. But this is due to the action of the toxins upon some vital organ already impaired. In these a severe local or general reaction is hardly ever seen. Here the reaction again bears some relation to the constitution. When the eusthenic impulses are in the ascendant a severe reaction is more likely ; when the dysthenic, a mild reaction.

With pneumonia there are three stages :

1. The bacillæmia.
2. The inflammation in the lung.
3. The restoration of the resistance factor.

The inflammation in the lung should be looked upon as an attempt on the part of the host to prevent, by the formation of anti-bodies, a bacillæmia developing into a septicæmia. But there is something more than this. For at a certain stage the resistance factor is restored and then occurs the crisis. A good reaction here too seems an asset. If an attempt is made to cut short the reaction, it seems to me that ill-health or some chronic bacterial disease is more likely to follow. But the influence of the toxins upon the vital organs and the impaired circulation upon the heart must be viewed in another light. It is harmful to have too severe a reaction, such as is seen in the healthy and strong, and equally so to have too slight a one, such as is seen in the aged and infirm.

The pneumococcus often flourishes in a soil where the eusthenic impulses are in the ascendant. These seem favourable to its growth and activity. Whilst its toxins may to some extent be stimulating the eusthenic powers of the body, rather I look upon them from an analogy with typhoid as paralysing the dysthenic powers, as a result of which the eusthenic powers may at times run riot. When this takes place much harm may result. When in pneumonia the reaction is satisfactory it is better to leave everything to Nature. That is what medical men were always taught a few years ago. It is at this stage that interference is meddlesome since it may worry the patient and so do harm. The medical man does well to leave the

patient in the hands of trained nurses and is content to hold a watching brief. But if the reaction is excessive and nothing is done, much harm may result. At this stage dysthenic drugs and measures are necessary. If the reaction is not sufficient, this is generally due to some failure on the part of the constitution to respond. It is seen so often in the aged and the weak. Eusthenic drugs and measures may be tried, but so often do little good. The trouble is that the patient cannot respond. Protein therapy by means of a vaccine or non-specific protein at this time fails, since some reaction on the part of the cells is necessary and this is not possible. The aim now is to maintain the strength, to protect the cells from the toxins, and to prevent any strain being placed upon the vital organs and whenever possible to diminish the work they have to do.

C. Typhoid Fever

The rise of temperature is more gradual but reaches a high point. During the attack the pulse is soft, the tension low, and there is severe mental and physical prostration. A leucopenia is to be expected. Around the ulcers in the intestine there is little congestion and no intense reaction is set up. It is very rare for pus to be formed in any amounts during the attack. After the attack the healing of the ulcers is not associated with much fibrosis and strictures are extremely uncommon. But prolonged impairment of the general health is likely to follow and the vitality remains low for many months. During this time an infection of some mucous membrane, characterised by little local reaction and little pus formation, is liable to arise. My experience of typhoid is too small to enable me to comment upon the effect of any inflammatory reaction that takes place. But with B. coli infections, an organism of the same group, tenderness and rigidity over the kidney, marked vesical symptoms or a high degree of acidity of the urine, are the signs of a severe local reaction in the urinary tract. If, provided the patient is not too ill, alkaline therapy is not

instituted until the symptoms have persisted for a couple of days, the infection clears up more quickly. Their presence has a favourable influence on the prognosis.

Typhoid fever is rare in infancy and childhood. When it occurs it runs a very benign course. This also applies to strong healthy people. When it arises in diabetes the outlook is good. It is the person with the hyposthenic constitution who seems more predisposed to typhoid. Before the onset the health will often be found to be impaired. It seems that when the dysthenic impulses are in the ascendant it gets the greatest hold and is most persistent ; when the eusthenic impulses are in the ascendant, it is not likely to be so severe.

When typhoid develops it prefers the constitution in which dysthenic impulses are in the ascendant. Its toxins either stimulate these or more probably paralyse those giving rise to the eusthenic impulses. The high temperature is an indication that the forces that set up a reaction are being stimulated. None takes place, for they are paralysed. This is the obvious state of the body generally during typhoid fever. It is shown clinically by the leucopenia and by the absence of any reaction around the ulcers and the failure to form pus. When a case of typhoid is watched and compared with one of pneumonia the practitioner must often put to himself the following question: Now here in pneumonia, that prefers those who are sensitive and strong, the severity of the reaction is doing the patient harm ; it is this which is going to destroy him ; it is this which leads to the formation of pus ; in the case of typhoid, that seems to pick out those who are not too robust, it is the absence of this reaction that is conspicuous; if I could but transfer this to the patient with typhoid, would not he soon get well ? But when pneumonia occurs in typhoid it is a serious complication. The reaction is essentially asthenic and so different from that which is seen in acute lobar pneumonia. It conforms to the type that is seen in the aged. This must be because those factors that are responsible for the reaction are paralysed

by the typhoid toxin, and are now unable to respond to the toxin of the pneumococcus. A reaction on the part of the tissue is just the thing that is needed. It is not possible to produce it except in the early stages. If the paralysing action of the toxins could be overcome, Nature herself would do the work.

From the start the aim is to maintain the strength, to protect the cells from the toxins, and to prevent any strain being placed upon the vital organs. For the time being the eusthenic powers of the body are paralysed. It is useless trying to stimulate them. It is here that phylaxis may play a big part.

A perusal of this chapter suggests that once a local inflammation such as gonorrhœa starts, it has to run its course. If everything is going on well, it is inadvisable even to attempt to modify it. It is unwise to attempt to abort it at this stage. This so often results in its becoming chronic. On the other hand the formation of antibodies seems to be indicated and should be attempted by whatever method the practitioner thinks best. With a sthenic inflammation such as pneumonia the local inflammation serves some purpose. Attempts should be made to modify it only when it is severe. As so often the disease begins as a general infection which becomes localised, the production of antibodies is already taking place. This should only be increased by artificial methods if the local reaction is very severe or is extending. Either of these I regard as an indication that insufficient antibodies are being formed. The practitioner should endeavour to protect the tissues as far as possible from the deleterious action of the toxins. In an asthenic inflammation such as typhoid the production of antibodies and of an increased reaction at the site of the inflammation is desired. Except in the early stages, this is not possible as the reacting powers of the body are paralysed. All that is attempted is to maintain the strength to protect the cells of the nervous system from the action of the toxins, and to liberate those that are already attached.

CHAPTER XIII

THE ACTION OF DRUGS

THE possibility of the following must always be taken into account :

1. Some action upon the constitution as a result of which the resistance factor is modified. Mercury in the bilious diathesis is a case in point.
2. Some direct action upon the local lesion.
3. Some direct action upon the organism.
4. The relief of symptoms leading to some improvement in the health.

The action of drugs in bacterial diseases has been attributed entirely to some antiseptic power. But the slight action of antiseptics when applied directly to a surface inflammation renders this unlikely. Some reaction with the tissues is a better explanation. Iodoform may be taken as an example. In phagedæna its action is sometimes so marked that it is looked upon as a specific, and when applied to foul septic wounds the improvement may be extraordinary, as the following case shows :

In Aug. 1933 I was asked to see at the Cardiff Royal Infirmary an appendix abscess that had been opened three weeks previously. The discharge was so foul that at first it was thought to be fæcal. Though a cavity was present that later needed counter-drainage, the offensive odour disappeared after the iodoform was applied on two occasions, the wound looked much cleaner and healthy granulations soon began to form.

Now iodoform itself has little antiseptic action when, placed in contact with bacteria, and consequently some consider that its action is due to the liberation of nascent

iodine, when brought in contact with a discharging wound. But iodine can be liberated in this way by other methods such as ionisation, and then it has little action. It is more probable that iodoform acts by setting up those reactions with the tissues, as a result of which certain processes that are hanging fire are stimulated and the inflammation is consequently overcome.

The possibility of a drug acting in this way has been lost sight of in recent years. Though of course the action is still upon the inflammation locally, the power to respond will depend upon the constitution, the state of the health, and the state of the tissues. For this reason a drug will not act equally well at all stages and at any age. Iodoform acts best in the hypersthenic and particularly if there is some tendency to plethora or to muscularity.

When a drug is applied to a surface inflammation it may increase the reaction, when it may be said to have some eusthenic action; or it may decrease it, when it may be said to have some dysthenic action. This is perhaps best illustrated by a reference to flavine and eusol. In the guillotine amputations that were sent over from France during the War, the wound would be covered with a thin greyish pellicle when the dressing was removed, if it had been soaked in flavine previously. There would be no signs of an inflammatory reaction and no tendency to the formation of granulations. When flavine is applied to a wound during an operation it aggravates the capillary oozing. It has no astringent or stimulating action and is definitely a dysthenic drug. This is also true for other dye preparations, such as brilliant green, and to a less extent for potassium permanganate.

Eusol may be taken as an example of a eusthenic drug. When applied to a wound, it leads to the absorption of sloughs and of blood clot and has some cleansing action. But it also stimulates the formation of granulation tissue when applied to a wound that is not reacting sufficiently. In the hyposthenic there is no better drug. Silver nitrate, collosol

silver, and certain preparations of zinc and mercury have a similar though less marked action.

Possibly when drugs are given internally they may act in the same way. This is illustrated in the treatment of syphilis. Mercury has a definite action, particularly if given in small doses for a long period. If given as soon as the chancre appears, secondary and tertiary lesions are unlikely; if taken for two years, it undoubtedly leads to a cure in the majority of cases. Though with certain types of chancre its action is quite definite, this is not so marked with the hard primary chancre in which there is much proliferation of connective tissue. Though, again, its action seems quite definite in the milder types of secondary lesions, such as the roseola and macular rash and in mucous tubercles, it is less evident in proliferative lesions such as rupia. It has little if any upon gummata.

Salvarsan acts best in the proliferative lesions of syphilis, and the more massive these are the more marked seems its action. When it was introduced, it was extraordinary to see lesions that had long resisted the intensive administration of mercury and iodide clear up in a few days.

We do not know how mercury and salvarsan act. The former probably has some eusthenic and the latter some dysthenic action. Whether this is upon the resistance factor of the constitution or locally upon the lesion is not known.

It is now my practice to give salvarsan only when lesions are present. If they are proliferative, as is so often seen in the hypersthenic, it is continued for a longer time. If the lesions are slight, as is so often seen in the hyposthenic, mercury is given as soon as they disappear and is continued for two years. Better results seem to be obtained by varying the treatment according to the constitution of the patient and the nature of the lesion.

The severity of syphilis depends not only upon the virulence of the spirochæte but also upon the constitution and health of the patient. If no resistance were put up, the

organism would enter and grow in the blood stream and the septicæmic state would arise. The chancre must be looked upon not only as the result of the activity of the spirochæte but also of the resistance of the tissues to overcome it. Fibrosis and ulceration are the evidences of this. When the chancre is extensive and particularly when there is any phagedæna, no secondaries may ever arise, for the spirochætes may have been destroyed by the resistance that is put up. If this does not take place, they enter and grow in the blood and the septicæmic state arises. The secondary eruptions should be regarded as the effort of the tissues to overcome this by the setting up of local inflammations. If the eusthenic impulses are in the ascendant, proliferative lesions are formed corresponding to the sthenic inflammatory state ; if dysthenic impulses are in the ascendant, the softer ulcerative varieties are formed, corresponding to the asthenic inflammatory state. As a result antibodies are formed that raise the resistance factor against the spirochæte. If this is not possible, secondary eruptions arise one after the other, from which the patient may eventually die. If a high resistance is attained, the spirochætes may be killed and the patient is cured. But it is unlikely that all are destroyed. Some may lurk in the tissues, and this would be most likely in the avascular areas. If at some future date the resistance factor becomes lowered by some impairment of the health or local injury, the spirochæte may become active. In this way the later sporadic appearance of gummata is explained.

Some look upon the secondary and tertiary lesions as manifestations of the same organism in a constitution that has been much altered. For in untreated syphilis changes in the cardio-vascular system become obvious in a couple of years. They probably start at the time of the septicæmia, though it is necessary for them to progress before they can be seen. As the constitution is something very delicate that is altered by slight changes, it also becomes modified.

Just as with the hypersthenic constitution proliferative lesions arise and with the hyposthenic ulcerative lesions, so when the constitution has become modified by the septicæmia of syphilis some change in the nature of the lesion will be expected, and gummata and not secondary lesions arise.

This view of syphilis means that so long as the resistance factor to the spirochæte can be maintained, the tissues are indifferent to their presence. If it becomes impaired, the syphilitic lesion arises. The variety will depend on whether the eusthenic or dysthenic impulses are in the ascendant. The whole aim of therapy is to modify these and bring the resistance factor to the normal. Then spirochætes may be destroyed or will at any rate be prevented from becoming active.

Arsenic and mercury are supposed to act by modifying the constitution. When one is indicated, the other may do harm, though there are times when it is advisable to give both.

The present method of attempting to destroy the spirochæte by giving mercury and arsenic, often in big doses for long periods, is to be condemned. It means much unnecessary therapy and may even do harm, by promoting the state in which the spirochæte flourishes. Persistent syphilis is still too prevalent, and there seems to be more congenital syphilis than before the War. Yet at that time little attention was given to the disease and few facilities were available for treatment. Nowadays there are plenty in all cities and towns. It can only be that the indiscriminate way with which the disease is being treated promotes that state in which the spirochæte flourishes.

Salvarsan also acts in streptococcal infections when the reaction is definitely sthenic and there are pain and congestion and a full bounding pulse. When the asthenic state supervenes it is useless and probably does harm. It also acts in staphylococcal infections with a sthenic reaction, such as osteomyelitis and perinephritis, and also in boils and carbuncles, where there is much congestion and a definite local reaction. It also helps to clear up the chronic forms of tuberculosis in which there is much fibrosis. It is stated to have an immediate action upon the lesions of anthrax, but I have had little experience of this disease. In gonorrhœa where there is much congestion and pain and particularly if there is much œdema of the meatus, one injection of salvarsan brings relief. It is doubtful if it

diminishes the discharge. If it is continued, it is my impression that the disease is more likely to become chronic.

In certain types of B. coli infections that do not respond straightaway to the alkaline therapy or that first tend to clear up and then hang fire, the intravenous injection of mercurochrome often assists. There is a certain form of chronic disease due to the B. coli in which administration of mercury by the mouth gives relief, particularly if taken in small doses over a long period. Mercury has no action when there is much fibrosis.

The preceding remarks suggest that salvarsan acts best when there is a sthenic reaction and a tendency to proliferation of the tissues, and mercury when there is an asthenic reaction and no proliferation of the tissues. They have little action when there is much pus. For the reasons given in Chapter III it is unlikely that salvarsan and mercury have any direct action upon the bacteria. Were they to act in this way, their effect should be greater in true septicæmia where there is no local lesion. For here the bacteria are circulating in the blood stream in direct contact with the antiseptic and their destruction should be easier. But it is in these cases that intravenous therapy fails. Just as flavine and eusol have some action upon a surface lesion, it is possible that arsenic and mercury have some dysthenic and eusthenic action upon the lesions when given internally. But it is equally possible that they act as alteratives and modify the constitution, and in this way restore the resistance factor to the normal. Then the tissues once again are able to deal with the bacteria that penetrate into them; and any lesions present tend to clear up. For instance, when mercury is given to those with the bilious diathesis in which there is a predisposition to infection with the B. coli it often cuts short the duration of the attack or may prevent its onset. Here the resistance factor becomes modified from slight causes and as a result bacteria become active. Mercury probably prevents this happening by restoring the resistance factor.

Those whose work brings them in contact with arsenic have generally a beautiful complexion and the skin is remarkably free from pimples. A practitioner whose clinical acumen I much respect tells me that it is his practice to give small doses of liquor arsenicalis or sometimes Donovan's solution for those who are predisposed to boils or carbuncles. It does good if taken for a long time. Years ago Donovan's solution was used as an alterative in such conditions. And by alterative is meant some drug that acts upon the constitution and restores it to the normal. Where a predisposition to certain bacterial diseases is present it raises the resistance factor. As a result the tissues become indifferent to bacteria that enter.

Tinc. ferri per. chlor. was given years ago in streptococcal diseases and this is still my practice. Manganese has undoubtedly some action in staphylococcal infections and particularly upon the more chronic forms.

Some practitioners prescribe iron, manganese, arsenic, or mercury for long periods, where there is any tendency to some chronic infection. There is something to be said for this practice I am quite definite that small doses of mercury given for a long time seem to diminish the liability to coli infections.

Sir James Paget has the following :

" Where then shall we find the lowest rates of mortality and other mischiefs. Perhaps you may find them in a class whom you may often study here. We have a large number of printing-offices in the neighbourhood of the hospital ; and every office employs many boys from 12 to 16 years old ; and hardly a week passes but we have one or more of these boys brought in crushed by the printing-machines. Fingers, hands, and arms are thus mutilated ; and I know no class of patients that recover more remarkably. Not only do they not die, but their wounds heal steadily and quickly ; they escape erysipelas and spreading suppurations and secondary hæmorrhages ; and often, when, to save any piece of a hand, we leave bits of skin that seem as if they could not live, they yet do live and grow good scars."

It would seem from this that small doses of lead over a long period in some way protect the patient against bacteria. As substances that resemble one another chemically have a similar pharmacological action, it is not unreasonable to assume that manganese, arsenic, iron, and mercury may have a similar effect. They probably act as alteratives and overcome the factor that predisposes to a certain type of bacterial disease and in this way modify the constitution. Their effect is probably due not to some direct action but to some reaction that is set up by the cells. Large doses are not indicated.

The method recommended of giving a blunderbuss mixture of many drugs has little to be said in its favour, for though one drug may do good another may do harm. Though mercury, for instance, seems to do harm in staphylococcal and streptococcal infections, and certainly when pus is present, it acts well in the bilious diathesis; arsenic, on the other hand, is beneficial where there is a predisposition to staphylococcal infections. Where either fails small doses of Donovan's solution, which is a combination of mercury and arsenic, may work wonders. But such a result is only occasionally obtained, for generally their action is opposite and not complementary.

CHAPTER XIV

PHYLAXIS

WHEN the tetanus and the diphtheria bacilli grow in the body they give rise to toxins that act upon the nervous system and are therefore termed "neurotoxins." Antitoxic sera can be prepared for both bacilli, and if given sufficiently early prevent the onset of symptoms. Once the disease is established and the nervous system involved, the activity of antitoxic sera is much diminished. It is consequently assumed that, as the toxins have become fixed to the nerve cells, they cannot be dislodged or that irreparable damage has been done. In the early stages of the War tetanus was common. Though cases treated by antitoxin did better than those to whom it was not given, few were really enthusiastic about its value. Towards the end of the War tetanus had become much less common. Though this was to some extent due to the better treatment of wounds, it was definitely due to the routine use of antitetanic serum as a prophylactic. At first it was given in one injection of 1,500 units, but later, better results were obtained from three injections of 500 units at intervals of a week.

It was assumed that the presence of the antitoxin in the blood over a period of three weeks would be sufficient to neutralise any toxin formed by the growth of the bacilli, or that it would inhibit their growth. But the greater part of the toxin reaches the central nervous system by passing up along the motor nerves that supply the area of the wound. It was therefore difficult to understand how a small amount of antitoxin in the blood—and towards the end of the week after the injection it would be very small indeed—could neutralise the toxin, particularly

as it would have difficulty in entering the nerves from the blood stream. Nor from what was known of the difficulty of freeing inflamed areas from bacteria was it likely that in the infected wounds that went on discharging for months the tetanus bacillus ceased to be active. Though there was never any question as to the prophylactic value of tetanus antitoxin, there was considerable doubt as to the way in which it acted. Whilst it undoubtedly combined with the toxin and so limited its activity, the whole of its action could not be thus explained.

The work of Billard on phylaxis shows that antitoxin becomes fixed to the nervous system, and in this way protects it from the action of the toxins. His work was based upon the observation of a shepherd that sheep, which had eaten the green shoots of the broom as they appeared above the snow in the spring, became immune to snake-bites. Working in the laboratory with sparteine sulphate, the active principle of broom, he found that a guinea-pig injected with sparteine could later be given more than five times the lethal dose of venom without any harmful results. He concluded that this was not due to the neutralisation of the venom by the sparteine *in vivo*. He showed that the sparteine combined with the lipoids of the nerve cells. As a result the venom could no longer enter the nerve cell. He assumed that the sparteine impregnated the nervous tissue like a dye and so protected it from the action of the toxin. To this protective action he gave the name *Phylaxis*. This protection persists for some time after the injection. He showed that this phylactic action could be produced by antitoxins. This offers an alternative explanation for the beneficial results obtained from a prophylactic injection of tetanus antitoxin.

When the neurotoxins have become fixed to the nerve cells in tetanus and diphtheria, it is difficult to dislodge them. It has been known for many years that the spasms of tetanus are controlled by administering chloroform. When it is stopped, the spasms recur with greater intensity and death

often supervenes. It has seemed that the temporary benefit is more than offset by the subsequent course of events. If, however, large doses of antitoxin are given at the same time, an improvement may follow, though none took place previously when the antitoxin alone was given. Billard has shown that when chloroform is administered, it combines with the lipoids of the nerve cells and sets free the toxins previously fixed there. These now circulate in the blood. Owing to the depressed state of the tissues no antitoxins can be formed to neutralise them, and they are not excreted to any appreciable extent. Consequently, when the administration of chloroform is stopped, they again enter the nerve cells and become fixed and do further damage. If, however, antitoxin is injected, this may be prevented.

These principles have been adopted by the French school in the treatment of tetanus. They inject antitoxin subcutaneously and 12 to 14 hours later induce chloroform anæsthesia, under which they inject antitoxin intraspinally. Better results are recorded from this treatment.

The work of Billard on phylaxis should receive attention, for it may be the clue to the treatment of certain toxic states. In the treatment of gonorrhœa the practitioner is largely concerned with a local inflammation. With a sthenic bacterial disease such as pneumonia, whilst the local condition counts, it is the immediate effect of the toxæmia upon vital organs and the strain to which these are subjected that give most concern. When it passes off there is little impairment of health provided no vital organ is damaged. In an asthenic bacterial disease, such as typhoid, it is the extreme prostration and the failure to produce a response that are most to be feared. When these are overcome prolonged asthenia, not always proportionate to the severity of the attack or to the care with which treatment is carried out, is apt to follow. It seems to some extent dependent upon the vulnerability of the cells of the nervous system to some neurotoxin. This is best illustrated by a comparison of tetanus and diphtheria

which are known to form neurotoxins. Tetanus gives rise to a severe sthenic reaction which is dependent upon the action of its toxins upon the nerve cells. When this clears up the impairment of the health is slight, considering the severity of the attack. Severe diphtheria offers a marked contrast. Not only is the paralysis likely to remain, but asthenia may last for years. The latter I also regard as due to the action of some neurotoxin upon either the sympathetic system or the nuclei at the base of the brain. In many of the asthenic bacterial diseases, particularly in those due to the B. coli, influenza and the common cold, possibly some neurotoxin is also produced. For the severe prostration at the beginning is out of all proportion to the disordered function in the vital organs. In the past we have been too concerned about the neutralisation of toxin circulating in the blood. As stated above, Billard has shown that if protective substances become attached to cells, neurotoxins may fail to act and thus we might forestall them. Even if they have got into the cell, the action of chloroform in tetanus shows that it is still possible to detach them. Nature can do this. The good results that are obtained by expectant treatment in the anterior poliomyelitis and diphtheria bear this out. Though where the nervous system is concerned, the powers of Nature are often limited. We should aim at assisting her in this.

Morphia in big does (half a grain at night) has been given for years in the treatment of pneumonia in the early stages, to relieve the pain and to promote sleep. The improvement is often out of proportion to what might be expected from this action. In the expectant treatment of acute cholecystitis and acute appendicitis, morphia is given as a routine to relieve the pain and to lower the metabolism. It undoubtedly does good. Whenever a rigor occurs, I at once give morphia to relieve the agitation. Patients always speak highly of the benefit derived. Paget, who suffered from an attack of septicæmia, eulogised the action of morphia. Patients

with acute sthenic bacterial diseases state that they feel much better after morphia, and there are rarely those unpleasant sequelæ that are seen when it is given to relieve the pain after an operation. During the terminal stages of an acute illness when it is obvious that the patient is going down-hill and there is little hope, my practice is to leave him alone, to stop stimulants and, if he is acutely conscious, to give morphia, as I believe no man should be allowed to die with all his faculties on the alert, unless he specially so wishes. At times the patient lives. Looking back on my cases, it seems that this is more likely to take place in those suffering from some sthenic inflammation due to staphylococci or streptococci. The improvement was at first attributed to the rest to the mind and body that occurred. But Billard's work offers some explanation of this action of morphia in pneumonia, the acute abdomen, and in bacterial diseases. For he has shown that certain drugs, as well as antitoxins, have a phylactic action against toxin. Morphia undoubtedly acts on the nerve cells by its solubility in the lipoids, and it is probable that once it has entered the cells it prevents substances such as toxins from doing so. This will account for the benefit derived from its use in certain septic states. For some of the ill-effects of those are undoubtedly due to over-stimulation of the nerve cells by the toxins. In all sthenic inflammations when the temperature is high and the pulse full and bounding, I prescribe morphia in small doses (gr. $\frac{1}{12}$ to $\frac{1}{8}$ six-hourly) throughout the 24 hours. It does good and the inflammation is more likely to become localised.

The value of Dover's powder in many of the asthenic fevers has been appreciated for years. The mistake is to give it only once or twice and not throughout the illness. Probably opium has some phylactic upon the nerve cells. In recent years I have prescribed small doses of opium throughout the 24 hours (2 minims of the tincture six-hourly) in all asthenic fevers. My impression is that the combination in Dover's powder is better. Hexamine was also shown

by Billard to protect the nerve cells from the toxins. Its action in coli infections is partly due to this. In this condition I combine it with small doses of opium, even when the urine is alkaline.

When a patient with asthenia is operated upon for the removal of some supposed focus of infection in the gall-bladder, the almost immediate improvement is at times difficult to explain. For though, where therapy is concerned, faith and hope always come in and can never be entirely excluded, in these cases their part is probably slight. In practically all the cases it will be found that some chloroform was given as part of the anæsthetic. May it not have freed the toxin from the nerve cell, as it does in the case of tetanus? Years ago spiritus chloroformi was given much more frequently than it is to-day. May its continued use not have some such action? It is well not to pass off as auto-suggestion, as is more or less customary to-day, actions of drugs which must still be regarded as empirical.

CHAPTER XV

ALKALINE THERAPY

ALKALINE therapy is indicated in acidosis, where there is a diminution in the alkaline reserve of the body and a tendency to the excretion of ketone bodies in the urine, and in B. coli infections where the urine may become markedly acid. Now these are two entirely different states.

During many acute illnesses there is a diminution of the alkaline reserve. This is particularly marked in acute specific fevers and in acute inflammatory states, especially in children whose urine is frequently found to contain ketone bodies. In those whose kidneys are functioning normally, the urine is acid. But, as in most acute illnesses there is disordered function of all the organs, that of the kidneys is also impaired and the degree of acidity of the urine need not necessarily be an indication of the state of the body. Whilst some improvement follows administration of alkalis by the mouth, this does not necessarily take place even when the urine becomes alkaline. For the primary cause is not the using up of the alkali but an error in carbohydrate metabolism, which is likely to occur in so many bacterial diseases, as the following examples show.

In diabetes any mild infection often leads to a severe relapse and larger doses of insulin are needed. When a severe boil, carbuncle, or other infection occurs in those previously healthy, it is not uncommon to find traces of sugar in the urine, and the sugar-tolerance test shows that there is an error of carbohydrate metabolism. This is the reason why small doses of insulin with glucose by the mouth produce much improvement. In some asthenic fevers, such as diphtheria and influenza, there is marked nervous pros-

tration. Though plenty of glucose is taken by the mouth, it has little effect. If, however, 10 per cent. glucose is given intravenously and insulin is administered afterwards, there is an immediate improvement in the sense of well-being and often in the general condition. No satisfactory explanation for this is forthcoming, unless it be that owing to certain changes in the nerve cells, due to the toxæmia, some product of carbo-hydrate metabolism is not able to enter. For this reason not only should alkalis be given in acute bacterial diseases, but also plenty of glucose combined with insulin.

In many acute B. coli infections the urine is very acid. This is most marked when there are tenderness and rigidity over the kidney, when there are marked vesical symptoms, and in children ; that is to say, in those who seem able to react well. The acidity is not due to the growth of the bacillus in the urine, for, when a profuse growth takes place outside the body and urine is used as a culture medium, the reaction is scarcely changed. This acidity is probably comparable to congestion elsewhere and should be regarded as the local reaction of the body to overcome the infection, for the B. coli does not grow well in an acid urine. It is not seen to the same extent in B. coli infections elsewhere or in septicæmia, for no other organ has the power to form acid like the kidney. And just as in an ordinary inflammation congestion is at first an asset, but becomes harmful if it is carried out to excess, so this acidity is to be desired since it denotes that the resistance is good and that the infection is being overcome. It is only disadvantageous if it is too severe or is too prolonged. It is easy enough to overcome this acidity by giving alkalis by the mouth. In such cases the prognosis is excellent. This acidity of the urine, however, is part of the local reaction and is at times to be encouraged. If alkalis are withheld for a few days, there is less tendency for the infection to become chronic.

It is my impression that in many B. coli infections,

and particularly when there is a septicæmia or the chronic stage is reached, early or prolonged treatment by alkalis does harm. Such patients do much better if at first all food is withheld and little fluid is given, or if they are treated by the ketogenic diet. Nor is there any point in carrying the alkaline treatment to extremes. All that is necessary is to counteract the acidity of the urine. The large doses that are given in order to get the pH of the urine up to 9 do no good locally and may do much harm. For it is not the bacilli in the urine but those in the mucous membrane that are the cause of the trouble. And they are not touched by the reaction of the urine. In addition, alkalis in big doses are very depressing and undermine the constitution and lower the resistance factor. When any local action is obtainable by therapy, it is always well to ponder as to whether its effect on the constitution might not more than counterbalance this. Those who may not agree with my view that big doses of alkalis are depressing should take them for several days, remembering that what may affect a healthy man moderately may severely affect one who is ill.

CHAPTER XVI

THE ACID STATE

HEXAMINE has been our sheet anchor in the treatment of urinary infections. As its action is supposed to be due to its being split up in an acid urine into formaldehyde, every effort has been made to change the reaction of the urine. There can be little doubt that hexamine has at times a marked action upon a urinary infection, and the improvement so often coincides with the urine becoming acid and formaldehydes appearing in it. But, as antiseptics have so little action upon a surface inflammation and as the amount of formaldehyde present in the urine is generally small, it is hardly possible in this way to account for the benefit derived from hexamine. Now hexamine has some action even when the urine is alkaline, and in addition it influences infections elsewhere, such as chronic cholecystitis. Here it is not split up into formaldehyde. Though it has some phylactic action and so protects the nerve cells from the toxins, it probably also acts by tending to create the acid state.

Clark of the Mayo Clinic had noted that the urine of diabetics and of those undergoing ketogenic treatment in epilepsy could stand for a long time without decomposing. This he attributed to its great acidity and to the ketone bodies it contained. This suggested to him the ketogenic diet for urinary infections. With this as little carbohydrates and as much fat as possible are given. The urine becomes very acid and ketone bodies also appear. To increase the acidity little fluid is drunk and much exercise is taken. Though many chronic B. coli infections clear up in a remarkable way, the diet has little action, if any, upon a staphylococcal or streptococcal infection. Some hold that the improvement is due to the increased acidity of the urine

and others to the antiseptic properties of the ketone bodies. But these would act only upon the bacteria present in the urine, and it is those in the mucous membrane that are responsible for the inflammation ; and they would not be affected by any change in the urine. Not only may a chronic infection in the urinary tract clear up, but also a chronic infection elsewhere in the nasal sinuses or the lungs ; and here the question of any antiseptic action of the urine does not arise. That of the blood can have little action, for though there may be some change in the alkaline reserve, the pH of the blood is normal and the amount of ketone bodies circulating there is extremely small.

Probably the ketogenic diet acts indirectly by creating the acid state. As a result the resistance factor of the constitution is modified and the infection is overcome. This acid state must be differentiated from the increased acidity of the urine that is produced by diminishing the amount of alkali and by giving acid-forming salts, such as ammonium chloride, ammonium benzoate, and sodium benzoate. For the improvement that now occurs is not nearly so marked as when the acid state can be produced by the ketogenic diet, and there is wanting that improvement in the general health and sense of well-being. There is more often a feeling of malaise, for the tendency is to poison the patient by giving large amounts of the drug. The acid state is due to some change in the constitution. It is only revealed by the condition of the urine and is not secondary to it.

During the day the reaction of the urine varies according to the amount of fluid that is drunk, and the kind of food that is taken. In some people the urine is persistently acid. Then the acid state is said to be present. This must not be confused with acidosis, which is pathological and is secondary to some change in the alkaline reserve. This acid state is seen in those of good health, especially if the constitution is hypersthenic with a tendency to muscularity or to plethora. These have a high resistance to B. coli infections but seem predisposed to staphylococcal and

streptococcal infections. In diabetes there is a tendency to acidosis and ketosis, and staphylococcic infections are apt to arise. There is less tendency to B. coli infections, which run a mild course and are quickly overcome. The prognosis of typhoid fever when associated with diabetes is good. These facts are consistent with our findings that the ketogenic diet is of value for B. coli infections but not for staphylococcal or streptococcal infections.

In Chapter IX it was pointed out that the resistance factor in some way depends upon the central nervous system. In the acid state there is a sense of well-being and the energy is high. This may be due to the ketone bodies having some action upon the nerve cells ; for they are soluble in the lipoids. They are produced when the ketogenic diet is taken and also during periods of starvation. Ketone bodies might in this way influence the formation of eusthenic impulses and so affect the resistance factor of the constitution. Is it not possible that recovery from a B. coli infection on the ketogenic diet is not due to the acidity of the urine or to the ketone bodies present there but to a change in the constitution ? Hexamine may act in the same way as the ketone bodies. For it contains the aldehyde group and is consequently soluble in the lipoids of the nerve cells. Billard has shown that it has some action upon them. If it leads to the development of eusthenic impulses and the acid state, an explanation is forthcoming for the clinical finding that when an improvement follows its administration the urine becomes acid at the same time. But the latter is secondary to the change in the constitution, and consequently the improvement is not just due to the liberation of formaldehyde.

At times acid. hydrochlor. dil., acid. sodium phosphate, and boric acid. have some action upon bacterial disease, not only in the urinary tract but elsewhere in the body. Acid. hydrochlor. dil. has sometimes an action in chronic ulcerative colitis so immediate that it is looked upon as specific. In 1923 I had two cases of B. coli infection of

the urinary tract that resisted all forms of local treatment, though there was nothing in the urinary tract to account for this persistence. An old practitioner told me at the time that he had occasionally derived much benefit from prescribing boric acid gr. xv t.d.s. This was given and the infection cleared up straightaway. I have prescribed it since with success, but this has only been occasional. It was difficult to account for this action, as the antiseptic power of acid. hydrochlor. dil. or boric acid in an acid urine is really negligible. It was possible that at the time of their administration the constitution was bordering on the acid state. Very little was required to produce it, and one of these happened to be the right drug. How they act is problematical. They are nerve tonics and possibly their action is analogous to that of ketones and aldehydes.

CHAPTER XVII

PROTEIN AND SERUM THERAPY

In this subject the utmost confusion prevails. Theory has outrun practice and is now given precedence in all the work. We are guided by views that are formed in the laboratory, where disease is induced in normal animals; whereas at the bedside of the patient, whilst importance must be attached to the disease it must always be remembered that before it could develop there must have been some preliminary modification of the constitution and of the resistance factor. It seems to be forgotten that bacterial disease is not necessarily fatal and that it does not always tend to become chronic. The majority of cases clear up if the patient is left alone, and the good results that follow therapy are not necessarily due to any antibodies that are injected. When some form of protein or one of its derivatives is injected, it stimulates in some way the formation of antibodies that not only prevent the onset of bacterial disease but also help to overcome it when present. This is possible only if the cells can react. But its action in the production of immunity is quite different from that in the curative treatment of disease.

The Production of Immunity

Here non-specific protein therapy is of little value and specific bodies are essential. A mild form of the disease is induced by vaccination. In prophylaxis against typhoid dead typhoid bacilli are used, whereas against tetanus and diphtheria the antitoxins are used. There is little doubt about the value of vaccination. The success in the War showed the value of typhoid inoculation and also of the

prophylactic use of antitetanic serum. If life over again were possible, most doctors would consent to be vaccinated; if there were an epidemic of typhoid or if there were another war, they would be inoculated: if they had a dirty wound, most would have an injection of antitetanic serum. Beyond this few would be prepared to go. The present method of inoculating wholesale against any disease that is prevalent is of doubtful value and is not free from danger. Even if it does raise the resistance factor for some particular disease, it may lower it for another. There is an appalling amount of ill-health to-day considering the good conditions under which people now live.

Curative Treatment

I will discuss only five methods—vaccines, antibactericidal sera, antitoxic sera, protein therapy, and protein shock.

Vaccines

When vaccines were introduced it was believed that they created opsonins that stimulated the leucocytes to engulf the bacteria or so modified the latter that they were more acceptable to the former. My experience with vaccines makes me doubt whether they have much specific action. Probably they act by some form of protein therapy.

Antibactericidal Sera

Whilst these may destroy bacteria *in vitro*, there is no proof that they have this function *in vivo*. It hardly seems likely, when the pathology of inflammation is considered, that they can have any action here.

Antitoxic Sera

Those for bacteria such as the bacilli of tetanus and diphtheria that form exotoxins are undoubtedly beneficial in the early stages. But when the disease is established the benefit is much diminished. Notwithstanding that diphtheria is now diagnosed at a much earlier stage, the

mortality is still very high and the morbidity very great. It must be remembered that before sera were introduced, these diseases were not always fatal. Whilst during the War everyone was quite certain of the value of tetanus antitoxin as a prophylactic, few were enthusiastic about its value when the disease was established. It is therefore strange to-day to find the enthusiasm for antistreptococcal (scarlatina) and antigas-gangrene sera, which are formed against bacteria whose toxins are by no means easy to liberate. Most of us can remember the enthusiasm when antistreptococcal serum was introduced and the excellent results claimed. Yet after a few years men were saying that they had as good results from normal horse serum and even when none was given. Claims were unfortunately put forward before either had been tried sufficiently long. Since the predisposing cause of bacterial disease is some constitutional error, obviously the value of any form of therapy depends not on theory based upon experiments on animals, but upon a long trial in the hands of competent clinicians. Only thus can it be decided whether the results are better than if the cases are left to good nursing and to Nature. I recently sought the opinion of men who had had much experience of these sera. They were not too enthusiastic, but used them because, when they gave them, they slept more soundly. This, after all, was not the point. It simply amounted to little more than that they were afraid that, if the case did badly, their conscience might prick them. It might be felt that, if they had been given, the patient would have lived. Though at times I prescribe antistreptococcal and antigas-gangrene sera, I have never been able to convince myself of their value. They do sometimes lead to a feeling of well-being; but, as the difficulty of displacing toxins already attached to cells is known, and since it is rarely possible to use them before the disease is established, it is difficult to understand how the antitoxin works. Eventually it will probably be found that their action depends upon some form of protein therapy.

Protein Therapy

I have always been impressed by the action of new tuberculin in genito-urinary tuberculosis, starting with small doses $\frac{1}{100,000}$ mgm. (T.R.) which are only slowly increased. Symptoms that have persisted for years clear up after a few injections. But at times they do no good or may even do harm. On the other hand, patients who have had it for months may ask for it to be continued. They feel better when it is being given. Tuberculin causes some reaction in the body which leads to restoration of the resistance factor to the tubercle bacilli. As a result the disease does not extend and that which is present clears up, unless there is a cavity that cannot contract. Should the tuberculin, however, lower the resistance factor, the disease goes ahead. It has to be kept in mind when it is being administered that not only is a disease being treated but also a patient who has to react.

In acute gonorrhœa the injection of sterilised milk may lead to the cessation of the discharge. This is more likely if there is a severe reaction. It seems to do good when there is marked congestion and the disease is going ahead. It is my impression that a course of vaccines or non-specific protein cuts short the disease by leading to the production of antibodies. Where the reaction is excessive, big doses are given; and where it is insufficient, small doses.

In an asthenic inflammation such as that due to B. coli, it seems that the disease is got under more quickly when a local reaction takes place. This I assume somehow stimulates the formation of antibodies. With this in view I give vaccines or non-specific protein in the early stages. But when the disease is established or has become chronic, the reactive powers of the tissues are paralysed. Little if anything happens now when either is injected.

Protein Shock

Some advocate the production of shock in protein treatment. But they do not differentiate between a severe

reaction and shock. When any protein is injected, there may be a severe general reaction, shown by a rise of temperature and malaise, a severe local reaction shown by an increase in the inflammation, or a severe reaction at the site of injection. A severe general reaction may do good, particularly if the disease is hyperacute. More often it seems to do harm. Such therapy is experimental, for it is not possible to predict what will happen. But protein shock is another matter. It is somewhat similar to anaphylaxis. I have seen only two cases which occurred in 1916 after an injection of antitetanic sera. The wounds healed in a remarkably short time. In other words, the shock shook up the system and suddenly restored the resistance factor. But it may lower the resistance factor and make the condition worse, or even prove fatal. Who, having seen anaphylaxis once, would ever attempt to produce it ? It is a terrifying experience. It bears little relation to the amount injected, and depends rather on some idiosyncrasy of the patient.

A condition corresponding to anaphylaxis is seen clinically when a gastric ulcer perforates. Now, when in certain people the resistance factor becomes lowered and chronic bacterial disease arises, a local inflammation is set up in the stomach. This constitutes the ulcer. They are said to have the ulcer diathesis, but rather it is a part of the bilious diathesis since it is so often associated with lesions of the gall-bladder, appendix, or colon. Operations for pyloric stenosis or hour-glass stomach give excellent results. But here surgery deals only with a mechanical obstruction, for the fibrosis means that the ulcer has already healed and the diathesis has been overcome. But when the operation is for an active ulcer, no matter how perfect the technique, the results are generally bad, for the diathesis is not touched. Consequently the ulcer recurs or breaks out elsewhere ; or some chronic inflammatory condition arises in another organ.

In perforated gastric ulcers the end results are generally

perfect. It is my practice to do as little as possible. Four stitches are placed over the ulcer, the free fluid mopped up, and the abdomen quickly closed. A gastro-enterostomy is not done. No prolonged after-treatment is carried out in hospital and it is rarely that I see my patients again. They have no trouble provided stenosis of the pylorus or an hour-glass contraction does not occur; and this is really due to excessive fibrosis, which is Nature's method of healing. It can be overcome by a gastro-enterostomy. Now the perforation means that the ulceration is very active; and though the surgery is really crude, the results are good unless excessive fibrosis occurs. Whereas in chronic gastric ulcer, notwithstanding perfect operative technique, the results are generally bad unless fibrosis is found at the operation. The shock of a perforated gastric ulcer is not due entirely to the pain caused by the irritating gastric fluid as it passes over the peritoneum, for it is not entirely relieved by big doses of morphia as is that due to severe colic. My impression is that at the time of the perforation the patient suffers from protein as well as ordinary shock. I think that the result is that the diathesis is suddenly overcome and that therefore the local inflammation subsides and the ulcer heals.

My view is that vaccines and sera act largely through the protein they contain. This acts in a non-specific way and stimulates the cells to form antibodies. This takes place only if the patient can react, which is not possible with all types of constitution and in all states of health. As this reaction is something definitely related to the constitution, it is unlikely that much guidance is going to be obtained from experiments on animals where the resistance factor is normal before the disease is created.

The indications for protein therapy in my practice are as follows:

1. In acute sthenic inflammation where the reaction is excessive locally or generally big doses are given. I regard the excessive reaction as an indication of the need for the production of antibodies.

2. In acute asthenic inflammation it does good if administered during the first few days before the reactive powers of the body are paralysed by the toxæmia. Once this occurs, protein therapy is valueless.

3. In a localised inflammation, such as gonorrhœa, protein therapy giving rise to a general reaction stirs up the formation of antibodies and should be given at the onset.

4. Where the local inflammation hangs fire small doses of protein do good.

CHAPTER XVIII

THE TREATMENT OF ACUTE INFLAMMATION

WHEN once an inflammation has begun and neither the organ nor the cause can be removed, it should be viewed as a contest between the patient and the bacteria. The practitioner finds himself much in the position of an active second in the boxing ring, who is definitely in favour of the patient. He knows what he wants accomplished. He may be able to give the most perfect advice. The difficulty so often is that the patient may not be able to respond because tissues cannot react. The difficulty may be only temporary and with a little coaxing the power may return. It is true that the patient does all the fighting, but the advice of the practitioner plays a vital part. Sir Anthony Bowlby and Sir Archibald Garrod in their rounds of the wards at St. Bartholomew's Hospital always laid great stress upon treating each patient as an individual and not just as a case of disease. In his recent book, *The Inborn Factors in Disease,* Sir Archibald has the following passage:

"The medical man trains himself or has been trained, by the example of those who taught him, to recognise the qualities and individual needs of his patients. He realises that each is an individual, and not merely a member of the human race. The task of the practitioner is far more than to apply the knowledge supplied to him from the laboratories; he does not merely ask himself or look to his text-books to tell him what is good for pneumonia, but calls upon his experience to guide him as to how he may best help the particular patient to come through his attack of pneumonia with the least possible damage."

Unless a practitioner grasps this he will never be able to practice medicine. Much of the art of medicine consists

in bringing ease and peace of mind to the patient. The practitioner must be extremely vigilant. He will point out to the patient that he realises what he has to go through and that he has his sympathy. Unfortunately it is necessary to build up the resistance. If he will but relax, take things quietly, and be content, the outlook will be so much the more favourable. The practitioner must be able to inspire the patient with faith and hope, for so long as these can be maintained, there is always some chance. They count for much even in bacterial diseases, and make a big difference to the prognosis. If the practitioner is only maintaining the confidence of the patient he is doing much, for so often it is the one thing that is needed. The nurse should get the patient to realise that he should make no effort. Everything should now be done for him. Those who have had pneumonia will appreciate this; and, if nursing did no more, it would justify itself in every way.

Though the inflammation has to run its course, the practitioner should have a definite plan for each case. If the reaction is not sufficiently great, it may be necessary to increase it. If it is too great, it may be necessary to decrease it. Each case must be dealt with in its own particular way. It is not possible to cut it short except by "shock" tactics. If at times these do good, they may also end in disaster. Those who adopt them are just trusting in luck. Throughout the illness the practitioner may be called upon to do nothing except hold a watching brief, but, however well the case is going, his vigilance must never be relaxed. He must be thinking of all possible complications that might arise and should take precautions to forestall them or to deal with them immediately they are detected.

A young and able practitioner told me recently that he regarded his attendance in a case of pneumonia as an absolute waste of time for himself, and a waste of money for the relatives. He misunderstood his rôle, for even where the pneumonia is a terminal event, as in the aged, his presence

can be a great comfort to the patient and relatives, and, even if his part is passive, he can do much to make the passage smooth. But even in a straightforward case where no active interference may be called for, he must always be on the alert. Anyone who has passed through an attack knows only too well that the practice of medicine by practitioner and nurse can be at such a time a great art. Probably there is no more difficult task than to stand by, do nothing, and yet convince the patient and his relatives that everything is for the best.

Though the attention of the practitioner is directed towards the inflamed organ, not only is it essential to nurse the constitution, but as far as possible the tissues must be protected from the action of the toxins. In this chapter only the main points in treatment are dealt with.

1. *The Maintenance of the Strength*

So long as the strength can be maintained there is a chance the disease will run its course before any vital organ is overcome, in which case the patient will get well. The room should not be too warm and should be aired regularly. So many sickrooms are so stuffy, particularly in winter. It is essential not to go to the other extreme and keep a patient, who was not too partial to fresh air when he was well, bathed in it when he is ill. At such a time it is better to keep to what he has been accustomed unless there is some definite contraindication. Draughts must be avoided. The bed should be so placed that the artificial light or the daylight is not in his eyes. Few if any visitors should be allowed. A sick man should not be called upon to make any effort.

When a man is up and about, every effort should be made to maintain the normal functions of the organs. This is generally easy so long as he has health. For one of the features of a healthy organ is adaptability, which means that it can respond with little extra effort to meet most of the conditions that arise. In bacterial disease the toxins affect all organs and adaptability is early impaired. Func-

tion is now possible only within narrow limits, and stimulation of organs is not necessarily good. For instance, the crisis in pneumonia is usually associated with profuse perspiration and the patient feels at ease. It is therefore assumed that during its course it is beneficial to set up perspiration, and liquor ammonii acetatis and blanket baths are advised. But perspiration occurs because the toxæmia has come to an end and the skin is able to function normally. It has never been proved that perspiration produced during the attack by stimulating the skin is beneficial. So often after it is over the patient feels weak. That produced by Dover's powder is in a different category, for some phylactic action comes in. The cells of all the organs correspond to the general condition of the patient. Hence there is disordered function in all organs, though some are no doubt affected more than others. At such a time the practitioner should put to himself the following questions :

1. If a certain function is possible by stimulating an organ, is it an advantage to obtain it ? May not the disordered function be of little consequence if the patient is at rest ?

2. May not any supposed advantage be more than offset by the indirect effect of treatment ? For instance, liquor ammonii acetatis and potassium citrate may upset the stomach and do harm.

Though many factors have to be considered during an illness, only the taking of food and of fluid, sleep, and the care of the bowels will be discussed.

(*a*) *The Taking of Food.* In a serious illness, such as typhoid or influenza, the patient eats little and much wasting follows. When recovery begins, the appetite improves and he eats more. As the wasting is attributed to want of food and the improvement to its being taken, attempts are often made to force it upon a patient who is ill. The loss of appetite is due to the toxæmia affecting the cells of the stomach, but the wasting is not due just to want of food. It is part of the disease. Improvement in appetite occurs because the patient is

getting well and all his organs are functioning better. Hence he desires more food. But this is secondary to the improvement in his general condition and is not the cause. A patient with an acute illness is often better with little or no food. This, however, does not apply to children. When acute appendicitis or cholecystitis is treated by the expectant method, no food is given for many days, and the reason is explained to the patient. Though the temperature is raised and an inflammatory process is going on, it is extraordinary how well the patient looks and what little wasting takes place, particularly if the patient has an equable temperament and does not worry. This is more noticeable with a sthenic than an asthenic inflammation. Anyone who lies quietly in bed, doing no mental or physical work, requires little food. In addition, when bacterial disease is present the cells of the stomach suffer from the toxæmia. If food is now forced, it probably will not be digested. The stomach is really in need of rest. Provided the patient takes plenty of glucose, it is of little importance whether he takes any other food for some days. It is better at this time to be guided by the appetite. When it is thought that sufficient food is not being taken, the appetite may be often stimulated by placing something that looks tasty in the room for him to see.

(*b*) *The Taking of Fluids.* If water has been withheld and there is dehydration, much improvement in the general state follows its administration, though this applies more to sthenic than to asthenic inflammation. Water is supposed to act by diluting the toxins, as a result of which the cells are less affected. It is hardly advisable to give the large amounts that some recommend. A writer recently stated that the minimum during the 24 hours should be 3,000 c.c. This amounts to five pints and is an extremely large amount for a healthy man. Even were it desirable to dilute the toxins to such an extent, a very great strain is being thrown upon the cardio-vascular system and the excretory organs at a time when they are affected by the toxæmia.

One of the failings in modern therapy is to think that because a certain amount does good, twice the amount will do twice as much good. Other factors, however, come into play and harm may really result. In an asthenic inflammation the withholding of fluids, or at any rate the giving of only those that the patient desires, is often beneficial in the early stages.

(*c*) *Sleep.* When the lungs are inflamed, it may at times be necessary not to allow the patient to sleep too deeply in case they become water-logged, but this does not apply when the inflammation is elsewhere. Some object to giving hypnotics on the grounds that the patient is not so alert during the day and is in consequence not so likely to take food. But since the phylactic property of morphia and opium were made known to me I feel that patients do better when they are given throughout the 24 hours. A little drowsiness in the long run seems to do little harm.[1] It may be that there is little to be gained by keeping the patient alert whilst the illness runs its course, and it is perhaps an advantage if his faculties are numbed. This certainly applies to those who are highly strung and who feel acutely. There is really little objection to giving hypnotics to produce good sound sleep. If the inflammation is sthenic, chloral is best, and paraldehyde if it is asthenic, though morphia and opium, given for their phylactic action, may be quite enough.[2]

(*d*) *The Care of the Bowels.* Normality is a standard fixed we know not how, and views that have been handed down are accepted as dogma. That the practice of maintaining the function of an organ, whatever the state of

[1] It is possible that the drowsiness at times due to the disease has been confused with that produced by hypnotics. The former is due to the action of the toxin on the cells of the brain or of some vital organ and is of serious significance.

[2] The practitioner should put to himself the following question: If hypnotics depress the faculties, may they not also depress those functions that are leading towards the restoration of the resistance factor and so impede recovery? It is my impression that when given in moderate doses they do not.

health, may at times do harm, may be illustrated by a reference to the bowels. Is it right to say that every man is better if his bowels are open each day? Even if this is true, should it be attempted during an illness? When a man is ill the toxins may affect function by acting upon the cells of the intestine. And the supposed disordered function may be quite suitable for the state in which the intestine now finds itself and the present state of the constitution.

Most healthy people have their bowels open once a day and are better for it. In the solicitors' room of a County Court, solicitors were discussing this point one morning. Some had had to rush to get there and in consequence had not been able to go to the lavatory. All were convinced that when the bowels were not open they suffered some discomfort and did not feel so fit. These men were healthy and well, and the discomfort could hardly be due to toxæmia. It must have been reflex and due to over-distension of the intestine and comparable to that which arises from the stomach if too big a meal is eaten quickly. If a man rests quietly in bed the discomfort disappears. On the other hand, there are quite healthy men who have the bowels open only every few days, especially as they get on in years. I saw a man, aged 92, for prostatic trouble, who told me that the bowels were open only when he took a pill, which was about every two weeks. This had been his practice as long as he could remember. Yet he was hale and hearty and for his years was mentally alert. Can it really be said that it would have been an advantage to him to have had his bowels open every day? If he were ill, what advantage would it be to upset what was normal to him? Such cases are more frequent than is often supposed. Paget has the following:

"Respecting constipation, I think its importance has been over-stated. Repeatedly, after operations for hernia, I have observed that no patients do better than those in whom, without any sign of abiding strangulation, the

bowels do not act for four, five, or even more days after the operation. And in cases of operation for fissured perineum and vesico-vaginal or recto-vaginal fistulæ, in which one used formerly more than now to keep the bowels at rest for many days, I never saw any general disturbance of the health due to the mere inaction of the bowels. It was, indeed, often remarkable that while the action of the bowels was arrested for ten, twelve, or more days, the patient passed through the ordinary process of recovery from the operation in exactly the same manner, with the same reaction, and the same gradual regaining of power, as those whose bowels act daily. From mere constipation therefore you need not anticipate any generally bad results. I do not recommend you to be altogether unmindful of it ; but you need not, as some do, consider it the matter of chiefest importance."

These words of Paget have always been kept in mind by me since a surgeon pointed out the disastrous effect that the giving of aperients had upon him after two operations in 1912, the first for a hernia and the second for an exostosis of the ear. He was thoroughly well purged the night before each operation and for the next six weeks the procedure was as follows : If the bowels were not open during the day, mist. senna co. was given the last thing at night. If this failed to act by the morning, an enema was given. If the bowels were not open the following day, the procedure was repeated. He felt convinced that if he were only left alone to adapt himself to the changed conditions of lying in bed, his bowels would have been open regularly as was the case when he was up and at work. He had little doubt that, if he had been called upon to face a serious illness, the treatment would have been harmful, as it made him ill and did not add to his fitness. He believed that the colitis from which he suffered later in life began at this time. I always advise those in charge of my wards not to be too drastic where the bowels are concerned, unless the patient has some discomfort or is showing signs of toxic absorption, which is very rare. I feel certain that this is to the advantage of the patient. Recently I removed the coccyx of a woman for

coccydynia and after the operation the bowels were not moved for twelve days. She was quite comfortable and looked quite healthy. No harm was done and the wound was given an excellent chance to heal.

Whilst the taking of an aperient by a healthy man may not have any ill-effect and may even be to his advantage, this need not necessarily apply to a man who is ill. For his intestine may be unable to function properly because its cells are affected by the toxæmia, and the drastic purgation, carried out to relieve the toxæmia during the treatment of an inflammation, may do much harm. The practitioner should be guided by bowel function in the past and consider that as normal for the patient. His confinement to bed is likely to produce some additional sluggishness for a couple of days. In addition the intestine is certain to be affected by the toxæmia and may be better for rest. My practice is to give an aperient at the start on the supposition that if it does little good, one at any rate will do no harm. I prefer small doses of calomel, gr. $\frac{1}{4}$ every half-hour until gr. 1 is given. The last thing at night half an ounce of a 20 per cent. solution of magnesium sulphate is given. If the bowels are not open during the following day an enema is given in the evening. From then on it is better to be guided largely by the condition of the patient and to give aperients only if there is a definite indication and not as a matter of form. The practitioner need be concerned only if the patient is uncomfortable or if the fæces are foul. The latter means that a certain amount of decomposition is going on, and intestinal lavage is probably advisable. One or two pints of 1 in 40,000 potassium permanganate may be run in each day. A wash out amounts to nothing more than a high enema, and the rigmarole performed to impress the patient and to make it appear scientific is better omitted. Should any disordered function persist, much improvement will often follow the taking of mild remedies, such as rhubarb and soda. Enemata are preferable to aperients, as they are less likely to irritate the intestine. But it is well at

times to consider whether the intestine may not know what is best for itself and be trying to carry it out.

Too thorough treatment undoubtedly does harm to a man who is ill. It is something of a shock that, when measures that are supposed to maintain the strength are abandoned because the case is hopeless, the patient proceeds to get well. Sometimes this corresponds with a crisis in the disease and is just a coincidence. More often it is the result of the patient being left alone for the first time since the inflammation began. As a result he is able to have proper rest.[1]

The practitioner should at times ask himself whether any advantage is really gained by having the patient disturbed. For instance, what is the good of having him bathed when he is very ill or having stimulants injected which have little if any effect. Some think the prick of a needle is a mere nothing. To test this they should try it on themselves. Let them watch the face of a sick man, particularly if the needle is blunt. This will reveal to them whether he is indifferent. We are not quite certain of the real value of much of our therapy. If there is any doubt, it is better to

[1] Those who feel so certain about the beneficial effect of their therapy would do well to read the article on "The Treatment of Carbuncle" by Sir James Paget. He points out the difficulty he had in deciding whether an extensive incision was beneficial or not. In order to prevent habitual self-satisfaction the surgeon should put to himself the question, "What would have happened if I had not made this incision?" He also refers to the value of watching patients who refuse to carry out advice, since then it is possible to observe the natural history of disease undisturbed by treatment. Paget was one of the greatest thinkers of surgery. He had both great practical experience and great clinical acumen. Yet he is always telling us how uncertain he is of the value of some of the measures he advises. Nature may do as much if she is left alone.

How much further on are we to-day? We certainly know much more about bacteria. Beyond that we have advanced so little. We haven't one test which can tell us whether the therapy that is applied is beneficial or not; nor one to tell us what the state of the patient will be to-morrow. We are still dependent upon experience and clinical acumen. There is nothing to suggest that our power to think has increased. It is unlikely that any evolution in powers of thought has occurred in a period of fifty years, as some are inclined to believe.

abandon it when the patient is ill. In this way he may be able to obtain that peace of mind of which he is in need.

In hospitals where nurses are being trained and so many patients are dealt with, a certain amount of routine is essential. But when the patient is ill, it should not be forgotten that harm may be done, since his organs cannot react. They are in much the same state as his general condition. At this time each case should be studied on its own. Those who have been ill in European countries pay their tribute to the nurses, whether German, Swiss, or British. Whilst they have been efficient they have always been humane and have considered the feelings of the patients. Sympathy seemed to be inherent in them. They had gained so much by having been trained at a time when attendance at the bedside of the patients was regarded as essential and when examinations played such a small rôle. I am a little doubtful if nowadays we are not witnessing some change now that education and a scientific training for nurses is being insisted upon and the passing of an examination is being stressed ; for sympathy and tact that are essential for a nurse cannot be acquired in this way. It is possible that efficiency is being sacrificed to officiousness. During an illness patients are still more dependent on good nursing than many think.

2. *The Protection of the Tissues*

If in a sthenic disease, such as scarlet fever, fluid and alkalis are withheld, nephritis is more common, for the toxins are more deadly if they are concentrated and the acid state persists. Therefore much water and big doses of alkalis are given. It is assumed that the cells of the organs are in this way protected. The four processes I use for this purpose are increased fluids, alkalis, glucose, and morphia. The first has already been dealt with.

(*a*) *Alkalis.* In most sthenic fevers there is a certain amount of acidosis. At this time alkalis have often a favourable effect, particularly as they have a dysthenic

action. But taken for a long period they are depressing, and if given in excessive doses too early, the infection is more likely to become chronic. Their administration in big doses is not devoid of danger and it is often better to overcome the acidosis by giving glucose and insulin. There is not the same indication for the use of alkalis in the asthenic fevers, apart from B. coli infections of the urinary tract. Potassium citrate is the drug usually recommended because it acts also as a diuretic, but it is unpalatable. It is doubtful if it has any greater value than potassium or sodium bicarbonate. It is the custom to prescribe equal amounts of sodium and potassium. But it is possible that more of the potassium salt should be given when the inflammation is sthenic and of the sodium salt when it is asthenic.

(*b*) *Glucose.* The value of glucose by mouth or rectum is now established in all bacterial diseases, and small doses of insulin often add to its value. It supports the carbohydrate metabolism. If in asthenic fevers 10 ounces of a 10 per cent. solution of glucose are injected intravenously followed by 10 units of insulin, the nervous prostration is overcome and the sense of well-being improves. In certain myocardial disorders glucose does good. When salvarsan is being given, the preliminary administration of glucose reduces the toxæmia and protects the cells of the liver. In toxæmic conditions I look upon glucose as protecting the cells of the liver, heart, and the nervous system.

(*c*) *Morphia and Opium.* In all sthenic bacterial diseases I give morphia gr. $\frac{1}{12}$ to $\frac{1}{8}$ every six hours from the beginning unless there is some definite contra-indication. It protects the nerve cells from the toxins. In an asthenic inflammation gr. 5 of Dover's powder is given every six hours through the illness. The subsequent depression and asthenia are then less marked. Hexamine also has some such action.

3. *The Withdrawal of Blood*

Years ago bleeding was resorted to in most inflammations. It was supposed to help to remove the putrid matter. Later

it was carried out whenever a fever was present, whether sthenic or asthenic. The amount of blood taken was sometimes so great that the patient fainted. So much harm followed that it was finally abandoned. It still has a definite if limited use, for it is one of the best dysthenic agents when applied in moderation to the right type of case, and it does much good. Whether it is carried out should depend not on the degree of fever, which seemed to be the indication in past years, but on the type of reaction to the inflammation. It is only of value when this is sthenic : it does harm when it is asthenic. Two or three ounces of blood or even less may be withdrawn from a vein with a platinum-iridium needle, and this may be repeated in 24 hours. It is often followed by an improvement in the general and local condition, particularly if the reaction is severe. In certain kidney diseases where the reaction locally or generally is sthenic, wet cupping undoubtedly does good. Though the amount of blood withdrawn is very small, it in some way relieves the congestion. It possibly acts as a counter-irritant. My experience of the use of leeches is limited, but they still seem to be indicated in the treatment of a sthenic inflammation.

4. *Rest to the Inflamed Organ*

There is no question of the value of this, particularly if the part is elevated, but in recent years it has been carried too far. The teaching has been that the inflamed part should be kept at rest until all evidence of disease has disappeared, but this has often been followed by development of marked adhesions. Everidge showed during the War the advantage of moving inflamed joints long before the suppuration had come to an end. Not only was more movement likely, but the inflammation subsided more quickly. This has since received the support of most surgeons. At Rollier's Clinic, Leysin, I noted that a certain amount of movement of tuberculous joints was allowed and even encouraged when the disease had ceased to be active. Though opposed

to the practice in this country, there was less wasting of the muscles and there was no tendency for the disease to flare up.

When epididymitis arose after a prostatectomy it was formerly my practice to try to keep the patient at rest in bed not only until all the inflammation had subsided, but until the swelling had largely disappeared. For I feared that it might flare up if he got up. But this was not always possible. Some patients insisted on getting up as soon as the temperature had become normal. Not only did they do better than those who were kept at rest, but the swelling disappeared more quickly.

In gonococcal arthritis if the joint is kept at rest too long, some degree of ankylosis is certain. If it is moved as soon as the acute stage is over, this is less likely and the inflammation subsides more quickly.

In chronic inflammation, and particularly if pus is present, many keep the patient in bed until the temperature has been normal for a week. If this treatment goes on for weeks, all the tissues throughout the body become very flabby. In chronic pyelitis I ignore small rises of temperature and allow the patient up and about much sooner than formerly. I am convinced that most of them do better for this. With the ketogenic diet exercise is encouraged. An occasional case now and again flares up, but this is the exception, and might have taken place had he remained in bed. The practitioner must be guided by what is best for the majority of his patients. When an inflammation is active or is extending, complete rest is essential, but better results are generally obtained if a certain amount of graduated movement is allowed as it tends to subside.

5. *The Application of Heat*

Dry heat has some action different from moist. Generally it is not so beneficial and tends to irritate the part. Fomentations wrung out of hot boric lotion are valuable, and the drier they are the hotter they can be applied. But even if they are immediately covered with jaconet and wool, they

retain their heat for less than half an hour, and the constant changing disturbs the part. This may be overcome to some extent by placing a hot-water bottle outside, but the pressure of this may be objectionable if the inflammation is acute or if the part is sensitive. A bath, particularly the sitz-bath, is of great value; but if the patient is left there for any length of time, it is a bigger strain upon the cardio-vascular system than is sometimes thought. Antiphlogistine is of great value, as it retains the heat for twelve hours. The skin should be first covered with a little oil and a piece of gauze spread over the antiphlogistine to prevent its sticking to the hairs. The heat from antiphlogistine is dry. If it is preferable to have it moist, a piece of lint should be wrung out of hot boric lotion, covered with jaconet, and the antiphlogistine then applied. Poultices have their use, but they are likely to make the skin soppy, and an aseptic field is very difficult to prepare if an operation becomes necessary. They are, however, very useful if economy has to be studied. Best of all is the electrical pad. Many excellent ones are now on the market and the amount of heat can be regulated. With them it is possible to maintain an even temperature right through the 24 hours.

It is not known how heat acts. It certainly leads to hyperæmia and an increased flow of serum and leucocytes. The relief of pain is immediate and must be due to some antispasmodic action. In addition, it seems to have some slight action as a counter-irritant. It is possible that the solution itself has some action. In a sthenic inflammation it is better to have the lint wrung out of a lotion containing boric acid or magnesium sulphate, which have some dysthenic action. In an asthenic inflammation it is better to sprinkle a few drops of turpentine or a little mustard over the surface. These have some eusthenic action.

6. *Passive Hyperæmia*

Bier has shown the value of this in an inflammation. It increases the stasis seen in the second stage. It does good

particularly early on when the inflammation is active and tends to spread; also immediately after an incision has been made. All that is needed is slight compression of the veins, to produce which a rubber bandage is applied over some lint. It should not compress the artery. The part should not become white: it should have a bluish discoloration and the pain should become less. In the case of an open wound such as that of a carbuncle or boil, passive hyperæmia may be produced by a suction glass. Only the gentlest suction is needed. The attempt to get considerable suction with the idea of removing the putrid material out of the inflamed area does harm. Some think that, when passive congestion is indicated, elevation of an inflamed part is not needed. This is not the case. There is some difference which as yet we are unable to appreciate between the passive congestion which results from Bier's treatment and that which arises when a limb is allowed to hang down; for the latter is harmful.

7. *Counter-irritation*

Irritants applied to the skin were much used in past years. They were supposed to withdraw putrid matter from the diseased organ. Two types were used: (*a*) *derivans* that drew it into the immediate neighbourhood; (*b*) *revulsiva* that led it into some remote part. It is possible, however, that their action was largely reflex, and was upon the local vasomotor system. Some think that the formation of pus locally sets up some form of protein therapy and so modifies the course of the disease. Herpes facialis, which is akin to a blister, has some action upon a case of pneumonia, for when it is marked the prognosis is better and the development of an empyema is less common. It is possible that it acts as a eusthenic counter-irritant. At times an incision acts as a dysthenic counter-irritant. Most surgeons can recall cases where the incision into an inflamed part revealed no pus and yet was followed by much improvement. The following case is an example:

A. J., aged 15, was admitted to the Cardiff Royal Infirmary, with acute pain in the left knee of four days' duration. All movements of the joint were painful, there was increased heat and a definite effusion. He was extremely tender over the neck of the fibula, but the radiogram showed no bony changes. There was no evidence of rheumatic fever and the onset was too acute for tuberculosis. Arthritis, probably due to the pneumococcus, was diagnosed. It was not possible to account for the tenderness over the fibula. He was treated with rest and passive congestion, but the swelling increased and the tenderness over the fibula was now intense. He was seen by me that afternoon. I decided that, if there was no improvement that evening, the fibula had better be explored. At 10 o'clock that night this was undertaken by Dr. J. R. E. James, the Registrar. There might have been slight œdema of the subcutaneous tissue, but no change in the bone was detected. The knee was aspirated and a small amount of sero-pus withdrawn. No organisms were detected and the culture was negative. The following day the pain disappeared, the temperature subsided, and in a few days he was able to move the knee freely. I can assume only that in some way this incision acted as a dysthenic counter-irritant.

A counter-irritant sometimes increases the reaction and sometimes decreases it. If some eusthenic action is desirable, it is best obtained by iodine, blistering, and dry cupping; if some dysthenic action is desirable, by an incision, wet cupping, or local bleeding by leeches.

8. *The Time for Incision*

No attempt is made here to deal with the question of excision as opposed to incision of an inflamed mass, such as arises in the case of appendicitis. That a timely incision into an inflamed mass may bring immediate relief and may lead to a cure does not need to be stressed. It is so evident in the practice of surgery. As a result surgeons taught that in an inflammation the sooner an incision was made at the point of tenderness, the better the outlook, as even if pus were not evacuated the escaping serum carried off the bacteria. But the danger of this soon became

apparent. It was really meddlesome surgery that served no useful purpose and was due to the desire of the surgeon to do something. On the other hand, a rapidly spreading erysipelas is rarely incised. Though the inflammation here is right under the eye and can easily be approached, few ever make an incision even when the disease is extending and death seems imminent. If the patient dies, no one suggests that life may have been saved by a timely incision. For not only may it aggravate the disease and lead to septicæmia, but the wounds take a long time to heal. Paget and Hutchinson, who were such careful observers, thought that in cases of both a carbuncle and boil it was better not to operate until they were ripe, when a small incision would be needed. Many who have had wide experience with early incisions and excisions have come round to this view.

Now that the purposive action of many of the phenomena of an inflammation have been realised, practitioners no longer aim at early incision of an inflammatory mass. Under rest, etc., this not infrequently completely subsides. Or if pus is formed that is not absorbed, a small incision has to be made and it quickly heals. On the other hand, if the inflamed products are under tension or if the pus is accumulating, it may lead to necrosis or to tracking, in which case much harm would result. In addition, at times pus aggravates the inflammation, which subsides when it is let out. But the making of an incision has its dangers; for when fresh tissues have to be opened up to approach the inflammatory mass, septic matter now passes over them and they become infected. This by itself may be sufficient to give rise to a virulent septicæmia. Also the incision may extend beyond the vascular area that is being established by the tissues in their attempt to limit the inflammation. If this takes place, the healthy tissues beyond are infected and the inflammation is liable to spread. The former is often seen when operating for osteomyelitis or for an abscess of some deep-lying organ, such as the prostate;

the latter, when operating for an appendix abscess after the third day. No matter what care the surgeon takes, at times it is not possible to avoid either. Surgeons have tried to prevent this by placing some oily emulsion such as bip over the tissues before the abscess is incised. Recently I have used the endothermy current. There is, I think, less tendency for the incised tissues to become inflamed, but it has not been used sufficiently long by me to be certain on this point. The time at which an incision should be made into an inflamed mass requires much judgment. This must be decided afresh for each case. If the pain persists or increases, it suggests tension ; so also does marked tenderness. These are about the only definite indications for urgent operation.

It must be kept in mind that the advantages to be gained by letting out pus are often more than counterbalanced by the risk of opening up fresh tissues. Rarely is there any urgency, and if there is any doubt it is often better to wait. Little harm can come from a delay of a few hours. No attention need be paid to those who say that life could have been saved had an incision been made a few hours previously. For when the inflammation is as virulent as this, the patient will die no matter what is done. There is no greater abuse of surgery than to operate on a patient who is dying. And unless pus is pointing under the skin there is always some danger when an inflammatory mass is incised.

Gas and oxygen or a local anæsthetic should be employed to produce anæsthesia whenever any toxæmia is present.

9. *The Treatment of the Wound*

When an incision is made there is usually at first some increase in the congestion and the œdema, though this is less if the endothermy current is used. At this stage the wound granulates better if it is left alone and not dressed each day. Whether this is due to the continued rest or to some action of the retained discharge is uncertain. In sthenic inflammation the gauze plugging may be left untouched for

a week or more. The continuous application of heat may be kept up by an electric pad : though at this time heat is not so necessary. The fear of a few years ago that the presence of pus would lead to repeated reinfection is unfounded. But when the discharge has a foul smell, it is probably better to irrigate with some very weak eusthenic drug. If pus accumulates and tends to track, a counter-opening may be advisable. Here again the danger that arises from incising fresh tissue must be given great consideration. Carrel's method of inserting small tubes and irrigating may obviate this. When it succeeds it is invaluable and the case clears up more quickly than if a counter-opening is made. In sthenic inflammation, irrigating with some dysthenic drug, such as weak flavine (1 in 4,000 in normal saline), does good. If sloughs form or the discharge is foul and much sero-pus is formed, then some eusthenic drug, such as Dakin's solution, should be applied. It is not used for its antiseptic action, which is not effective on the bacteria lying in the inflamed tissues. The lotion may act by the continuous application of heat, but more probably by some reaction that takes place with the tissues.

Pressure on the edges to get rid of discharge may help if done gently in the subacute or chronic stages, but never in the acute stages.

It has been said that since the inflammation starts to subside and the wound to heal when the slough comes away, it should be our aim to assist this. But a slough separates naturally because a layer of granulation tissue is being formed, and this takes place only as healing is making progress. Manipulation of a wound hinders rather than assists this. At one time it seemed to me that the various antisera might work when applied directly to a wound, but I have now come to the conclusion that they have no action.

10. *Inflammations of the Skin and Mucous Membranes*

Erysipelas is a surface inflammation, at first limited to the skin. As a certain amount of absorption normally

takes place through the skin, any action antiseptics have upon an inflammation would be most evident here. Even if one penetrated, it would be immediately removed by the local lymphatic circulation. This is scarcely realised by those who stress the penetrating power of their particular favourite. I nowadays apply 1 per cent. brilliant green or 1 in 1,000 flavine upon the supposition that some dysthenic action takes place, though it is difficult to be certain whether this is really the case. The direct application of certain antisera appealed to me very much, for they could be applied in great concentration for any length of time and some absorption would be expected. The method of bringing them in direct contact with the disease seemed preferable to the usual intravenous route. I could not convince myself that any beneficial action was not due to the natural process of recovery. In the Cardiff Royal Infirmary some time ago, many were enthusiastic for this procedure. Most of the staff have now abandoned it.

When a mucous membrane is inflamed, it is the bacteria in it and not the pus and the bacteria on the surface that are causing the trouble. Even if antiseptics have any penetration power, they would be immediately removed by the local circulation of lymph. To expect a weak antiseptic to act upon bacteria that are safely ensconced in a mucous membrane, merely because the solution can be placed in contact with it, is hardly less vapid than to expect a rocket to hit the moon because it flies off in its direction. If a drug has any action, it is probably due to some reaction that is set up with the tissues.

In the treatment of gonorrhœa limited to the anterior urethra weak potassium permanganate (1 in 10,000) has some action if the reaction is a little too great, and zinc permanganate (1 in 10,000) if it is not sufficient. Yet neither of these has any action upon a culture of the gonococci in a test tube that would not be obtained by plain water. In all probability their effect is due to some reaction with the tissues, the potassium salt having some dysthenic and

the zinc salt having some eusthenic power. For this reason I use the former in the hypersthenic and the latter in the hyposthenic. Silver nitrate, 1 in 10,000, will often clear up an infection of the bladder, of the pelvis of the kidney, or of the posterior urethra, so much so that at times its action appears specific. In this strength it has no antiseptic action. The effect must be due to some reaction with the mucous membrane. It may be necessary to use the solution hot, at other times quite cold; but if a feeling of mild burning is produced, an improvement is likely to take place. It is not advisable to go on increasing the strength under the impression that because good follows a slight reaction, much more will follow if it is severe. So often this does harm; and if benefit is not obtained from a strength of 1 in 2,000, some other drug should be tried. Many have thought that this action of silver nitrate is due to the silver itself, and various preparations have been substituted, such as the organic salts and the colloidal silver preparations. All do not act in the same way. It is this substitution of one salt of a metal for another that has given rise to so much wrong thinking in therapy. Whilst it is possible that they have a greater antiseptic power, they do not act in the same way upon the mucous membrane and consequently may not be nearly so effective. Just as it is found that some bacteria will affect only certain mucous membranes, so it is possible that each mucous membrane will react in a particular way only to certain drugs. For silver nitrate has little action upon an inflammation of the anterior urethra, and potassium and zinc permanganate upon inflammation of the bladder or posterior urethra. This may be dependent upon something connected with their development, for the bladder, posterior urethra, and pelvis of the kidney, which react with silver nitrate, are derived from the allantois, whereas the anterior urethra, which reacts with the permanganate salts, comes from the genital tubercle. Consequently it might at first be thought that certain drugs act with a mucous membrane derived from

the epiblastic and others with one derived from the hypoblastic layer. But many ophthalmic surgeons are quite definite that in gonococcal conjunctivitis silver nitrate is the drug of choice and that potassium permanganate has no action. Why a local reaction arises at one place and not at another is still a mystery.

11. *The Internal Use of Drugs*

If the writings of the great leaders of our profession during the last century are carefully read, it will be found that they had a certain faith in drugs in the treatment of inflammation. They claimed for them no specific action. They merely pointed out that at times their administration led to much benefit, though they were not prepared to lay down indications for their use. Paget, for instance, eulogised morphia in septicæmia, and he also advocated iron and potassium in what are now known to be streptococcal infections. Their views should be given serious consideration. For they were acute observers who studied most carefully the reaction of the constitution in therapy. When nowadays I am a little uncertain as to whether a drug has any action, if I can find some support in their writings I take it up with greater confidence.

At times iron salts have some action in a streptococcal infection. They were abandoned by our generation because they had little antiseptic action and we failed to understand how such a drug could act upon bacteria. It was also felt that if they had some action when the disease was established, they should have much more if given in the early stages. Again, salvarsan given intravenously (·3 grm.) or intramuscularly (·45 grm.) has at times an action in streptococcal and staphylococcal infections, but only if the reaction is definitely sthenic in its general and local manifestations. At times it acts upon a B. coli infection where there is a severe local reaction.[1] Again, if B. coli infections

[1] A preliminary course of protein therapy seems to increase the action of salvarsan, particularly if it has given rise to a severe general reaction.

of the urinary tract do not clear up straightaway, the intravenous injection of 10 c.c. of 0·4 per cent. mercurochrome often does good. Now, iron, arsenic, and mercury have no action upon the bacteria in the strength in which they are in the blood. In all probability they react with the constitution when it is in a certain stage and restore the resistance factor by some eusthenic or dysthenic power. As a result the tissues can become indifferent to the bacteria they contain and the disease clears up. It does not follow that these drugs will have this power at all stages. Rather they seem to act best when a definite reaction has already been established. If given earlier on, their action seems to be slight. Apparently the constitution is not then capable of responding to the full.

Unfortunately we have no method for estimating the constitution scientifically. We assess it clinically by the reaction that takes place when disease is present. Until a few years ago my therapy in bacterial diseases was based upon the assumption that for a particular bacteria a certain drug was needed and rational therapy would be possible only when bacteria could be further classified. In recent years I have come to the view that though the type of bacterium counts, so does the reaction of the patient. Because the principle underlying this is not known, this work is bound to be difficult. In clinical work, general impressions can only be reached at the end of a lifetime of work. My views, reached after a few years, are put forward in the hope that they may serve as slight guidance to those who feel inclined to take up this work. My contribution might have been much greater were it not that a few years ago, when my work seemed to be reaching completion, circumstances over which I had no control took away my opportunities, and a long illness interrupted my line of thought.

Though repeated references have been made to the reaction with the tissues that is at one time eusthenic and at another dysthenic, this is, after all, in the present light of our knowledge little more than a phrase. It is only putting

into words what are, or rather what are believed to be, observed phenomena. Unfortunately the underlying principle is as yet a mystery.[1]

[1] Once an inflammation has been overcome, it is not wise to assume that immediately it disappears health is regained. Generally this is brought about very slowly, as is very evident in the case of pneumonia. It applies, however, to all bacterial diseases. A little care exercised at this stage and a change of air will prevent many from becoming chronic. This subject has already been dealt with in Chapter XVI of *The Constitution and its Reaction in Health.*

CHAPTER XIX

THE TREATMENT OF CHRONIC INFLAMMATION

UNLESS there is some preceding pathological lesion in an organ or one has developed during the attack, an inflammation becomes chronic only if the impairment of the resistance factor persists. If the eusthenic impulses are now in the ascendant, as is seen so often in the hypersthenic, fibrosis follows. If the dysthenic impulses, as in the hyposthenic, ulceration follows. Here, as elsewhere, the object of the inflammation is to raise the resistance factor. When this is restored, the inflammation clears up and leads to no further trouble, provided no pathological condition is present that cannot be overcome by the healing powers of Nature—such as when a cavity is formed the walls of which cannot contract or come together, or when fibrosis takes place around the duct of a gland. A cure is then possible only by removal of the organ or dilatation of the orifice. This is shown so well when an infection of the urinary tract secondary to a stricture or an enlarged prostate clears up as soon as the obstruction is overcome. But even when the resistance factor is restored and the inflammation has disappeared, the former becomes impaired from slight causes, such as the season or weather, and especially by anything that leads to fatigue. At such a time the inflammation tends to recur. A chronic inflammation may give rise to :

1. Pain.
2. Discomfort due to disordered function.
3. Toxic absorption.

Each of these may affect the health. Whilst the symptoms to some extent depend on the size of the lesion and its site, they vary with the activity of the inflammation. There is

much controversy as to the amount of toxæmia to which a chronic inflammation can give rise. One school maintains that it can act as a focus of infection that undermines the health and gives rise to asthenia and to degenerative changes in other organs. Its followers give wonderful statistics of results from operations. But these results are not obtained by equally competent surgeons, though the technique for the removal of an organ that is chronically inflamed does not demand considerable skill. All surgeons have had cases where the removal of a chronically inflamed organ is followed by much improvement in the health; but in these cases it will generally be found that there is considerable disturbance of local function, that pus is present that cannot escape, or that the inflammation tends to recur in a subacute form. When relief follows removal of an organ that is chronically inflamed, something more than the mere relief of a toxæmia may come into play, for the persuasive powers of the surgeon cannot be discounted. In addition, the patient obtains peace of mind. For the organ may have given rise to slight pain and discomfort which constantly remind him of its presence. And he may worry that it may be the precursor of an acute attack or the indication of some serious disease, such as cancer.

Much of the confusion that exists in regard to the relief to be obtained from the removal of an organ that is chronically inflamed is due to our failure in past years to differentiate between chronic inflammation, chronic bacterial disease, and the functional disorders that are part of a neurosis. When a chronic inflammation has been present for some months, there is always fibrosis or ulceration which is evident to the naked eye. Chronic bacterial disease is described in the next chapter. The neurotic is in a separate category. There is here no question of any inflammation or bacterial activity. When his nervous system is deranged, disordered function is present in one or more organs, and this is frequently confused with inflammation. He believes that his ill-health results from this organ, and were it to be removed

he would regain his health. It is true that some relief may follow an operation. But too frequently the disorder recurs elsewhere and it is not long before he desires another operation. There is an occasional case where peace of mind seems permanent. But experience teaches us that this is relatively rare, and it is better not to operate. But a new type of patient has come to the front in recent years, owing to the efforts that are being made to educate the public on medical matters. As a result some are being frightened. They come to feel that, as there is nowadays so little risk in operating, it is better to have an organ removed rather than run the risk of disease. For instance, they are told that, if appendicitis is operated upon within the first twenty-four hours, no patient should die. They read in the newspaper of the death of prominent people from appendicitis. They begin to wonder whether it may not be advisable to have the appendix removed and soon convince themselves that they are the subjects of incipient disease. It is not long before they induce some surgeon to operate. After the operation they have the perfect health they had before. They feel better because they are relieved of something that worried them. Now these are the very people who talk so volubly in hotels and on golf courses about the great benefit derived from the operation. If attention is paid to them, a false impression may be obtained of the relief to be expected from operating for chronic inflammation.

When a practitioner is treating a case of chronic inflammation he should keep in mind that, if the resistance factor is restored, the trouble will clear up, provided no pathological lesion is present that Nature cannot heal. He therefore should put to himself the following questions :

1. How much is due to a local lesion that can be overcome by a minor operative procedure ? The clearing up of a pyelitis by the passage of a ureteric catheter is an example.

2. How much is due to some pathological lesion that can be overcome only by the removal of the organ ?

3. How much of the ill-health is due to persistence of the

impairment of the resistance factor that allowed the inflammation to become chronic ?

4. How much of the ill-health is set up by changes due to the chronic inflammation ?

Few cases require so much judgment in their treatment as chronic inflammation. Less help is received from recent advances than some think. There is no test that tells us anything about the state of the constitution or of the resistance factor. The practitioner has to rely on his clinical acumen. If only the right line of therapy can be found and the resistance factor restored, the patient will be saved much suffering. This is the aim of nursing, attention to the rules of health, and therapy. But it is wrong to prolong this treatment when the local condition is such that an operation is essential. On the other hand, if the operation is done before the resistance factor is restored, not only may the inflammation recur locally, but it may arise elsewhere, and the last state of the patient is worse than the first. This is seen in the surgery of gastric ulcer. When the persistence of symptoms is due to stenosis of the pylorus or an hour-glass constriction, a permanent cure follows gastro-enterostomy. Fibrosis means that the ulcer has healed and that the impairment of the resistance factor that led to its appearance has been overcome and surgery is not treating a local inflammation, but a mechanical obstruction that is secondary to it. When the ulceration is active, the end-results are poor whether a gastrectomy or gastro-enterostomy is done ; for the impairment of the resistance factor remains and ulceration persists or recurs elsewhere in the jejunum. The ulceration should be regarded here, as elsewhere, as the means by which the resistance factor is restored. It is therefore obvious that in the treatment of chronic inflammation operative surgery can play only a minor rôle, and therefore conservative treatment should be given a good trial at the beginning.

The possibility of a complication supervening has to be faced. For should this happen, the practitioner may be

blamed. Each organ has its own particular feature. The perforation of a gastric ulcer is an example. Perforation, however, is rare whilst treatment is in progress, and it sometimes follows gastro-enterostomy. The possibility of an acute flare-up or of the onset of malignant disease generally receives special consideration.

Is a Chronic Inflammation likely to become Acute?

Whilst it cannot be said that an acute inflammation that may be a menace to life will not arise, it is relatively rare. An acute inflammation generally arises in an organ that was previously normal. It is true that, as life goes on or should an illness develop, the chronic inflammation may become more active and more extensive. On the other hand, to counterbalance this it should be realised that the inflammation may clear up.

Is the Inflammation likely to become Malignant?

It is necessary to differentiate between chronic inflammation and irritation such as may arise from a jagged tooth, for whilst the latter undoubtedly predisposes to malignant disease, the former does not. When chronic inflammation and malignant disease are associated, it is probably no more than a coincidence; for both are very common and consequently at times occur together. The removal of an organ for chronic inflammation has been practised to an appreciable extent only in recent years. If cancer were caused by inflammation, it would have been extremely prevalent in the past and the relation between the two would have been established. Attempts to do so nowadays are based upon observations of those who are out to support some type of operation and cannot be relied upon. For instance, some say that cholecystectomy should be performed for gall-stones, as early cancer is so often present. But the operative treatment of gall-stones was rare fifty years ago and cholecystectomy is much more recent. If cancer

of the gall-bladder is so often associated with gall-stones, it should have been a very common disease years ago, but it was then rarer that it is now. Some claim that pre-cancerous changes are often present with a chronic inflammation ; though quite what is meant is uncertain. When the difficulty of diagnosis between early cancer and chronic inflammation is borne in mind, but little attention need be paid to those who claim to be able to distinguish a pre-cancerous condition. The relation between cancer and a chronic inflammation is so remote that it need be given only slight consideration when the question of a conservative treatment arises.

Treatment

The patient should be told at an early stage that once an organ has become inflamed some discomfort and pain may return when the health becomes impaired. This should not be regarded as a recurrence of the inflammation. For the mucous membrane responds to slight atmospheric changes for many months, particularly if fibrous tissue has been formed. A patient is not ill one day and well the next. Before good health is regained the period of convalescence is longer than many think. During this time some recurrence of the symptoms is certain. If he will but take things quietly and pay attention to the mode of living, they clear up. Anything that improves the health undoubtedly influences the local lesion. It must be explained to him that any ill-health present is not necessarily due to the inflammation becoming active. It is more likely to be due to some vulnerability of the constitution that persists for months after an illness clears up. It is this that causes the inflammation to flare up. The regaining of health is often only a question of time, and a holiday in the mountains or by the sea works wonders.

Warmth to the part is essential. Cold air should not be allowed to play on the surface, even when the weather is warm. For abdominal inflammations, the wearing of the

old-fashioned cholera belt night and day does good. The bedroom should be warm; it is better to use flannelette sheets for many months and to have a hot-water bottle placed in the bed. If the pain returns at night, pressure from a hot-water bottle often brings relief. One should be handy by the side of the bed. It is a great mistake for a patient to think of hardening himself at this time. This is more likely to do harm than good. Local massage does help. Slight friction of the skin may be sufficient though deeper kneading may be necessary.

Counter-irritants

Counter-irritation may give much relief. It must be applied to a part in intimate nervous connection with the inflamed part. A surgeon who for years had a cholecystitis tells me that the application of a blister to the right side of the epigastrium, or to the tip of the right shoulder, brought much relief when the pain was intolerable. At first he attributed the relief to the production of a surface pain, for it is well established that when two pains are present only the more intense is felt, and for some reason a surface pain is always more tolerable than a deep one from an internal viscus. But later he came to the conclusion that the relief was greater than could be so explained and was due to some reflex vaso-motor changes set up in the gall-bladder, which seemed to have a favourable influence on the inflammation. Counter-irritation of all degrees is obtainable from that of iodine to the actual cautery. Older practitioners to whom I have spoken are positive about its value in the occasional case, and cases where a seton or an issue brought much relief are recorded. But formerly there was not too much care in the selection of the case, for exact diagnosis was difficult. Counter-irritation was applied indiscriminately and was abandoned because it was thought it acted only by suggestion. But the possible reflex action upon an inflammation should be kept in mind, for a eusthenic or dysthenic effect can be maintained in this way.

The Use of Drugs

Tinc. opii in small doses, minim 1 t.d.s., will often give relief. If there is a tendency to fibrosis, some dysthenic drug, such as arsenic, does good ; and if there is a tendency to ulceration, some eusthenic drug, such as mercury. They do not act by a direct attack upon the diseased area, but by modifying the constitution. It is perhaps better to give small doses over a long period, though at times myosalvarsan intramuscularly or mercurochrome intravenously has an action that is not produced by small doses.

The Ketogenic Diet

The value of this in chronic coli infections is established. With it there seems little doubt that when pathological changes are present in an organ such as the kidney, they clear up provided that they are not too extensive, that no stone is present, and that there is no obstruction to the outflow of urine. It is not necessary to give the extreme diet advised by some in order to get a high acidity of the urine. This leads to nausea, undermines the health, and so does harm. All that is necessary is to modify the constitution, as a result of which the resistance factor becomes changed and the infection overcome. When the health is in a certain state slight measures are quite effective in producing the acid state. Boric acid in small doses may clear up a coli infection of the urinary tract, and acid. hydrochlor. dil. at times acts like magic in ulcerative colitis. It seems rather that they have to be given at a particular time, for they do not act so well if given too early.

Operative Treatment

It is not possible here to outline the indications for this, for they are special for each organ and each case must be decided on its own. The most an operation can do is to overcome or remove a local disorder. It does not by itself give a man a constitution nor does it overcome the impairment of the resistance factor that allowed the inflammation

to arise and to persist. It is wrong for surgeons to teach that the future of the treatment of chronic inflammation is in the earlier application of the knife. There is a time when an operation is indicated, but this is late in the disease, when the resistance factor has been restored and a local pathological lesion that does not clear up is present. If an operation is performed too early, the disease is likely to recur. I am convinced that the majority of the cases that are subjected to operation would be as well off if they had been left alone. The operating surgeon is inclined to talk about the evils that would have arisen had conservative treatment been followed. Practitioners who see so many of these cases over a number of years know how rarely complications are seen except as terminal events.

Many of our therapeutic measures will be more successful when it is realised that they act upon the constitution and only indirectly upon the disease. They have to be applied to the right type of patient at the right time. Once this is grasped, those who are chemically minded may come to our aid. When Erhlich discovered salvarsan, he based much of his work upon the supposition that drugs of a certain composition, being soluble in bacteria, would destroy them. Whilst their action may be partly due to this, some is due to indirect effect upon the tissues. Now the reaction that takes place when bacterial disease develops depends partly upon the constitution and partly upon the type of bacteria. In Chapter VII it was shown that with gram-positive bacteria a sthenic reaction is the more likely and with gram-negative an asthenic reaction. As the staining power of bacteria depends upon their composition, so may the reaction depend upon the production of some chemical that is formed as they grow. Possibly some drugs act by countering this. When watching a chronic inflammation that refuses to heal, I always recall the extensive syphilitic lesions that resisted all forms of therapy. Their removal by operation seemed to be indicated. It was useless doing it, for the disease recurred locally or broke out elsewhere. The gumma was

really an effort on the part of Nature to restore the resistance factor. Then came salvarsan. What had previously taken months was accomplished in a night. It is surely not inconceivable to anticipate the introduction of some such drug for non-specific chronic inflammation such as gastric ulcer. Could we but know what takes place when a gumma clears up after salvarsan is given ! The same thing is also seen in chronic inflammation under certain forms of therapy. Instances have been given in Chapter III. Our trouble is that we do not know what takes place, though we are fairly certain it is not a direct attack upon the bacteria. Could we but grasp the principle, the way might be clear for a great advance and we should be able to apply the right treatment to the right patient at the right time.

CHAPTER XX

THE TREATMENT OF CHRONIC BACTERIAL DISEASE

THE chronic bacterial disease discussed here is not that previously described in Chapter XI which arises as a terminal event, but that which at times is spoken of as a subinfection or a diathesis and which has been described in Chapter X. There is no clear-cut line between it and chronic inflammation. So many of the cases can fall into either class. In a chronic inflammation there is a definite reaction leading to fibrosis, ulceration, or the formation of pus. Until its onset the health was generally good and the constitution seemed normal. The impairment of the resistance factor can be looked upon as something temporary. If it is overcome and the health restored, recurrence of the inflammation is not expected unless there is some definite exciting cause. If chronic bacterial disease has existed for many years, the characteristic feature is the absence of a local reaction. This is well seen when it affects the gall-bladder. For though gall-stones may be present, there is rarely any marked fibrosis or ulceration and pus is generally absent. In such cases the ease with which the resistance factor is impaired is the conspicuous feature. For many years there may have been slight impairment of the health which at first was easily restored. Then comes the infection. Its onset may have been connected with some period of strain, such as puberty. Eventually a time comes when the infection appears after the slightest mental or physical strain or even a change of weather. Now infection can be avoided only by living most carefully. If the slightest risk is taken the infection will recur. The ease with which this takes place constitutes the diathesis.

Here the constitution is primarily at fault. When it is affected, the resistance factor becomes impaired. As a result bacteria invade the mucous membranes. The infection now leads to a mild type of inflammation, the object of which, like that of inflammatory processes in general, is probably to raise the resistance factor. At first many mucous membranes are affected, but there comes a time when only one is picked out, the so-called weak organ for this patient.

No good will be attained by removing this organ, for the defect in the constitution that led to the impairment of the resistance factor is not touched, and no operation of itself can improve the constitution. Rather by leading to asthenia it may do harm. Removal of the affected organ, so often the desire of the patient, can do no good apart from the faith and hope it inspires. It may end in disaster, for the infection is certain to recur. This may take place in some vital organ, or a chronic bacillæmia with a worse state of health may arise. Such a history was common in years gone by, when surgeons thought they could overcome asthenia and restore health by removing a local infection.

Many of these patients are temperamental, emotional, and highly strung. At one time they were of an extremely fine type, with any amount of energy, though this may not be so obvious when ill-health is present. But some weakness in the nervous system when they are subjected to any mental or physical strain would be evident to a close observer. Possibly the primary defect rests in the central nervous system. For this system seems to be the basis of the constitution, and in this book some evidence is brought forward to indicate that the power of the tissues to withstand infection by bacteria and to overcome it is in some way connected with the central nervous system.

Each case should be viewed from the following aspects :

1. The maintenance of the tone of the central nervous system.
2. The restoration of the resistance factor.
3. The local bacterial disease.

The Local Disease

The patient must be told that this is not the cause of his ill-health but results from it, and should be regarded by him as a barometer that indicates its state. An operation is to be avoided, even if a local lesion, such as gall-stones, is detected. The great chances are that the infection will recur. For by setting up a mild form of inflammation Nature attempts to restore the resistance factor. The local treatment referred to in the last chapter may be tried, but does no more than relieve the symptoms. It does not in any way modify the impairment of the resistance factor that allows the infection to develop.

The Treatment of the Resistance Factor

In these cases certain drugs often do good, if taken in small doses over a long period. If the right drug can only be found, it is possible to give much relief. Mercury should be administered at the beginning to the hyposthenic and arsenic to the hypersthenic; sometimes a combination is the best. We do not know how they act. They certainly have no antiseptic action. They are described as "alteratives," which means that they alter the constitution and maintain the resistance factor. But giving a name does not explain an action. Hutchinson's teaching, that it is not the quantity of the drug but the effect on the organism that really counts, should be kept in mind. Take mercury as an example. It probably does not act by anything that it does directly as by some change that it sets up in the cells. If no response is forthcoming with a small dose, this may be due to the cells being unable to respond, and a larger dose may do harm, if over-stimulation takes place. Therefore gr. $\frac{1}{20}$ of hydrarg. cum crete three times a day is enough at first, and the dose should be only slowly increased. Rarely is more than gr. $\frac{1}{6}$ needed. Whether it should be continued throughout the year or given only in certain seasons is problematical.

The Treatment of the Central Nervous System

In past years no direct treatment of the nervous system has been possible ; for it was not realised that before drugs could act upon the nerve cells, they must be soluble in the lipoid membrane. If chemists would but give their attention to the production of aldehydes and ketones that act in this way, the building up of the nerve cells may be possible.[1]

Magnesium in small doses seems to have some action. Much importance should be paid to the way of life, and attention to little details counts much, as adaptability is definitely impaired. These patients are easily upset by slight causes such as exposure to the sun and exercise that ordinarily do not give rise to any trouble. No doubt much would have been prevented had good advice been obtainable round about puberty. For puberty is not just a matter of sex, as some suppose. A tremendous change now begins in the constitution and the nervous system, and any small weaknesses are revealed. The children of those who are known to suffer should receive special consideration. In the advice he is able to give, the practitioner holds a privileged position. He should rely, however, on his powers of observation, on his knowledge of human nature, and on his clinical acumen. For where the individual is concerned the advances of science and deductions from animals give little help.

The hypersthenic finds it difficult to relax, for he has too much vitality. Whilst he is all the better for playing those games that test the wind, he should be encouraged to direct part of his activity into the quiet ways of life, and hobbies that lead to this should be cultivated. The hyposthenic never has any excess of vitality. Whilst he is good at games round about 14, his want of stamina is likely to become evident at puberty. From then onward he is never quite the same. Not only does he fall away at games, but a liability to some infection develops. It is questionable whether excessive exercise and the playing of strenuous games should again be undertaken by such a one. At any

[1] T. E. Hammond, *The Constitution and its Reaction in Health*, p. 145.

rate round about puberty they should be abandoned. It is much better to point out to him that his health is not really robust and that those things that men can ordinarily do without much effort really take too much out of him and are undermining his constitution. The trouble is that often he is most ambitious about his games. Though it is unlikely that youth will ever appreciate advice that seems opposed to its views, there may come a time in the quiet of the evening—and this is particularly likely when the health is not too good—that its value will come home. Some of us wonder to-day whether this excessive culture of physique and of health is not really undermining the nervous system. Probably never in the history of this country have chronic bacterial diseases been so rampant, and probably never have the conditions of living been better.[1]

Treatment by Operation

Whilst the performance of an operation for chronic inflammation may yield a brilliant result if done for a certain pathological condition when the resistance factor is restored,

[1] A medical man relates his experience to me : At the age of 11 he was operated upon for tuberculous glands. He quickly got over this and devoted himself to work and games. At 14 he was a star turn at Rugby and boxing. At puberty there appeared a slight crack in his constitution, after which his stamina was never the same. This he attributed to colds and some gastro-intestinal disturbance that arose, which he tried to overcome by cold baths, keeping the windows open, etc. His father, who had perfect physique and health, warned him that as he had been unable to carry out these himself, they were more likely to do the son harm. Though at 21 the latter was again able to play in first-class company, looking back on his life he is quite certain that the playing of strenuous games and the attempt to harden himself to overcome the infection did him much harm. He should never have gone on with them. Much of the ill-health that he later suffered from came about in this way. Though he was constantly in the hands of doctors from the age of 11, he cannot recall one who advised the giving up of games. They certainly advised him not to do too much work, but they rather encouraged the playing of games. How much more would he not have suffered in these days ! If the practitioner will only have a chat with parents and observe them carefully, he will often get valuable information about the children. There is no biochemical test or any instrument that gives him the slightest help when studying the constitution.

in the case of chronic bacterial disease it never does any good and may be disastrous. The surgeon must make up his mind on this point. It has been proved beyond dispute that, though there may be a little temporary improvement due to the faith and hope inspired, the last state of the patient is worse than the first. It is useless to talk of the preventive aspect of the operation, since complications are not likely. In chronic bacterial disease they so rarely occur. Every operation is a bigger strain upon the nervous system than many realise, and asthenia may last for 6 to 12 months. It takes away from the patient that vitality of which he is so much in need and which, owing to the state of his health, he may never regain. It is just as rational to attempt to cure gout by removing a uratic deposit as it is to try to cure a patient of chronic bacterial disease by removing the affected organ. This should be done only if there is an acute flare up and life is at stake.

CHAPTER XXI

CONCLUSION

ANYONE who reads this book will be struck by its incompleteness, for so many things are omitted and others are just touched upon. No attempt is made to give a complete account and only certain principles bearing on treatment are outlined. The points dealt with are those that I have pondered over at the bedside of my patients during the last few years. My own fragmentary knowledge is relied upon and little reference is made to the work of others. Statements are made dogmatically for the sake of clearness. In clinical medicine the exceptions to any rules laid down are too obvious, but to mention them only leads to confusion. Though treatment seems simplified by leaving so much to Nature and by applying eusthenic and dysthenic measures only when they are indicated, it is by no means easy to know what to do when it comes to a particular patient. For not only has the state of the bacterial disease to be considered, but also the constitution of the patient and any idiosyncrasy he may have.[1]

The difficulty is that the latter may only be revealed as the disease progresses. Even if age alone is considered, it is obvious that treatment at one stage of life cannot be exactly the same as at another, for the power of the tissues to respond generally diminishes as the years go by. Paget pointed this out to us. He says :

[1] Paget says, *Selected Essays and Addresses*, p. 70 :

" This is not a mere question of doctrinal pathology. It is among the first necessities for success in practice that, in the several phenomena of a disease observed in any patient, you should be able to estimate what belongs to the disease and what to the man. A farmer may as well expect success if he sows his fields without regard to their soils or to the weeds that may ' of themselves ' come up in them, as one of us may expect it if we treat diseases without exactly studying the constitutions of those in whom they occur."

" Respecting the treatment of senile scrofula little need be said. I believe that whatever is useful for scrofula in the young, is not indeed useless, but less useful in the old. As age advances, all medicines that act by increasing the activity of organic processes become, as it seems, less potent : and so iron and cod-liver oil and iodine have comparatively little influence. Even high mountain air and sea air become, as age advances, less invigorating, and the more so the more old age is attended with infirmities that hinder active exercise. As age advances rest and warmth and good food become constantly more important than any kind of air."

And what applies to scrofula applies also to bacterial diseases.

The medical profession is supposed to be slow in bringing to the bedside of the patient the great advances of medical research. The difficulties with which it is faced are not always realised. For the practice of medicine is an art based upon an inexact science ; and, though a knowledge of medicine is easily acquired, its practical application is often difficult. In my practice I am still following methods that were taught me as a student and which were no doubt carried on years before. Though the great claims of research workers are known to me and most of the writings are followed, it is with difficulty that I grasp what they talk about. So little seems to have any practical bearing. I point out to my house-surgeons and dressers how much it is to be regretted that, with all the suffering I am called upon to treat, I can discover in recent work so little that is of value at the bedside of the patient. They are at a stage in life when the brain is receptive and open to new ideas, and, if they could come and tell me where it is that I fail to make use of these great claims of science, no one would be more grateful. So far none has returned. It is probable that when they are faced with the problem of bringing help to a particular patient, they find themselves lost. It is so easy to talk in the abstract or to pile up data, as is now the tendency in research. It is another matter when the welfare of a patient, who puts his trust in one, is at stake.

There must be few of our profession who have not stood at the bedside of one, passing out from some bacterial disease with young ones dependent on him, who would not at times have given almost all they possessed if the remedy could be produced that would put the patient right. It is so easy to talk of the reaction of the constitution in the abstract. It is a different problem at the bedside. There is not one test that really helps the practitioner to know what remedy to give. If one is tried and a reaction is obtained that is not desired, it may do considerable harm, and may be the very thing that will prevent the patient from recovering.

A patient with a bacterial disease is a sick man, and something that may not impair the health of an animal or a healthy man may do him serious harm and may cripple him for life. If this happens, he suffers; it is not the practitioner who has to linger on in life with his vitality impaired. That is the reason why the practitioner is reluctant to try on his patients remedies he knows he would not try on himself were he ill. He is not willing to experiment with a sick man. His life is too precious for that. Scientists forget that they are working on animals, in whom disease is artificially induced. Before it started, the constitution was sound and the resistance factor was adequate. When this is the case, recovery takes place as soon as the exciting cause ceases to act. If scientists want a disordered constitution on which to experiment, why do they not go to sick animals? There are any number of these; and after all, if things go wrong with an animal and the vitality is lost, it can be put to death. This is not possible with a sick man. When scientists can put right animals in whom disease has appeared as in man we know not why, the medical profession will listen more eagerly to their claim; for they will be trying to come to grip with that constitutional factor that allows disease to develop. When this can be restored, the disease will clear up unless very serious pathological changes have supervened.

It is not so easy as some think to decide whether any form of therapy works. If a patient improves, this may be due to Nature, or to the delayed action of some measure that was discontinued. My house-surgeons are more certain than I am about the benefit to be obtained from many forms of therapy. They think that if they were not employed the disease would necessarily extend. But most bacterial diseases are self-limiting and tend to subside if Nature is left alone. There are few of us who have not at some time or other taken up something with enthusiasm believing it is the thing, only to abandon it later when we realise that we have attributed to therapy what was due to Nature. It is useless to reason from a few spectacular cases. When only a few of a series get well, the underlying principle has not been grasped. Those who read the works of Paget and Hutchinson will realise the difficulty they had in coming to a conclusion, and they were among the greatest thinkers that surgery has known. So far as bacterial disease is concerned we are just in the same position as they were when they looked at the carbuncle, with the exception that we can now name the bacteria giving rise to it. There is not a single test that tells us what the condition of the patient is or what it will be in a few days' time, and what line of therapy we shall adopt or whether improvement or harm will follow the administration of a remedy. We still have to rely on our experience and clinical acumen. When a good result follows therapy, the careful practitioner puts to himself the following question: Might not this have occurred if I had held my hand? When a bad result follows: Might not this patient have been better if nothing had been done? These questions are not always easy to answer when the experience is great. For experience teaches us to respect Nature. She does so much if she is given a chance.

In 1913 sensitised vaccines were the rage because a house-surgeon who was dying from a cellulitis of the neck made a spectacular recovery after their administration. But though they were subsequently given to many hundreds of

patients they benefited very few. At the West London Hospital in 1913, a woman was admitted with advanced rheumatoid arthritis of the hands and feet. She had severe pyorrhœa, and after her teeth were extracted she recovered in an extraordinary way. Since then I have seen teeth removed for many conditions, but more harm than good has followed. A few years ago I had done a few hundred appendicectomies without a death and then had ten in a couple of weeks. This caused me to modify my line of treatment and so far with great success. But am I now on the right track or is it that a little luck is with me, as was the case years ago? Time alone can give the answer. Assuming that I had changed my views when I started that series of a few hundred I would have been justified in thinking I was working on right lines. Nor is help always to be gained from a comparison with statistics published years ago. For at that time often only the more serious cases were seen by the practitioner, and the milder ones were treated by remedies in the home.

It is easy to attribute an improvement to therapy that is entirely due to the reaction of the patient or to some change in the nature of disease. For diseases change from one age to another. Scarlet fever thirty years ago was very fatal and associated with much morbidity. In recent years it has become quite mild without any change in therapy. What might have been attributed, had some specific remedy been introduced?

This June in the Cardiff Royal Infirmary lay an elderly obese patient from whom I had removed a kidney for a pyonephrosis two weeks before. The wound was still discharging but was hanging fire. Some eusthenic drug, such as eusol, seemed indicated. On my round a few days later there was a marked improvement. Naturally I was inclined to regard it as an indication that my views on therapy were now right, until I found I had forgotten to order the treatment. The improvement was due to a natural reaction on the part of the patient.

The same month there was a case of erysipelas in the isolation ward. No improvement had followed salvarsan intramuscularly and the local application of brilliant green. The patient was drowsy and was going down-hill. It seemed that he would die. As he was a young man and a reaction still possible, a drastic revision of the treatment was decided upon and morphia and antitoxic sera were ordered. When I saw him three days later there was a marked improvement in both the general and local conditions which it was only right to attribute to the sera. But the sister was quite definite that the patient had begun to perspire before she went off duty, and she had noticed that there was an improvement in the general condition. It was not until later that evening that sera was given. Here a change in treatment synchronised with a crisis. Whilst in these two cases it was easy to reach a decision, this is not always so.

The Achievement of Science

We are brought up in an age that believes that we can accomplish anything if only we will it. But men forget that the achievements of Science are entirely materialistic. This was seen so well during the War when the instruments and methods that were devised for destroying men reached perfection and the killing of men became an art indeed. In recent years she has given us numerous drugs for diminishing vitality, but of these we had plenty, and none is better than morphia or opium. But Science has taught us nothing about life. She has only described certain phenomena that are associated with its activity, and she certainly has not created any form of life. She has not given one drug that can directly increase vitality. Nor has she given us an instrument to measure the different grades of vitality in man. When I ponder over this question of life and vitality the achievements of Science seem so puny and small. What is the advantage of being able to measure the size of electrons and the speed of light and to send messages round the globe when we are unable to measure vitality or to

give man anything to help him in his fight? Since the days when bacteria were first discovered research workers have shown us how many varieties there are and have also revealed to us certain phenomena associated with their activity. But they have introduced singularly little that can impede the activity of bacteria when they grow in the body. This failure of research is well shown in the case of the tubercle bacilli, for it is fifty years since it was discovered by Koch. Though this has helped us very much in the diagnosis of tuberculosis and in the elucidation of certain points connected with its pathology, it has given us no help in treatment. This remains much the same as fifty years ago, apart from a few operations that have been introduced.

As the practitioner stands by the bedside of his patient he is only too well aware that, compared with the great advances that have been made in the diagnosis of disease and in the investigation of disordered function, the relief he is able to bring his patients by the adoption of modern scientific methods is extremely small. Much of our failure to-day is no doubt due to the fact that research workers have left the bedside of the patient and are now content to work in laboratories. As a result they concentrate on the discovery of causes and the elucidation of phenomena, and the practical bearing of medicine, namely the cure of the patient, is at times forgotten.

The Bearing of Operative Surgery upon Bacterial Disease

There can be no question of the value of a timely operation in bacterial disease. This is so evident in acute appendicitis. But a mortality of 3 per cent. is still too high for the treatment of inflammation. It is useless to attribute this to the inability of the practitioner to make an early diagnosis or to the failure of the patient to apply for treatment as soon as he feels ill. A study of the daily press shows that death occurs too often among those favourably placed who from the start will have the best medical advice. Practitioners

tell me that nowadays the surgeon is concerned only with operating and getting away. He rarely exercises any judgment in the selection of the case. If things go wrong, he merely regrets that he was not called in earlier. Having removed the appendix, apart from telling them to keep the patient in the Fowler position and to put him on rectal glucose, he gives no further advice. We know little of the ætiology of appendicitis and are uncertain as to whether it always starts as a local inflammation of the mucous membrane or whether it sometimes does not begin as a bacillæmia that becomes localised in the appendix. But before it can arise there must be some impairment of the resistance factor, and the shock and asthenia that follow the operation are certain to add to this. The chances are that appendicitis does not differ from bacterial diseases in general, and certain types undoubtedly begin as bacillæmias. The inflammation is to be regarded as an effort to overcome this. If in such a case the appendix is removed, septicæmia may follow. Other cases should be regarded as terminal bacterial diseases. Appendicectomy should not be undertaken in either of these conditions. When an inflamed mass is present, as is likely after the 48th hour, many surgeons now carry out the expectant method. They maintain that the inflamed mass is probably shut off and that an operation will open up fresh tissues and flare up the inflammation. With this I am in full agreement. For such a line of treatment conforms to that carried out in inflammation in general, and since adopting it my results have improved. A lowering in the operative mortality can come only by the surgeon refusing any longer to be just an operative hack. He should exercise more judgment in his selection of cases for operation and should take some responsibility for a failure. Inflammation here does not differ from inflammation elsewhere. There is no one line of treatment. There is a time when the patient can be saved by an operation. There is a time even in the early stages when he can be saved only if it is not carried out. When a death occurs,

the surgeon should not blame the practitioner and say that, if the diagnosis had been made earlier, it need not have taken place. He should remember that an operation is apt to stir up an inflammation and death might have been prevented if he had held his hand. For however severe a case of peritonitis may appear, it has a way of becoming quiescent and of clearing up if nothing is done, provided a nurse is available who realises that at such a time the patient wants rest and that her duty is to see that he is not disturbed. Appendicitis is a less severe bacterial disease than peritonitis, and Nature is always doing her best.

Those who have the future of surgery at heart should now and again review the procedure that is generally adopted to see whether some very obvious flaw may not be visible which habit leads us to ignore. Three instances only will be referred to here.

(*a*) *Acute Pancreatitis.* For this an incision is made into the peritoneum overlying the gland. As a rule the latter is not incised since pancreatic secretion, which is extremely irritating to the tissues, would be liberated. If gall-stones are present, they are removed and the gall-bladder is drained. What is the object ? Bile itself is non-irritating and drainage of the gall-bladder has no influence on an inflammation in a gland so far away as the pancreas. What is to be gained by draining the inflamed products that are lying behind the peritoneum right into the peritoneal cavity ? Surely this breaks across all principles of surgery. If with acute pancreatitis an incision is necessary to relieve tension, this should be made through the loin. But so much healthy tissue has to be cut through that this is not advisable. Consequently in acute pancreatitis an operation is rarely indicated. Inflammation here as elsewhere is by no means always fatal. Nature herself may work wonders, if she is given just a chance.

(*b*) *The Present Aspect of Tonsillectomy.* As the bacterial conception of disease developed, medical men began to look round for the source of the bacteria. Their passage through

an intact mucous membrane was problematical. If there was a diseased organ they were more likely to come from this. In some children with enlarged tonsils and adenoids much improvement in the health followed their removal. They were consequently assumed to be the cause of ill-health. In children with rheumatic fever, tuberculous glands of the neck, and other diseases, enlarged tonsils and adenoids were often found which were believed to be the source of the bacteria. It was felt that if the tonsils and adenoids had been removed earlier, disease might have been prevented. Their removal was therefore suggested. But such surgery was essentially experimental. It could be justified only as the results were observed over a number of years. It was never suggested that it should be carried out as a routine. It was advisable only in certain selected cases after a consultation between the practitioner and the consultant, when the health of the children and the bearing of certain points in the family history could be passed in review.

After the medical inspection of school-children was established quite a number were found to have enlarged tonsils and adenoids. It was promptly believed that these were vestigial structures and that under the conditions that civilisation imposed they were likely to become the seat of pathogenic bacteria. If they were removed in time ill-health would not occur. As a result " T. & A. " clinics were set up by municipal authorities at which operators attended and undertook to do so many cases per session. This in my opinion has led to a grave scandal, for as yet we are uncertain that removal of the tonsils is really harmless. Nowadays it is necessary to remind people who talk of the strain of living that civilisation did not really dawn with the Great War nor did evolution reach its climax at the time of the Victorians. Civilisation is age old and so are the problems incidental to it. The evolution of man occurred about half a million years ago ; it is at least five thousand since he came into his present image. If structures are

merely vestigial they should by this time have shown signs of disappearing. After all, the conditions of living to-day are much better than they were only a hundred years ago. Consequently there should be less tendency for even vestigial structures to become inflamed. Enlarged tonsils and adenoids are really the reaction of lymphoid tissue to bacterial disease. They arise only when the resistance factor is impaired. The object of the inflammation is to restore this. Once this is brought about they clear up. If they are removed before this takes place, the infection only lights up elsewhere. A surgeon tells me that at 23 he had his tonsils removed for recurrent sore-throat. They were definitely diseased and full of pus. Since then he has had bronchitis from which he never suffered previously. He is able to overcome this by taking a holiday ; but what is going to happen to the children of the poor who are not so favourably placed ?

Diseases are even more common among those who have had their tonsils and adenoids removed. It is no good saying that had the operation not been done the ill-health would have been worse. The experience of practitioners, who worked in days before this modern craze for operating arose, does not bear this out. It may be necessary to remove the tonsils and adenoids if they obstruct respiration or if they are full of pus. Otherwise it should be kept in mind that tonsils and adenoids become enlarged only when the resistance factor is impaired. It is much better to direct the treatment towards the cause of their enlargement. If this is not overcome, ill-health is likely to persist and disease will eventually arise.

(*c*) *Curettage.* Curetting or scraping a surface ulcer or sinus was at one time performed to stimulate the healing power. The practice was abandoned as the results were so poor. No surgeon who understands anything of the pathology of bacterial disease or the principles of operative surgery would attempt it in the case of an internal organ. For if bacterial disease is not completely removed, it always

recurs. Gynæcologists frequently perform dilatation and curettage for affections of the uterus. The rationale for this is not obvious to me. For the factor in the constitution that led to the inflammation is not being touched. It is difficult to understand why a procedure which does harm in sensitive organs is still carried out on the uterus. In my search for truth I frequently ask practitioners what their experience is. Some think the operation does good after an incomplete abortion. This is comprehensible since a foreign body is removed. Otherwise they regard the operation as simply a money-making stunt.

Those who think that improvement in the treatment of bacterial disease will come from earlier or more extensive operation would do well to ask themselves how they contemplate this will be brought about. For though an operation like gastro-enterostomy restores function, the greater number of operations consist in cutting something out of the body. They do not put anything in. There is no suggestion that any operation restores the constitution. Rather it undermines this, temporarily it is true, by the asthenia to which it gives rise. A surgeon will always be controlled in his activity by the following factors :

1. *The Anatomical Approach.* For instance, in the case of the pancreas he has to go through the peritoneal cavity or the loin. Nothing he can do can overcome this. It is useless giving much thought to the treatment of an inflammation here or claiming any great results from a certain method of approach until it is very evident that an operation is equally effective in the case of a more superficial structure such as the skin. A carbuncle or erysipelas is still left untouched and yet the majority of patients recover.

2. *The Importance of the Organ.* It is useless our pretending that a patient is better off without an organ. It is only in so far as this is a source of discomfort or is a danger that an operation brings relief. Every operation is followed by scar tissue, and to some this is just as uncomfortable as disease.

3. *The Pathology of the Disease.* No operative procedure

by itself modifies the pathology. If the organ cannot be completely removed and the disease is still active, it is certain to recur.

4. *The Constitution of the Patient.* Where this is primarily at fault, nothing that operative surgery does will change it. Rather, owing to the asthenia that follows every operation, a further impairment of the constitution is likely to arise and the disease breaks out elsewhere.

A consideration of these points will show that little improvement is to be expected in the treatment of bacterial disease from earlier operation or from any modification in technique. But much improvement will ensue if the surgeon will but realise that, if an operation does at times assist Nature, it also at times does harm. The idea that has sprung up in recent years that the surgeon should operate to give the patient his last chance should be immediately abandoned. At this stage an operation does more harm than good. A death after an operation for bacterial disease is at times a great reflection on the judgment of the surgeon. It is in the exercise of greater judgment that the future of surgery lies. Whilst operative technique may have reached perfection, it is really only a small branch of the art of surgery. As the surgeon ponders over the treatment of bacterial disease, he becomes too well aware that there can be no suggestion of surgery having reached finality. We are really only at the beginning. As he tries to decide on what type of case to operate and at what time the operation should be done, he realises how imperfect is his knowledge. At such a time he has to rely on his judgment, which is so liable to lead him astray. Nothing that has been introduced in recent years gives him any guidance. Where experience counts for so much, there never can be such a thing as finality.

The Position before Us

Some forms of therapy have a very definite action, but our difficulty is to be able to apply them to the right type

of patient at the right time. In the past we have gone astray in assuming that a direct attack on disease was being made, whereas a reaction on the part of the patient was being set up. The more I ponder over the question of bacterial disease the more convinced am I that we have only to grasp some principle that may be only just evading us to make a big advance. Up to now it has eluded us.

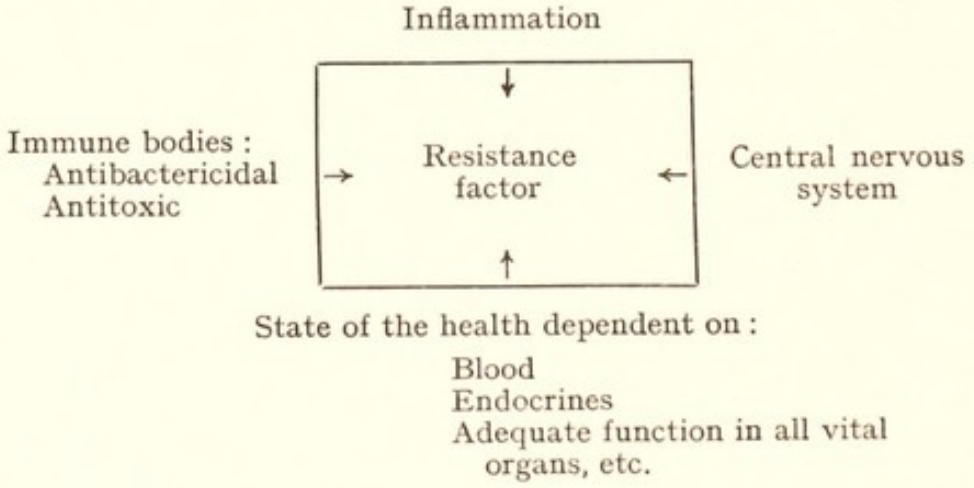
When a bacterial disease is studied, it is well to look upon it from the following points of view :

1. The local reaction.

2. The general reaction as a result of which the anti-bactericidal power of the blood is raised.

3. The response of the constitution as a result of which the resistance factor is raised and the tissues can again be indifferent to bacteria that enter them.

The last is brought about by maintaining the health, and by good nursing, and is the aim of therapy. It can take place only if the patient can react. It is to this reaction that attention should now be directed. As some of the reasoning in the previous chapters indicates, it is in some way linked up with the central nervous system. What it is we do not know, and in calling it the resistance factor we only give it a name. For the time being it should be regarded as the focus to which all things converge.



At such a time it is well to recall the difficulty in the treatment of extensive syphilitic lesions before the War when

it was assumed that the local destruction of tissues was too great and that treatment should have been started at an earlier stage. After the introduction of salvarsan, gummata that had resisted other methods cleared up at times as if by magic. In recent years B. coli infections that had resisted previous forms of therapy and in which doubtless there were changes in the kidney have cleared up under the ketogenic diet. Now both this and salvarsan will ultimately be found to modify and raise the resistance factor of a particular type of constitution against a particular type of bacillus. In this way established disease is overcome. Probably by working along such lines the next advance will be made. This might take place during our lifetime if those interested in research would leave the laboratory and deal with sick animals or return to the bedside of the patient. For it is here that the reaction of the constitution plays such a vital part. Inflammation in all its aspects is responsible for the greater part of disease. If the principle underlying the reaction of the tissues could only be grasped, a great advance might be possible.

I do not claim to have put forward anything original, but only hope that something in these chapters may stimulate men to think clinically and independently. When at the beginning of this century bacteriology seemed to be showing us the way to much knowledge and a great advance, we were inclined to smile at views put forward by men of eminence who had lived just a generation before. They seemed so naïve. Yet nowadays some are going back to their writings and are amazed at the wisdom there revealed. The power to think is not our prerogative. It probably does not vary from one generation to another, and we are not really greater thinkers than our fathers. Many are inclined to agree with Albert Schweitzer, who tells us in his *Autobiography* that the power to think is really on the wane. Some would do well to try to grasp what was in the mind of Paget and his colleagues. For at that time the aim of medicine was the cure of the patient. Nothing more was

attempted. Though research has taught us much about the activity of bacteria, it has told us practically nothing as to why disease should arise in one person and not in another. The bacterial conception of disease has lead us sadly astray in therapy, and it is only by returning to the bedside of the patient and facing the problem that there confronts us that medicine will come into her own again.[1]

[1] Those who consider this line of work worth following up should read the writings of Paget and Hutchinson already referred to in the various chapters. Also the address on " The Diatheses ; the Personal Factor in Disease," delivered by Sir Dyce Duckworth before the Faculty of Medicine of Paris (see *The Lancet*, vol. i, 1908, p. 699). And the writings of Sir Archibald Garrod, Dr. A. F. Hurst, and Dr. J. A. Ryle, which serve to bridge the gulf between the older doctrine of the diathesis and the modern conception that, important as may be the bearing of the constitution, the onset of bacterial disease is in some way linked up with the state of the central nervous system.

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Printed for H. K. Lewis & Co. Ltd. by
Hazell, Watson & Viney, Ltd., London and Aylesbury.

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PUBLISHED BY

H. K. LEWIS & Co. Ltd.

136 GOWER STREET, LONDON, W.C.1.

ESTABLISHED 1844

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