ANNIVERSARY OF THE ROYAL SOCIETY.

ADDRESS BY LORD LISTER.

THE anniversary meeting of the Royal Society was held on St. Andrew's Day.

LORD LISTER, in the course of his presidential address, referred to some of the more distinguished Fellows who had died since the last anniversary. In mentioning Sir William Flower, whom he described as a man of noble and generous nature, ever ready to give his aid and counsel to those who sought it, he said that the arrangements of museum collections was a matter which engaged Flower's earliest attention. One well qualified to speak on the subject had said "the arrangement and exhibition of specimens carried out by Flower in both instances" (the Hunterian Museum and the Natural History Museum) "was so definite an improvement on previous methods that he deserves to be considered as an originator and inventor in museum work. His methods have not only met with general approval, and their application with admiration, but they have been largely adopted by other curators and directors of museums, both at home and abroad." How beautifully he carried his ideas into practice had been, Lord Lister said, a matter of familiar admiration to all who have followed the development of the South Kensington Museum under his hands.

PREVENTIVE INOCULATION.

LORD Lister then observed that one of the most interesting scientific gatherings which the Society had held was the meeting for discussion at which M. Haffkine brought before it his experience and views with regard to preventive inoculation. Lord Lister continued: The first subject with which he dealt was the application of that system of treatment to cholera. He went out to India six years and a half ago with the object of testing there a method which he had recently elaborated. Applying Pasteur's principles of the "atténuation et renforcement des virus," he had succeeded in obtaining the microbe of cholera in two very different degrees of intensity—one so virulent as to produce, when introduced in small quantity beneath the human skin, the most violent inflammatory disturbance, and even mortification, at the seat of inoculation, the other so mild as to cause extremely little reaction or inconvenience. And he had ascertained by experiments upon himself and some scientific friends that if a little of the milder form of the organism was injected hypodermically, and followed a few days later by a similar dose of the more potent variety, introduced, it might be, at a place remote from the site of the first operation, the whole system of the human body had in the interval undergone such a change, that the second potent injection was unable to produce more effect than the original mild one.

This was a perfectly definite and a truly astounding fact: but there were many who doubted whether it would prove applicable for the prevention of cholera. To understand these doubts, it is necessary to bear in mind some very important distinctions that have been established regarding artificial immunity to infective diseases. Pathogenic microbes produce by their growth in organic media poisons or toxins, varying according to the nature of the microbe concerned, but often of astonishing potency; and it is commonly by means of these poisons that the infective diseases produce their fatal effects. The toxins, which are purely chemical products, can be separated by filtration from the microbes that produced them, and animals naturally highly susceptible to their action can be completely protected against them by the administration of successively larger and larger doses. When thus rendered proof against the poisons produced by the microbes, they are secured against the chief causes of their fatality.

But besides this antitoxic immunity, a strikingly different kind of protection against infective diseases may be produced. If, instead of the toxins, the bodies of the microbes themselves are administered to an animal, it acquires a wonderful power of repelling the assaults of that particular kind of micro-organism, which is thus rendered incapable of obtaining a footing among the tissues of the creature. This kind of protection has been termed by Metchnikoff anti-infective immunity. The antitoxic and anti-infective forms of immunity appear to be quite independent of each other. An animal may be brought to a very high degree of protection

against the attacks of a microbe, and yet remain perfectly susceptible to the poisonous action of its toxin.

Now cholera is essentially a toxic disease. It is by the poison which the cholera bacillus produces that the fatal symptoms are occasioned. Hence it might appear at first sight as if an antitoxic treatment could alone give promise of success in dealing with it. Haffkine's injections, on the other hand, prepared with the bodies of the microbe, were essentially anti-infective, not antitoxic.

Haffkine, however, felt confidence in his method, and resolved to give it a trial in India, where the dreadful disease is in some districts awfully prevalent; and he pursued his object in spite of wellnigh insurmountable difficulties with an enthusiastic perseverance and an heroic self-devotion which should never be forgotten. How fully his efforts were crowned with success was evident from the striking statistics which he brought before us, confirmed as they were by Professor Simpson, now of King's College, who had shared his labours in India, and was present at the meeting.

Now that we know the success of these preventive inoculations for cholera, we are perhaps able to explain them. It appears to be established that the cholera bacillus invariably attacks the mucous membrane of the intestinal canal. And if it be admitted that this is always the primary site of its invasion, we can well understand that the anti-infective inoculation, by securely protecting the mucous membrane against the invasion of the microbe, may prevent it from ever developing in the body and from ever producing its deadly toxin.

These considerations enable us to understand Haffkine's position with reference to plague. The plague bacillus, like that of cholera, can be cultivated apart from the animal body in artificial media. Living plague bacilli could of course not be injected; but it is a happy circumstance that their life is not essential to their efficacy for producing anti-infective immunity. Cultures of the microbe could thus be used after being subjected to a temperature high enough to ensure their death, and prevent the possibility of communicating the disease with them.

But another important point claimed his attention. He had noticed in his cholera statistics that among the comparatively few persons who were attacked in spite of inoculation, the disease was as fatal as in the uninoculated. Or, to speak technically, while the absolute mortality was immensely reduced by the inoculations, the case-mortality was unaffected by them. This he attributed to the purely anti-infectious character of his cholera inoculation; and it occurred to him that if he could combine, in the case of plague, the antitoxic with the anti-infective element, he might not only diminish the number of attacks of the disease, but also render them less deadly when they did occur, by robbing the plague toxin of its power for mischief. With this object in view he resolved to cultivate the plague bacilli for so long a time as to allow of an accumulation of their toxin in a concentrated form in the liquid in which they grew; and having devised an ingenious and effective method of culture, he continued it for five or six weeks. He expressly disclaimed any wish to regard the theory that led him to this practice as more than a guess. But whether well founded or not, his guessing has been followed by striking success. It is difficult, when inoculations are practised on a large scale, to obtain accurate statistics as to the relative aggregate mortality among the inoculated and uninoculated; but with the case-mortality it is otherwise. Many patients with plague were admitted into the plague hospitals; and it was easy to learn which of them had received inoculation and compare their cases as regards the proportion of recoveries with those which had not been so treated. The result has been to show incontestably that the case-mortality in the inoculated is less by 50 per cent. than that in the uninoculated. Thus Haffkine's anticipation in that respect seems to have been fully justified.

At the same time the number of attacks appears to have been greatly reduced by inoculation. He brought before us certain comparisons that had been instituted in gaols and elsewhere that had, as he said, the precision of laboratory experiments; where the inoculated and uninoculated were in all other respects under identically similar conditions, and all were under strict supervision, the observations being controlled by independent witnesses. And although the numbers

here were not very large, the facts were extremely convincing. Taken altogether, the evidence brought before us tended to the conclusion that this system of preventive inoculation is, under proper management, capable of reducing the mortality in a plague-stricken district by between 80 and 90 per cent.

At the close of his discourse Haffkine referred with confident hope to typhoid fever. Considering the close analogy that exists between that disease and cholera, he early predicted that the protective method which had proved successful with the one would answer with the other. Indeed, he was only prevented from dealing with typhoid himself on the same lines by the persuasion of friends, who urged that he was already overtaxed by the cholera work. His suggestion has been more recently acted on by Professor Wright of Netley, who has developed with great zeal and ability a method of procedure which appears full of promise. As a member of the Plague Commission he had large opportunities for applying it in India; and although sufficient time has not yet elapsed for testing fully its protective efficacy, he clearly established its freedom from any immediate injurious consequences. Meanwhile, some earlier trials, though on a limited scale, have proved so satisfactory that our army authorities have seen their way to recommending the system to our soldiers going out to South Africa, where the disease is grievously prevalent, and we may fairly anticipate that many a gallant life will thus be preserved.

How long the protection caused by these protective inoculations will last is at present somewhat uncertain. It will no doubt differ in its duration in different diseases. In the case of cholera it appears from Haffkine's results that it continues for upwards of a year. In plague so far as can be judged hitherto, it would also seem to last for at least a twelvemonth. With typhoid there are not yet materials for forming an estimate.

I have thought it not unfitting to dwell upon this subject of preventive inoculation on the present occasion, because, while it is of supreme practical importance, it is in many directions of high scientific interest.

CLINICAL RESEARCH IN LONDON.

THE MIDDLESEX HOSPITAL. *Cancer Investigation Scheme.*

LAST week the quarterly court of Governors of the Middlesex Hospital sanctioned a scheme already considered by the Managing and Medical Committees for the systematic investigation of cancer.

The new Cancer Research Laboratories will be in full working order by the end of the year. The accommodation provided for the purpose of the scheme includes pathological and chemical laboratories, and a director's office. The laboratories, which are situated in the recently-built Cancer Wing of the hospital, are fitted up very completely; and the work which it is proposed to do will be carried on under the most favourable conditions. The permanent staff of the laboratories will consist of a director, an assistant to the director, and a registrar. It is also proposed to afford facilities to others who may be specially interested in this part of pathology, and are qualified to carry on original work in connection with it. Mr. Alexander Foulerton, F.R.C.S., has been appointed Director of the Laboratories, and an advertisement inviting applications for the other posts appeared in the *BRITISH MEDICAL JOURNAL* of December 2nd. The Governors of the Middlesex Hospital are to be congratulated on the public spirit which has prompted them thus seriously to make an effort to deal with what is in many ways the most terrible disease which afflicts mankind, and we are glad to be able to add that a generous donation of £1,000 from Mr. Arthur W. Davis has already been placed at their disposal for the furtherance of the objects of the scheme.

According to this scheme a Cancer Investigation Committee is to be formed, consisting of the surgeons to the hospital and the lecturers on medicine, surgery, and pathology, the director of the Cancer Research Laboratories being the scientific secretary. This Committee would superintend the issue of reports, the business of the laboratories, and the election of members of its staff. The responsible director will be aided by an assistant and also by a medical officer and

registrar, who would have access to the wards for the purpose of obtaining information needed for the department. Three rooms already existing in the Cancer Block are suggested for laboratory accommodation: one as the director's office, the second as the chemical, and the third as the bacteriological and microscopic laboratory, but yet larger premises are held as desirable.

The necessary expenditure for preliminary alterations and fittings in the three rooms considered suitable for research purposes is estimated at £465, the annual expenses at £650. The latter include a salary of £250 to the director, £100 to his assistant, at least for the first year, £100 to the medical officer and registrar, with £100 for board and residence. £30 is apportioned to the laboratory assistant, whilst the estimate of the maintenance of the laboratories is £70.

The framers of the scheme also suggest the scope of the investigations.

(a) Every case of cancer and sarcoma in the hospital is to undergo a systematic bacteriological and histological examination. The results of this systematic examination would be applied to an attempt to formulate a classification of sarcomata, hitherto very unsatisfactory, and to the investigation of the causes of both forms of malignant disease.

(b) As respecting causation, the framers of the scheme note that in the case of carcinoma recent theories not universally accepted as to a blastomycetic causation require investigation. The arguments in favour of them have been very ably urged by Italian pathologists, and careful bacteriological examinations are required, if only for the purpose of obtaining negative evidence. The theory of a protozoal causation has now been practically abandoned by pathologists, and probably would not require any further investigation. The older theory as to the direct origin of carcinoma from normal epithelial cells as the result of a perverted or irregular overgrowth, and independently of the influence of any parasites from without, would seem to offer the line of research from which definite results might most probably be expected.

(c) As to the causation of sarcoma, a knowledge of the pathology of that form of malignant disease is even less definite than in the case of carcinoma. We have reasonable grounds for assuming that all varieties of carcinoma are, at any rate, manifestations of one and the same kind of morbid action. But with regard to sarcoma, there is reason to believe that the term, as ordinarily used, includes the results of more than one morbid process. Recent investigators (Curtis, Busse, and Nello Biargi) have shown that some of the cases, which clinically would be classed as sarcomata, are definite instances of yeast infection. And there is also presumptive evidence that some of the cases which are clinically recognised as "lympho-sarcoma" may similarly be caused by a parasitic infection of some sort. On the other hand, there is no reason for supposing that all cases of sarcoma are due to a parasitic infection. The relation of some cases of sarcoma to chronic inflammation, arising independently of the action of micro-organisms, would require investigation.

The scheme urges the value of a precise and scientific tabulation of cases of malignant disease in connection with public health statistics. It is urged that it is not advisable that the term "cancer" should any longer be made to include sarcoma in the Registrar-General's returns, which are still of very small value in assisting to the formation of a correct judgment as to the age and sex incidence of both diseases. Systematic examination of the blood and quantitative examination of the urine in malignant cases are also indicated as specially suited for laboratory investigation.

The Medical Committee have accepted in a general sense the above suggestions for the pursuit of investigations on malignant disease.

THE WESTMINSTER HOSPITAL. *Clinical Laboratory.*

A new departure has been recently taken at Westminster Hospital with regard to the Pathological Department, and the Governors are taking steps to place the whole of that department on a footing conformable with the modern advances of that branch of scientific medicine. A clinical laboratory is being constructed which will be in working order early in the New Year, and the Governors are sparing no expense to render it thoroughly efficient. At the same time it is recognised that