

The study of the natural history of disease the basis of all advance in its treatment : being the address in medicine delivered at the Annual Meeting of the British Medical Association at Manchester, July-August, 1902 / by Sir Thomas Barlow.

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Barlow, Thomas, Sir, 1845-1945
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Publication/Creation

London : Printed at the office of the British Medical Association, 1902.

Persistent URL

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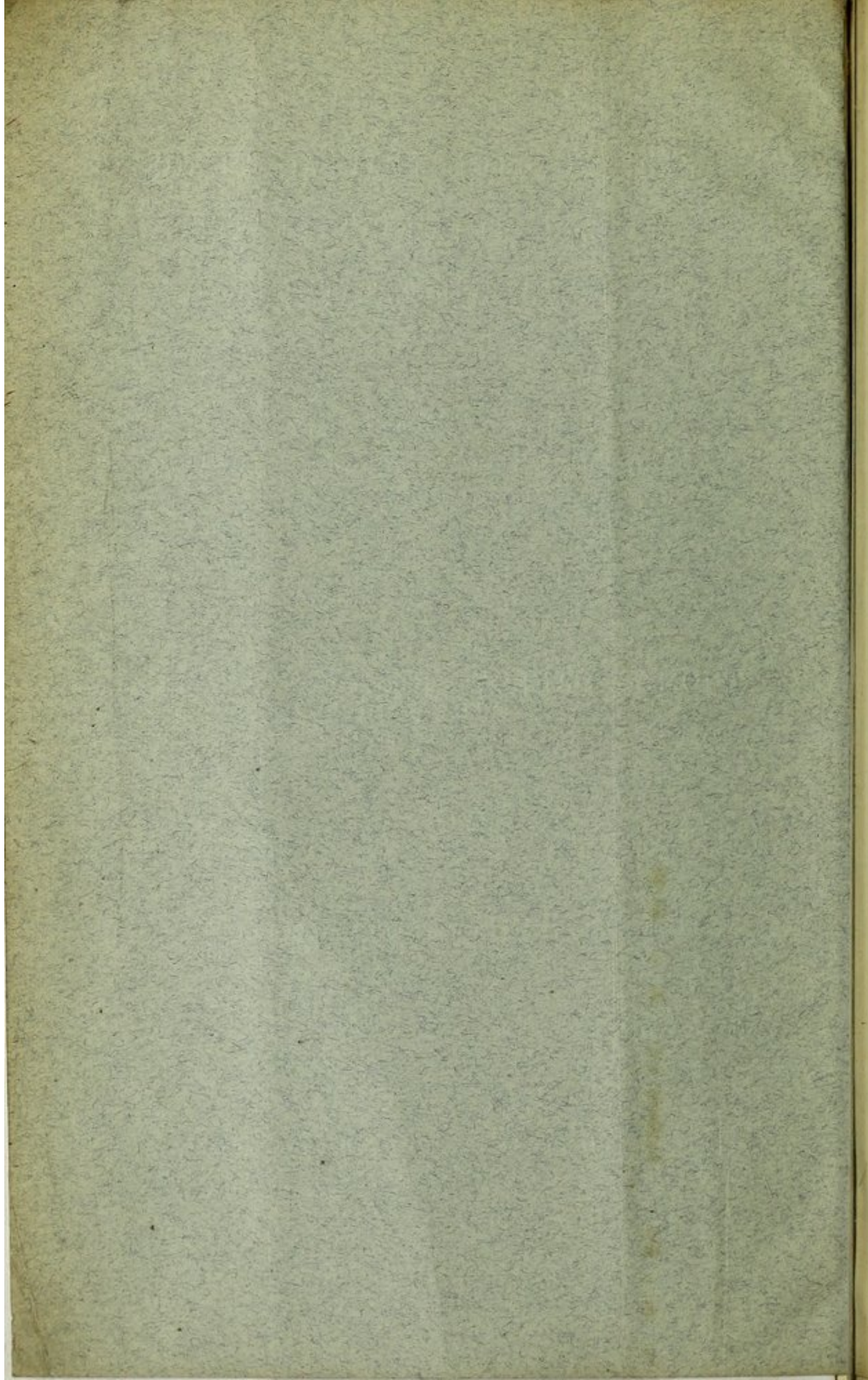
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THE STUDY OF THE NATURAL HISTORY
OF DISEASE THE BASIS OF ALL
ADVANCE IN ITS TREATMENT.

*Being the Address in Medicine delivered at the
Annual Meeting of the British Medical Association at Manchester,
July-August, 1902.*

BY

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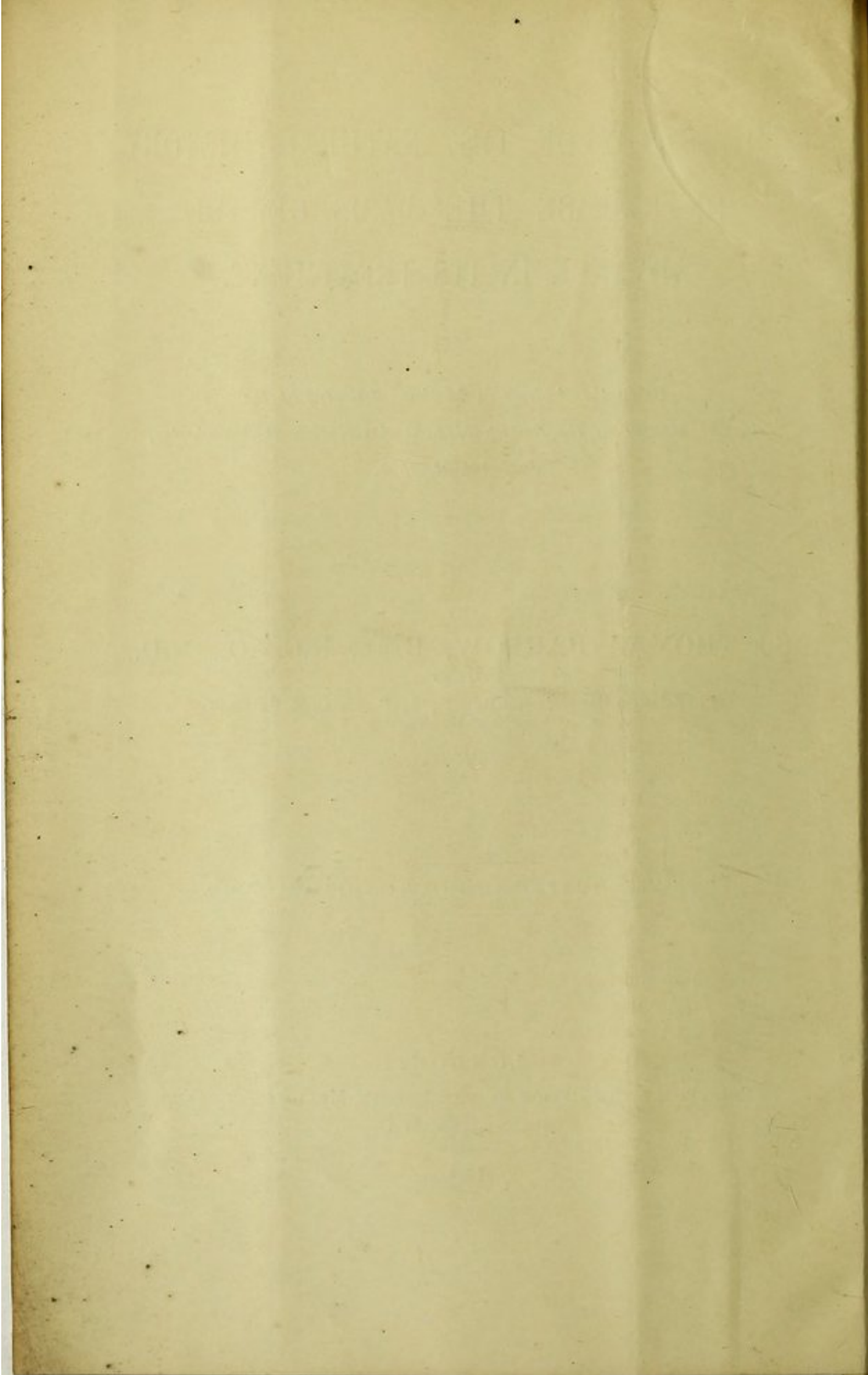
Reprinted from the BRITISH MEDICAL JOURNAL, August 2nd, 1902.

LONDON :

PRINTED AT THE OFFICE OF THE BRITISH MEDICAL JOURNAL,
429, STRAND, W.C.

1902.

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THE STUDY OF THE NATURAL HISTORY OF
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IN ITS TREATMENT.

TWENTY-FIVE years ago the British Medical Association met in this city, and the Address in Medicine was given by one who fitly represented the Manchester School, and whose name is illustrious amongst the leaders of our profession in the Victorian epoch. William Roberts had many remarkable gifts, but the combination in his mental equipment of infinite painstaking in homely detail and of philosophical insight and foresight gave alike to his public utterances and to his conversation a suggestiveness and charm which can never be forgotten.

The address which he gave at that meeting was a notable example of this. It was a masterly discourse on the acute specific diseases in their relation to contagium vivum which subsequent research has left intact, and which in many ways was prophetic as to future developments. *Nihil quod tetigit non ornavit.* The recollection of his discourse gives humbling, reflections to one who has to take up the parable where Roberts left it.

In the address which you have asked me to give it would be impossible even to enumerate all the advances which medicine has made during the quarter of a century which has elapsed since we last met in this hospitable city.

EMPIRICISM AND SCIENCE IN THERAPEUTICS.

We live in worrying times, and we have often to possess our souls in patience. There are those who still maintain that

medicine has no claim to the title of an exact science, and yet some of the most estimable of our fellow-citizens do all that lies in their power to hinder the employment of one of the methods which contribute towards making medicine an exact science. On the other hand, in view of the striking development of some of the modern applications of the physical forces, there are not wanting those who sneer at us as bigots and obscurantists when we hesitate to write a blank cheque for the reckless employment of these modern applications in diseases of which our knowledge is very limited.

But let us reflect how strange and varied has been the progress of practical medicine, by which I mean all that body of knowledge concerned with the cure and the prevention of disease. The history of the earliest efforts in the relief of pain is wrapped in mystery. Perhaps they were not unlike the sports or spontaneous variations which are claimed by the Darwinian hypothesis as the first steps in the development of species, those variations which were useful being perpetuated by a survival of the fittest. But at all events—and let us frankly admit it—the basis of our practice is empiricism, and the basis of all our practical life is empiricism. But there is good empiricism and bad. The good empiricism continually strives to follow Nature's lead, and shed that which is foolish and useless while preserving that which is essential. And good empiricism, by carefully recording cases, noting the results of changes made first by chance and then by design, may at length assimilate to a truly inductive process, even though there are many unknown quantities. But as Nature herself seems sometimes to fail, and leaves behind vestiges and survivals in our bodily conformation which may give rise to trouble, so we also in our treatment sometimes preserve methods of long past utility which may now and again be harmful.

How much we owe to the good sceptics—or, in other words, the independent observers—of whom Sydenham was one; and of whom, in our generation, there was no finer example than Sir William Gull. These are the men who have taught us to look disease straight in the face with our own eyes, and to realize what is its natural cycle, and ask ourselves within what limits we can reasonably hope to modify it. And as a warning against becoming self-centred and self-opinionated,

let us never forget Bacon's wise aphorism: "For as they were men of the best composition in the State of Rome which either, being Consuls, inclined to the people, or, being Tribunes, inclined to the Senate; so, in the matter we now handle, they be the best physicians which, being learned, incline to the traditions of experience, or, being empirics, incline to the methods of learning."

In the period of half knowledge the practice of medicine has often cut a sorry figure. For theoretical lines of treatment, based on incomplete physiological and chemical data, have often produced melancholy failures.

But the outcome of the new experimental pathology of the last quarter of a century, controlled by clinical observation, applied and tested by clinical experience, has justified us in claiming that at length our work has ceased to be fairly described as groping in the dark, and that in some definite instances medicine has justified for itself the designation of an exact science.

In drawing attention to some recent notable advances in the healing art, I will ask your consideration and support for this thesis:—the advances in the treatment of disease have been real and satisfactory in proportion as they have been harmonious with the complete knowledge of the natural history of disease. I do not say that good treatment owes its origin entirely to pathology—far from that; it has often antedated pathology—but in proportion as pathology has become complete it has rationalized good treatment and refined it, separating, so to speak, the ephemeral from the permanent, the accidental from the essential, as well as the harmful from the beneficent. Moreover in these last days in not a few instances the true pathology has laid down new therapeutic lines which have been justified by experience.

BACTERIOLOGY AND TREATMENT OF DIPHTHERIA.

Let me choose as my first illustration one of that group of acute specific diseases to which in his discourse Sir William Roberts gave his chief attention, though he did not refer to this number of that group. I will ask you, as practical men, whether there is any disease within your knowledge in which bacteriological investigation has made so profound a change in our attitude as to the malady and its treatment as it has in diphtheria?

Recall, I pray you, the chaotic and bewildering state of doctrine on this disease only a dozen years ago. There were the endless, and not altogether academic, disputes as to the difference between croup and diphtheria; as to whether there was a true membranous croup which was different from laryngeal diphtheria; and as to the diagnostic differential signs of diphtheria which appeared to elude the most careful anatomical definition. Malignant diphtheria of the throat was easy to diagnose, but as to the nomenclature of mild cases simulating follicular tonsillitis, and of the throat exudations complicating scarlet fever, an experienced man was the last person to dogmatize. It was only, at length, by studying cases in epidemic groups, and especially by noting the paralytic sequelae, that we learned how widely we had to cast our net in order to include examples in which there had been no visible membrane at all, though there might in some of them have been exudation in the post-nasal region, and, for a time, thin irritating discharge from the nostrils.

How exceedingly diverse were our opinions as to its etiology. We were never prepared to deny that exposure to cold was a cause, and after cold came drains. Drain poisoning, serious as it is in lowering vital resistance and preparing a suitable soil, has been often made to bear more than its fair share in the immediate causation of specific disease, and diphtheria was a notable case in point. Sir William Jenner, whose enlightened doubts were nearly as valuable as his absolute statements, would never admit that the direct relationship of diphtheria and drain emanations was proved. But the confident assurance of many people on this doubtful point was often exceedingly mischievous, for though it led to sanitary investigations and helped sometimes to bring about sanitary improvements, it also led to the quiet ignoring of other possible sources of the disease. There was a time, not many years ago, when cases of membranous croup were treated in children's hospitals in ordinary wards, and there were those who stoutly maintained that these cases were not contagious.

The further study of epidemics led to the conclusive proof that in some cases the disease was disseminated by milk. Then came the observation that epidemics were often followed by sporadic cases, or preceded for a time by mild and ambiguous sore throats. Country villages and isolated homes gave their quota as well as crowded streets.

By degrees, even in apparently sporadic cases, we came to attribute more and more importance to insidious personal contagion, and to see that the disease was maintained and transmitted by the moving to and fro of slight cases, especially in schools and places where children were closely aggregated. Increase of the disease seemed to correspond with the period when compulsory school attendance was enforced, and there grew up a strong presumption in favour of the tenacity of infective material associated with bedding and clothing.

If there were wide differences of opinion as to the signs and causation of the disease, how varied were the different lines of treatment. One recalls the routine administration of antimonials and emetics in laryngeal cases which held sway so long, probably on account of the confusion in diagnosis. The cases that were benefited were those of simple laryngeal and tracheal catarrh with spasm, but the true membranous cases were almost certainly made worse. It was but slowly that the consensus of opinion grew in favour of quinine and iron and other tonic methods. The local applications were multiform, and who does not remember the pitiful struggles of many a tender child at the swabbings which were fruitlessly and repeatedly applied. Many of the stronger local applications were actually mischievous. The continuous steam kettle and the tent and the irritating and headache-producing antiseptic inhalations come back to us, and make us realize how often we lowered the constitutional vigour of the patient while we vainly attacked the local disease.

The fear of cold air in the treatment of laryngeal affections was also maintained in respect to faucial diphtheria and a room temperature over 70° day and night, moist like a tropical hot-house, was so constant that it required some hardihood to break through these cast-iron conventions.

When the bacillus of diphtheria had been isolated by Klebs and the inoculation of it in animals had been demonstrated by Loeffler to produce diphtherial lesions, the first step had been taken in unravelling the skein. Let us consider how these discoveries, followed by those of Klein, Roux, Sidney Martin, and others, illustrated and explained the puzzling clinical facts. First, the polymorphism of the bacillus is very suggestive. The long and short varieties it has been shown, may occur as pure cultures or side by side, or in successive cultures apparently one form may be replaced by the

other. Though these varieties cannot as yet be correlated to different types of membrane, yet their discovery prepares us for considerable variation in gross naked-eye characters.

Secondly, the variation in virulence of the bacilli going down to an actual vanishing point with little morphological alteration has its transcript in clinical experience. When, in an ordinary case of faucial diphtheria the nose becomes affected and a thin ichorous discharge appears at the nostrils the gravity of the case is always increased. On the other hand there are cases of children attacked with thick fibrinous exudation obstructing the nostrils in which the Klebs-Loeffler bacillus has been identified and yet there is little constitutional disturbance and apparently very slight infectivity. There is a form of chronic diphtherial ophthalmia with thick exudation which presents many similar features.

Thirdly, the detection of the diphtheria bacillus in the secretions of the throat in cases at first clinically indistinguishable from follicular tonsillitis gives the clue to the puzzling cases which the study of epidemic groups had brought home to us—namely, that paralytic sequelae can occur when most careful observation has failed to identify any antecedent visible membrane. The persistence, sometimes for months, of the bacillus in the fauces of those who have passed through an attack of diphtheria when all membrane has long since disappeared, gives us the clue to the occasional prolonged infectiousness of those who have had this disease, and seems to enforce the need of special arrangements for diphtheria convalescents. It is the experience of those interested in day school epidemics that a slight nasal discharge associated with imperfect resolution of the lymphatic glands are the clinical danger signals to be looked for, and which suggest the bacteriological investigation for continued sources of dissemination.

The detection of the diphtheria bacillus without exudation in the fauces of doctors and nurses attending cases of this disease is one of those valuable and suggestive facts which emphasize the importance of keeping the mouth and throat clean, and of maintaining the vital resistance of the attendants by good food, regular sleep, and plenty of fresh air.

In the old days how often the risks of the diphtheria nurse contracting the disease have been increased by the close,

stuffy sick room, the long uninterrupted hours of attendance, and the inadequate meals.

Moreover, the tenacity of the bacillus and the fact that cultures can be made from membrane that has been in contact with a textile fabric even after some months, accentuates the importance of destroying as much as possible in the way of contaminated clothes, and of not being content with perfunctory disinfection.

But we are further indebted to the bacteriologists for solving some of our clinical difficulties by demonstrating that not all false membranes are diphtherial. The streptococci, for example, seem capable of giving rise to pseudo-membranous deposit. The exudation occasionally present in early scarlatinal throats, which are extremely red and swollen, is not generally true diphtheria, and this harmonizes with what is found clinically, that the exudation seldom spreads, and that paralysis does not supervene.

On the other hand, the secondary membranous exudations which sometimes supervene in measles and in the late stage of typhoid appear often to be due to true diphtheria bacilli. But further investigation seems to be required as to the virulence of, and the dissemination from, the secondary cases. Thus far as to the bacilli. But the skein becomes still further unravelled by the discoveries of Roux, Yersin, and Sidney Martin on the toxin of diphtheria. The first two observers separated the toxin from the bacilli, and produced by inoculation many of the symptoms of the disease, but *minus* the formation of false membrane.

Whether, as Sidney Martin maintains, the bacilli at the local site of the disease elaborate a ferment-like body, which, subsequently affecting the tissues, digests them, and the products of this digestion constitute the toxins, or whether, as others hold, the bacilli themselves elaborate the toxins, is not material. The solid gain to knowledge is that for the most part the mischief is elaborated locally at the site of the diphtheritic membrane, and not to any great extent by multiplication of the bacilli themselves in the blood and other tissues.

This leads us to see the justification of the researches of Behring and his fellow workers which eventuated in the practical application of the methods of immunization and the preparation of an antitoxin.

It is beyond my purpose and outside my province to go into the complicated questions of the preparation and standardization of diphtheria antitoxin. But surely it is right, in this meeting of practitioners who have to deal with disease, to insist on the revolution which this treatment has made.

The statistics are striking enough, for they show a reduction of mortality between one-third and one-half. But statistics are not the only test upon which a doctor bases his practice. The manifest alteration after the use of antitoxin, even in a most unfavourable and ultimately fatal case, is convincing enough to an informed person that we have here a fundamental remedy of enormous potency.

When, within forty-eight hours, we see a young subject with malignant diphtheria accompanied by secondary infections which are on the verge of setting up septicaemia, so far relieved after the use of the remedy that the glands are reduced in size, the cellular tumefaction of the neck is lessened, the membranous exudation is arrested and begins to separate at the edges, the tongue is more moist, and the general state ameliorated, we know that something has been done to control the disease processes with which no previous treatment with which we were acquainted was in the least degree comparable.

Furthermore, in cases in which tracheotomy has to be performed, not only are the mortality statistics improved, but we see for ourselves that the membrane formation ceases to spread, and the tube, which has formidable disadvantages of its own, can be withdrawn much sooner, and the risks of ulceration and stenosis can be thereby lessened.

Moreover, those of us who were doubtful about the expediency of intubation in this disease, on account of the difficulty of providing for the evacuation of the membrane below the tube, are now only too glad to admit of its applicability, because of the gradual melting away of the membrane.

Since the introduction of the antitoxin, the urgency of local applications to the fauces has become lessened to a marked extent. We are told that antitoxin only neutralizes the toxin, but does not destroy the bacilli themselves. A weak mercurial solution which attacks the bacilli, though it coagulates the albumen, and an alkaline solution which favours the solution of the membrane, seem to be all that are needed. By too much zeal in local applications, we interfere with the

protective action of the phagocytes, and the old corrosive applications are entirely ruled out.

With continued experience the limitations of antitoxin are becoming more and more clearly understood. A careful man seeks the assistance of the bacteriologist in every doubtful case, but does not wait for his report, for he knows that the certainty of success depends on the remedy being introduced early, say within the first three days, and that the risks of its employment are insignificant. The existence of secondary infections makes him far more anxious, and he feels compelled to warn the friends on that account, but it does not prevent his applying the diphtheria antitoxin even in very grave cases. Experience does not seem to support the concurrent use of antistreptococcus serum.

As to the rashes, the pyrexia, and the joint pains which appear up to the second week after the injection, they seldom give rise to anxiety when we are prepared for them and recognize their nature, nor do they require special treatment. We know now that they really depend on the serum *per se*, and not on the special antitoxin. As might be expected, there are occasionally inflammatory incidents from imperfect aseptic precautions in the injections, and such incidents ought not to occur, but let us remember that there are also like risks which occasionally arise with hypodermic injection of morphine and other remedies, and these we accept.

Some of the earlier objections as to the effects of antitoxin seem to have been made by those who were inadequately familiar with the symptoms of diphtheria itself. Everybody knows that albuminuria is common in diphtheria, and that suppression of urine is not rare, and there is no reason to believe that antitoxin has any effect at all in producing them.

May I here, in speaking of suppression of urine, by way of parenthesis refer to a practical point in nursing—namely, the extreme difficulty in inducing nurses to give abundant plain water to patients suffering from diphtheria and other febrile illnesses generally, and also to the importance of aiding renal secretion and quenching thirst when there is distressing vomiting by giving weak saline rectal injections?

As to the incidence of diphtherial paralysis in cases treated by antitoxin, it seems reasonable to suppose that many of those who develop paralysis after antitoxin would otherwise

have died before there was any chance for the paralysis to become manifest.

Goodall has shown, however, that there are no more fatal cases of paralysis in those treated by antitoxin than in those not so treated. It seems probable from Martin's researches that the diphtheria toxin begins to affect the nervous system very much earlier than would be supposed from the obvious clinical manifestations, and possibly, when once initiated, the neuritic changes go on in spite of antitoxin, just as in some other forms of peripheral neuritis they persist and go through their own evolution after the removal of the cause.

Of the prophylactic value of the diphtheria antitoxin for those in a family or institution where there is a case of diphtheria, we can only say that there seems now a large body of experience in support of its efficacy, although the period of immunity conferred does not exceed three weeks.

TETANUS.

While the diphtheria antitoxin treatment is in every way the most satisfactory of all the serum methods, the other members of this group of therapeutic measures are full of suggestion, and it is worth while briefly to consider a few of them.

Thus, with regard to the tetanus antitoxin, although the experiments on immunization of animals have not furnished us with a successful method of dealing with the severe and acute cases of human tetanus, yet some benefit has been gained in the subacute forms.

It is interesting to observe that the tenacity of the combination between the toxin and the nervous tissues which was shadowed forth in diphtheria is in tetanus the dominant factor. It would appear to be the tissues of the central nervous system for which the toxin has a special affinity, and the later investigations point to the necessity of subdural injections into the cerebral substance itself, as well as into the cellular tissue, and to the employment of far larger doses of the antitoxin than the first immunization experiments suggested.

OTHER EXAMPLES OF SPECIFIC REMEDIES.

In the other examples of this kind of treatment we have to depend on very incomplete data. For example, in rabies we

are still ignorant as to the micro-organism, which we are none the less convinced is the cause of the disease. But the knowledge that the poison is lodged in the cerebro-spinal tissues has led, in the hands of Pasteur and his pupils, to the most fruitful results. The working hypothesis that in the dried spinal cord of an animal that has died of rabies the micro-organisms are destroyed, but that the immunizing substances remain active, seems to have been justified by experiments based upon it, and by its applications.

There surely can be no doubt of the prophylactic value of Pasteur's methods so far as those who have been bitten by rabid animals are concerned, although no beneficial effects follow their employment in the developed disease. But when a complete analysis of the life-history of the organism has been attained, we may fairly look for still greater results in the therapeutics of this disease.

Is it unreasonable to suggest the same thing with respect to the great triumph of English protective medicine—namely, vaccination? One of the best results of the recent Royal Commission was that it gave the *coup de grace* to the easy optimism of those of us who considered that there was finality in what had been already accomplished, and that nothing more was needed than to continue on the old lines.

But the most recent methods of preparation with the carefully regulated glycerination, and the getting rid of so much of the secondary infection, for which we are indebted to Copeman, mark an enormous advance in the practical application of vaccination.

Who can doubt that there are still further triumphs in store for us when the organism has been discovered and its natural history has been completely worked out?

Of plague, cholera, and typhoid I will not speak, for the inoculation methods are still *sub judice*.

With respect to the employment of antistreptococcus serum we are met by the most various testimony. Some cases of erysipelas and puerperal fever, and some of those most desperate cases of acute septic mischief following on infections from necropsies, have been strikingly benefited by the use of injections of this serum. Some cases of infective endocarditis appear to have improved, but a great many others have shown no response whatever.

It would appear that although streptococcus is the organism

common to many forms of septicaemia, and although morphologically no differences can be established according to the lesion from which it is derived, yet that there must be many different strains, and that the serum of an animal that has been immunized from one strain will not necessarily prove beneficial to an animal subject of another strain. Meanwhile it would seem that in any case of formidable septicaemia, when there is substantial reason to doubt whether the patient can cope with it successfully, we are not justified in withholding the use of antistreptococcus serum, which should be recently prepared. This is pre-eminently one of the subjects in which we may look for notable advances from fuller knowledge of the natural history of these organisms.

THE TREATMENT OF TUBERCULOSIS IN THE LIGHT OF MODERN DISCOVERIES.

Koch's great discovery of the tubercle bacillus in 1882 has been so far reaching and comprehensive that the simplification which it has brought about in our knowledge and in the mode of grouping of a great body of facts seems almost incredible. The most important outcome was that it confirmed the doctrine that tubercle should be placed amongst the chronic infections and so helped us to realize, in some sense, the kind of enemy with which we had to deal.

With respect to the tuberculin treatment, it cannot be denied that the results obtained have been on the whole unsatisfactory and tentative. When we consider that under the most favourable circumstances both forms of tuberculin can only claim to set up fresh activity in the neighbourhood of pre-existing tuberculous lesions with which fresh activity the reaction temperature is associated, it is clear that the result must be, to say the least, problematical. With localized subacute and indolent lesions such as we get in lupus we might fairly expect that such increased activity might sometimes be followed by improvement, and that has unquestionably been observed also in some cases of tuberculosis of joints. But with respect to visceral lesions there is always some risk of dissemination following this renewal of activity and of the setting up new inflammatory action and necrosis instead of fibrosis in the lesions themselves.

The importance of the tuberculin injection as a test for the

tuberculous lesions in cattle seems to be very great indeed, but the justifiability of the employment of this test in the human subject for the determination of a doubtful lesion is, I think, open to question, although it has been extensively employed without proof of harmful effect.

The most important pathological fact bearing on the therapeutics of tubercle is the enormous frequency of unsuspected tubercle as proved by investigation after death of persons dying from other causes than tubercle.

Thus necropsies on people dying from surgical injury and every form of acute and chronic disease show in a great many cases one or more old tuberculous lesions. And the younger the subject the more frequently are tuberculous lesions found. Thus from the careful synopses published by several skilled pathologists, it would appear that about one-third of the children under 12 years of age who die from all causes in the children's hospitals show tuberculous lesions.

The first reflection that forces itself upon us is the enormous frequency of unsuspected tuberculous illnesses that occur in the population around us.

The second and equally important reflection is that there exists a tendency in the human subject to spontaneous limitation and arrest; and the third reflection is that there is an extreme frequency of local limited tuberculous deposit as compared with the generalized disease.

How, then, if tubercle has gained admission are we to aid Nature in this spontaneous tendency to limitation and arrest?

Let us by no means deny the possible utility of fresh attempts at serumtherapeutics nor the tentative use of disinfectants introduced into the blood stream, such as the formaldehyde plan of Dr. Maguire. These methods may prove beneficial in the concomitant and secondary infections even if they do not control the tuberculous process pure and simple. Also we are grateful for all that the surgeons have done in respect to glands and joints and abdominal tuberculosis, and for the recent applications of Roentgen rays and Finsen's methods to cutaneous tuberculous lesions.

But surely the teaching of pathology is that the fortifying of the general resistance of the individual is the most important indication of all. Real true advance always tends to simplification, and the great fundamental therapeutic remedies

are the employment of fresh air, sunshine, of good food, and of regulated exercises. This, surely, is the inwardness of what has been called the sanatorium treatment.

Let us gratefully recognize what Brehmer and Dettweiler and Trudeau and Walther have taught us; but in this meeting of the British Medical Association it is fitting that we should remember that sixty years ago an Englishman—a village general practitioner, George Bodington, of Sutton Coldfield—taught, both by precept and by the results of actual experience, what were the proper methods of treating phthisis.

The measures upon which he relied were that the patient should live most of the day in the cool open air; that his rooms should be thoroughly ventilated, and in temperature not vary greatly from that of the outer air, that daily driving or riding, and, as soon as possible, walking should be enjoined; that a generous diet should be given, and that all this should be carried out under the assiduous daily and even hourly supervision of a doctor living under the same roof or close by.

Bodington's criticisms of the orthodox antiphlogistic doctrines of his time were as sensible as they were trenchant, but it may be questioned whether in his rebound from them he did not attribute undue value to sedatives and alcohol as adjuncts to his treatment. But the main lines which he laid down are admirable.

But let us now consider in detail what we have learned from recent sanatorium experience in our own time. First, we have learned the value of hyperaëration and of establishing tolerance to cold and to exposure to variations of temperature. The value of hyperaëration is not summed up in its affording more effective oxygenation to the lungs, parts of which are *hors de combat*, though that counts for a great deal. The access of free air is also a natural and wholesome stimulus to the nervous system. It increases the appetite and lessens the languor and exhaustion of a chronic febrile disease which the still, warm air of the old sick room did nothing to relieve. The getting rid of the liability to catarrhs of the upper passages by free exposure to pure fresh air had been known to us apart from phthisis, if we had only had the sense to apply it, and the enormous difference between sitting in the open and sitting in a draught was an old story which we ought to

have remembered. The daily exposure to free, cool air has also been shown to have a direct benefit in lessening pyrexia, diminishing sweating, and improving sleep. And can we exaggerate the value of the immeasurably greater intake of direct sunshine which this treatment ensures as compared with any ordinary mode of life?

With regard to the employment of exercise, the time when it is taken, and the exact amount of it, the sanatorium experience has shown us that the most important therapeutic indications depend on the careful record of temperature.

With regard to food, we find that the exaggerated fastidiousness which is so hard to deal with in phthisis is less of a difficulty under sanatorium treatment than under ordinary conditions; that the number of patients who are unable to assimilate milk is exceedingly small; and, finally, that the enforcement of large mixed meals, at any rate for a period, is on the whole justified by the results of chemical investigation and of the actual well-being of the patients.

But, further, there is the educational side of the sanatorium. The patient is instructed as to the importance of the disposal of sputa, and as to the methods by which a phthisical patient may live with his fellow-creatures without risk to them. Surely the imperative necessity of enlightened and unremitting medical supervision in work of this kind is self-evident. Whether there will be evolved any better method of carrying out these indications for the treatment of phthisis in its early and middle stages remains to be seen.

So far as the rich and well-to-do are concerned it will probably be found that the sanatorium fulfils the rôle of a school which shall educate them in methods which can subsequently be carried out efficiently at home if the conditions are favourable.

But with respect to the poor, it is only now and then that the home conditions even in the country admit of adequate early treatment and for them in the immediate future we have to look forward to the multiplication of sanatoria.

It seems desirable that we should speak more guardedly about the *cure* of consumption and insist rather upon its *arrest*. In that way we throw upon the individual as well as upon the enlightened community the vital necessity of a prolonged after-care of the tuberculous subject.

This is another of the instances in which bacteriology has

given scientific emphasis and direction to rational therapeutics for we remember how many of our patients in spite of having increased greatly in weight and general nutrition and of having improved enormously in physical signs, nevertheless continue after their sanatorium course to expectorate once a day sputum containing some tubercle bacilli.

But even when the general nutrition leaves little to be desired, when, so far as physical signs are concerned, the lungs are dry, when the temperature is normal after exertion, and at every part of the day, is it wise to adopt the optimistic tone, and assure the patient that he is as sound a man as ever?

We cannot, even in the most promising cases, exclude the possibility of the reawakening of activity around old foci, nor of entirely new local infections, and we must continually hark back upon the old text of maintaining the resistance at its maximum.

Meanwhile for the poor man there is the question of bread winning, and there is the danger of relapse when he returns to unhealthy surroundings.

The question must be faced whether systematized arrangements can be made for open-air occupation. Whether this can best be done in colonies like the epileptic colonies, where horticulture is taught, or by some method comparable to boarding out, requires much consideration.

It is also clear that to meet the full needs of the poor there ought to be some form of special hospital provision made for incurable and rapidly advancing cases of phthisis. These are certainly not suitable for the sanatorium, and it is unfair to frustrate the true work of the sanatorium by sending such patients thither.

On the other hand, with our present arrangements of general hospital and infirmary wards, the contiguity of cases of acute and curable disease with those of advanced phthisis in which there is copious expectoration is always an anxious matter, even when precautions are taken.

We may nevertheless be grateful to the bacteriologists for enabling us to give the confident assurance to many a poor consumptive that it is the dried sputum and not the moist material which is the most important, and if the devoted wife who is nursing a consumptive husband will only carry out scientific cleanliness, if she will strive for the greatest amount

of ventilation possible, and if she will do her best to maintain her own personal resistance at its maximum, her risk becomes almost a negligible one.

Looking still further ahead, it is clear that the community is beginning to realize the necessity of going to the root of the matter, and of seriously attempting to prevent consumption as well as to cure it.

First as to the prevention of infection, voluntary notification has been established, in Manchester, under Dr. Niven's able organization, with very great success. There seems to be very little difficulty in securing disinfection of rooms after a fatal case has occurred in the abodes of the poor, and experience would seem to show that, with tact, notification of phthisis during life may be followed by sanitary inspection, and by much useful guidance as to ventilation, cleanliness, and disposal of sputum.

The example of some of the Latin races has been often quoted to us in respect to the popular estimate as to the infectiousness of phthisis, but Heaven forbid that our people should, in consequence of any such teaching, become prudential cowards, and treat the poor consumptive as a leper and a pariah.

There have been undoubted cases of hardship in the way of summary dismissal of young people from places of business on account of cough and the suspicion of phthisis. It ought to be an honourable understanding that no employer should dismiss such a person without using his best endeavours to secure admission for him or her to a sanatorium or to some adequate equivalent of the sanatorium.

Passing from the care of the individual sufferer and the protection of his immediate neighbours to the wider claims of the community, let us do our utmost to secure in our towns the greater access of sunshine, and not only strive for large open spaces but for free space round our dwellings; let us face the question of free air in our houses, and workshops, and schools, and all public buildings, and wage unceasing warfare against the lodgement of dust in theatres and all public buildings, and insist on the importance of moist cleansing as distinguished from mere sweeping of dusty material.

There must come many changes in our modes of home life in large towns, in our house architecture, and lighting, warming and furnishing. Surely these are not altogether utopian and foolish forecasts to keep before us, and when substantial pro-

gress has been made and the public conscience has been quickened and enlightened the sanatorium may be regarded as a temporary and provisional arrangement only, and more may be done in the way of rational home treatment, even at its outset. At any rate, it is certain that there will be less of it to treat.

With regard to the relation of human tuberculosis to that of the lower animals, Koch's remarkable deliverance has no doubt led to much searching of heart, but we must possess our souls in patience and wait for the results of further and more exhaustive investigation.

Meanwhile, let us do all we can to prevent the relaxation of the hard-earned sanitary regulations which have been obtained for the protection of the community in respect to cattle. There can be no doubt of the wrong done by allowing milk to be supplied from a cow with a tuberculous udder; and the value of the tuberculin test for revealing this disease has been definitely proved. The instruction to our patients to scald their milk should be given universally, although we may condemn the prolonged and repeated sterilization at high temperatures which have lately become fashionable.

But I must confess that for my own part I have not yet been convinced that the abdominal tuberculosis of young children is in any large amount the result of infection pure and simple from tuberculous milk. Human tuberculosis absolutely limited to the alimentary canal and to the mesenteric glands is not a very common disease. I believe that for young as well as old the entrance of tubercle is in far greater proportion by the respiratory tract, and that its resting place is in the bronchial glands and the lung alveoli, and that in a large number of cases the infection of the mesenteric glands is a secondary one or part of the general infection. Also the habit of swallowing the sputum, which is so constant in children ought to be taken into account in the consideration of the production of intestinal and mesenteric tubercle. Three colleagues of mine at the Children's Hospital, Great Ormond Street, who had held the post of pathologist there—namely, Dr. Colman, Dr. Batten, and Dr. Still, have published the results of their investigations, and these all point in the same direction.

The carefully-recorded observations of Dr. Carr, Dr. Guthrie, and Dr. Northrup likewise show the great preponderance

of bronchial glands as the common site of tuberculous lesions in children.

The most important antecedent and predisposing conditions for tuberculosis amongst the children of the poor are measles and whooping-cough, and the close, stuffy rooms in which they are treated and in which their convalescence takes place.

The response of children to open-air treatment is if anything more striking than that of adults, and I believe that it will be found that they are more tolerant of exposure to wind than adults are. The importance to healthy children of passing a great part of the day in the open air has been gradually apprehended by the rich, and the poor have been compelled to learn it by their home conditions, but neither rich nor poor have as yet appreciated how large a slice of every twenty-four hours of a child's life is passed in the bedroom. The traditional fear of night air and of wide open windows, which is perhaps the survival of ancient malarial experience, has still to be unlearned in this country. Moreover, we should never forget in our large manufacturing towns the importance in children of paying regard to the unhealthy mouth cavity, which is due to bad teeth and inflamed gums and likewise to morbid conditions of tonsils and naso-pharynx, which make open pathways for the admission of tubercle, and lead to localized and limited infections of the glands of the neck. Surgery has done a great deal to help us in dealing with advanced lesions; but surely cleanliness of the mouth in the large and complete sense, improved ventilation, the early instruction in nose-breathing and timely change to hills or seaside after acute specific illnesses and chronic catarrh ought to anticipate and prevent surgical interference in a large number of cases.

Clinical observations ought in future certainly to be carefully made as to the relation of tuberculous milk to the infection of the glands of the neck, but it is exceedingly difficult to get conclusive evidence.

What is the practical bearing of the later investigations with regard to the bearing of heredity on tubercle? We have here a conspicuous example of the fact that the more complete our knowledge of the natural history of a disease, the more clearly we realize that observations which at an earlier period seemed absolutely conclusive in one direction, become susceptible of other interpretations.

As we know tubercle now, we must admit that, if there were definite inheritance of tubercle, it would imply a direct transmission of a tangible material from parent to child which would be capable of subsequent dissemination.

Now to say that it is impossible that tuberculous material should exist in the newborn child would, no doubt, be an ultra-dogmatic and unjustifiable statement, but it must be infinitely rare. It is certainly significant that in infants under 12 months old tubercle is not very common, as we should expect it to be if congenital tubercle occurred. It is in the second year that tubercle becomes very common indeed.

The successive attack of several members of a family by tubercle, instead of pointing necessarily to an inheritance of the disease, is often explicable by their being subjected to the same or similar infective conditions. Is there, then, no inherited tendency to develop tubercle at various periods of stress—what has been called inherited vulnerability? That we cannot deny—though it is impossible to prove—but strictly this amounts to nothing more than saying that a given child is delicate and unstable, and all delicacy, whether the parents be tuberculous or not, means weakened resistance to the inroads of disease.

This is not an academic question; it is a practical one. Sensible moralists will remind us that the doctrine of original sin is responsible for the excuse and wholesale condoning of much wrong doing. In our domain we know how often the abject acceptance of the doctrine of heredity has taken away the courage and initiative alike of doctors and of responsible relatives in dealing with delicacy of constitution as well as with pronounced tuberculous disease.

THE PRACTICAL RESULTS OF THE SCIENTIFIC STUDY OF MALARIA.

In the whole range of medicine there is scarcely a disease which illustrates our opening thesis more forcibly than does malaria. The story of the investigations of our countrymen, Manson and Ross, are fresh within our memory.

Up to a certain point the life-history of the malarial parasite had been made clear by the observations of Laveran and Marchiavafa.

The amoeba-like bodies enter the red corpuscles, live on the haemoglobin, and divide into spores. The latter burst through the envelope of the corpuscle, become disseminated in the blood serum, and repeat the process of the parent organism.

But other forms do not develop spores, and in some species these assume within the corpuscles a crescent-like shape. When the crescent-like bodies are observed for some minutes on the warm stage a change of shape takes place, and motile filaments are observed to escape from them. It was at this point that Manson's insight led him to join issue with the Italian observers, who looked on this stage as one of degeneration, whilst Manson claimed that it suggested another life cycle of the organism within the body of some host other than man, which host should be the means of communicating the parasite to man. That intermediate host, he reasoned, must be a suctorial insect, and he predicted that it would prove to be the mosquito.

Ross's investigations established the truth of this hypothesis beyond any cavil, and narrowed down the number of possible hosts to gnats of the genus *Anopheles*.

The next inquiry was to ascertain the important facts as to the habitats of the *Anopheles* and its mode of life.

Ross, in the expedition sent out by the Liverpool School of Tropical Diseases, was able to show that the larvae of these gnats were to be found in shallow pools which were not big enough or permanent enough for fish, and yet were not small enough to dry up between showers. The drainage or filling up of these pools in the neighbourhood of human habitations, or systematic destruction of the larvae by the application of paraffin, appeared to be the readiest way of dealing practically with the problem.

The further verification of the mosquito theory was finally set forth by the results of an expedition planned under Manson's direction, and carried out by Drs. Sambon and Low of the London School of Tropical Medicine. The objects of this investigation were twofold:

1. To arrange for the transmission to London, with proper precautions, of specimens of *Anopheles* which had been infected with malaria, and to arrange for a healthy person to be bitten by them, and to watch the result as to the induction of malarial fever.
2. To instal two healthy persons in a malarial district

through the whole of a fever season, providing them with efficient protection against mosquito bites, and to note the result. Ostia, in the Roman Campagna, was chosen for the erection of the experimental hut, which was constructed with the greatest care, and furnished with wire netting, so as to be absolutely mosquito proof. No quinine or other prophylactic was taken.

Both these sections of the investigation were absolutely conclusive.

In two subjects in London a sharp attack of ague was induced by puncture by the infected mosquitos, and Drs. Sambon and Low, with precautions as to clothing, and as to avoidance of exposure to mosquitos at their feeding times—namely, just after sunset and after sunrise—sojourned through the fever season with impunity.

It is not too much to hope that these researches will jointly give a definiteness and a purpose to attempts made to deal in an effective way with one of the greatest scourges of mankind. But it is not in prophylaxis only that the elucidation of the life-history of malaria has been useful. Slipshod use of the term malaria has been responsible for many culpable blunders in diagnosis, so that many illnesses have been described as malarial which had no claim whatever to this designation.

We also see now that the specific effect of quinine on true malaria is most definite when it reaches the blood as soon as possible after the sporulation of the amoebae has taken place, and the young organisms have escaped from the corpuscles into the serum.

We realize, again, that the anaemia which may come perilously near to being pernicious as the result of the corpuscular destruction may still persist after the organisms have disappeared, and that it is in this condition that arsenic finds its chief utility. We are still in the dark as to the true relation to malaria of that mysterious disease blackwater fever, which has so much in common with the mild paroxysmal haemoglobinuria of our own climate. But its refractoriness to quinine is quite in harmony with the hitherto negative results as to the presence of malaria parasites in the blood.

MALTA FEVER.

In Malta or Mediterranean fever we have another illustra-

tion of how complete exhaustive pathological investigation has led to the rational separation of a given disease from every other. The discovery by Bruce of the life-history of the micrococcus melitensis settled once for all the specific nature of this intractable but not very fatal illness, and separated it entirely from typhoid and malaria.

ACUTE RHEUMATISM.

The microbial origin of acute rheumatism was strongly maintained at the meeting of this Association as far back as 1887 by Dr. Mantle, and its clinical analogies with other infective diseases have been repeatedly set forth. The recent researches of Drs. Poynton and Paine seem to have established the existence of a specific diplococcus in the blood, in the valves of the heart, in the pericardial exudation, in the joints, and in the subcutaneous nodules of acute rheumatism. From pure cultures of this organism intravenous inoculations in rabbits have been followed by clinical manifestations and by non-suppurative lesions similar to those with which we are familiar in acute rheumatism. This seems to be a real contribution to the natural history of the disease, and when we have learned something about the rheumatic toxins and about the changes which supervene upon their formation, we shall probably get a more satisfactory explanation of the action of the salicylates than is at present forthcoming, and we may hope for further light as to the treatment of the complications and refractory forms of this common disease.

THE DIFFERENTIATION OF MENINGITIS.

Bacteriology has done a great deal towards the elucidation of the somewhat confused groups of meningitis. Setting aside the septic cases which arise in connexion with otitis and bone disease and injury, as well as those severally dependent upon syphilis and tubercle, there remain :

1. The epidemic cerebro-spinal fever in which the characteristic organism is the diplococcus intracellularis.
2. The rapidly acute forms, often vertical, but sometimes cerebro-spinal, which are associated with pneumonia, empyema, and ulcerative endocarditis, in which the pneumococcus is the characteristic organism, and

3. The sporadic subacute form especially found among young children, often limited to the posterior region of the base of the brain, but sometimes also spinal, which is usually unaccompanied by any visceral disease whatever. In this form Dr. Still has isolated a diplococcus, allied to that of the cerebro-spinal fever, but with some definite differences.

There is scarcely any group of diseases in which the resources of therapeutics have been so discouraging. It is true that in the first and third of these forms there have been a certain number of recoveries, and, although for my part I would not relinquish the use of mercury, yet it seems doubtful whether drugs have played any important part in the recovery of the successful cases. Although lumbar puncture and drainage from the cervico-occipital region have temporarily relieved pressure symptoms, they cannot as yet be strongly urged as curative measures.

May we not reasonably hope that serumtherapeutics will one day find some tangible success in this group of intractable diseases?

The late Dr. Washbourn, whose premature loss we all lament, had succeeded in making an antipneumococcus serum, and it has also been prepared and used in Italy. But the results hitherto obtained, so far as pneumonia is concerned, are inconclusive. I am not aware that there is evidence as to its effect in the form of meningitis depending on the pneumococcus.

"ORGANOTHERAPY."

Washbourn was cut down in the beginning of his prime; but we have lately lost another physician in the ripeness of years after a long and distinguished career. With the name of Dr. Ord must always be associated the merit of having given the first systematic and detailed account of the disease which he called by the name of myxoedema.

As you will remember, it was Gull who, in 1873, gave the first clinical description of this malady, and in his brief and striking paper with remarkable insight he recognized its affinity with cretinism. But Ord made an elaborate investigation, both pathological and clinical, of several cases and described the atrophic condition of the thyroid gland. And then came a remarkable series of researches. Reverdin and

Kocher showed that the outcome of surgical removal of the thyroid for various diseases was the unlooked for cachexia strumapriiva. Horsley proved that myxoedema could be experimentally produced in monkeys by removal of the healthy thyroid. The various attempts to ingraft the thyroid failed from absorption, but presently George Murray proved that hypodermic injections of extract of fresh thyroid were followed by subsidence of the symptoms of myxoedema, and finally Mackenzie and Fox showed that the gland could be equally advantageously administered by the mouth.

The analyses of Hutchison and others will probably pave the way to a still further simplification by indicating which are the really efficient constituents of the gland material, and some of the alterative effects in diseases other than myxoedema may perhaps be explained by the unexpected organic combination of iodine which is found to be present in this gland.

The relation to exophthalmic goitre, though not yet satisfactorily worked out, is clear enough to show where true lines of fruitful investigation will almost certainly lie.

The investigations of Schäfer and Oliver on the suprarenal body have revealed to us the existence of an internal secretion concerned apparently in maintaining the tone of muscular tissues generally, and especially of those of the vessel walls. And although they have not yielded a cure for Addison's disease they appear to have given us a haemostatic agent of considerable local potency.

HOW ADVANCE MAY BE MADE IN THE FUTURE.

Hitherto we have stood on more or less solid basis of established fact, though there have been many gaps in our knowledge, but it would be interesting to forecast a few of the probable directions in which research in the forthcoming generation is pretty certain to add to the common stores.

With regard to nervous diseases, it seems almost certain that some of the acute types will be brought still more into line with the specific fevers. Anterior poliomyelitis, for example, which occasionally affects two or three members of a family simultaneously, and which shows some striking relationships to the exanthemata, will almost certainly prove to be an acute infective disease.

The nervous sequelae and complications of the exanthemata

are a mine of clinical wealth and suggestion. For they point not only to disseminated foci of cerebral and spinal hyperaemia and extravasation, but also to later changes at first insidious but sometimes far reaching, dependent on the dissemination of the toxic products of bacillary growth.

It may well be that more developed clinical observation may elicit that in the long latent period which we have assumed to exist between an infective disease and its sequelae there has been a real continuity of morbid process translatable by signs and symptoms which one day will be obvious enough. In locomotor ataxy, for instance, it will be strange indeed if the latent period does not reveal some intermediate clinical and pathological changes.

The great group of peripheral neuritis (towards the elucidation of which we are pre-eminently indebted to the Manchester School, especially Dreschfeld, Ross, Bury, and Reynolds) is indeed a meeting place for many etiological factors, but it is especially suggestive as showing the parallel effects produced by toxins which are the outcome of bacillary activity, and by inorganic and organic material introduced by way of the alimentary tract, and perhaps by poisonous products elaborated in the body itself by faulty metabolism.

Now with respect to the therapeutics of these diseases, the elucidation of their natural history has unquestionably done a great deal by teaching us what cause to remove, and so prevent the further extension of the malady, even in some cases up to a fatal issue.

Still it must be confessed that some members of the group show a singular tenacity in going through a certain evolution, even when the peccant cause has been removed. This may seem a disparagement of my original thesis, but knowledge is always justified, and it is something to be able to say that, although remedies have not hitherto materially modified the process, yet that, the cause having been removed, we are tolerably certain that, provided there is no extension to the medullary centres, the cycle will come to an end, and that recovery will ultimately be complete. Further elucidation may yet show a definite method of shortening the morbid process. But if the more complete knowledge of the natural history of these and other obscure nervous diseases does not in the immediate future pave the way to definite antidotes for them, it will at least save us from many a blunder. We

shall learn to leave for a time the morbid process severely alone and to concentrate our therapeutic efforts on food and on the improvement of the general metabolism of the patient.

Can there be any reasonable doubt that we are on the eve of a fuller elucidation of cancer, and that when the history of the organism which we suspect to be behind it has been learned, then the fragmentary and isolated pieces of knowledge which have been painfully and slowly acquired during past generations will slip into their proper places like the blocks in the puzzle of a child? But if the history of previous discoveries in our science goes for anything, this, again, will be an instance of the convergence of work of experimental pathology, biology and chemistry, and of clinical medicine and surgery in their widest connotations.

Gentlemen, I have finished my task. I have tried to drive home the thesis that the advances in the treatment of disease have been real and satisfactory in proportion as they have been harmonious with the complete knowledge of the natural history of disease. I have given various instances in support of this thesis, and others could be given. If we are agreed, what is our duty arising out of this conviction? Surely that we ought to do all that in us lies to maintain, to develop, and to defend experimental research in alliance with clinical work.

Our countrymen are waking from their complacency, and beginning to realize that in our great industries it is imperative, if we would keep our place, that well-directed scientific research should be liberally and steadily maintained. And shall it be said that in the care for the life and health of the community, the noblest and most precious of all industries, we are to be left crippled and poverty-stricken by the absence of suitable equipment?

We need trained workers, not only in our great university laboratories, which are more or less efficiently equipped, but in every large centre of population it is essential that there should be those who are capable and ready to bring special knowledge to bear on the problems of the public health, and that there should be the necessary means to enable the work to be done.

It is not the genius of the English people to look to the State to do everything. Whoever reflects on the trend of political thought must see that more and more devolution

of the national work will go to the municipalities of the country. Let us carry the municipalities with us in an enlightened crusade. That the public bodies are ready to do the right thing so far as their powers permit, and if the plans suggested are practicable, is abundantly manifest in this and other great towns.

And for far-reaching researches in the advancement of pathology which lie beyond the proper limits which the municipal bodies could consider may we not look to the generosity of Englishmen? How much has been given for hospitals and charitable institutions but how little for the endowment of research which will help to lengthen human life and mitigate its physical ills!

The British Medical Association has an honourable record in its yearly series of timely and generous grants to individual workers for special research; and some invaluable work has been fostered and helped in this way. Might it not in the future seek to co-operate with municipal bodies, and through its widespread local branches supply the stimulus and perhaps the pecuniary assistance required to push forward investigation in local laboratories, and to afford the direction, and countenance which solitary workers so much need?

Let us fain hope that the day may come when to the other beneficent functions of this Association there may be added some form of systematized, continuous, and widespread local organization for the scientific study of the problems of disease.