Medical research in wartime / by Sir Edward Mellanby.

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MEDICAL RESEARCH IN WARTIME*

BY

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In his address to celebrate the centenary of Ludwig Mond, in whose memory this lectureship was founded, Prof. Donnan summed him up as an "eminent investigator, creator of new industries, princely benefactor of science, great patron and lover of art." This is a fine epitaph. It is also said that Ludwig Mond "cared little for words but much for deeds." This is rather hard on his lecturer, but possibly the censure might be mitigated if the lecturer confined his attention to the deeds of others, especially if such deeds represented the successful application of knowledge gained by research to such practical issues as the prevention and cure of disease and injuries in man.

I should first like to stress the fact that, even in wartime—or at least in war as at present developed—medical and biological research has concerned itself wholly with the defence of man against disease and injury and with the promotion of his safety, efficiency, and comfort. It is necessary to point this out because of the endless references in religious, theological, and even philosophical addresses, particularly those broadcast nowadays, to the prostitution and degradation of science, especially for purposes of war. There is indeed some suggestion that there exists in science and scientific men a kind of wickedness not shared by the humanities and by those engaged in their study. This state of affairs, of course, has nothing to do with science as such, since it is only systematized knowledge, and, like any other knowledge, can sometimes be turned to the benefit and sometimes to the harm of mankind, according to the demand of human nature. If society is so arranged and the public mind so determines, scientific knowledge can be used so as to be wholly beneficial. Whatever the future may hold in this respect it can be claimed that, even in wartime, medical research and its participants come to the bar with clean hands and that their work has, up to the present time, only conferred untold benefit upon mankind and has not been directed to his maiming and extermination.

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When the attention of the Secretary of State for War was recently drawn to the fact that he had not mentioned either the health of the Army or the work of the Royal Army Medical Corps in his survey of Army activities when introducing the Army estimates, he replied that this was because the Army's history in this respect for the past year had been a blank, to the immense credit of the Army medical and nursing services. Well, that is one way of looking at it. But to anybody with a knowledge of the history of war, who realizes that, even so late as the South African War, more soldiers died of disease than were killed in battle, and that before that time many of the greatest campaigns between nations were settled by the incidence of disease among troops and civilians rather than by arms, the modern official attitude towards this greatest enemy of man must be regarded as at least worthy of comment.

Disease in Earlier Wars

Napoleon started his Russian campaign with an army of half a million men. When the retreat from Moscow began there were not more than 80,000 fit for duty (Oct. 19). By Dec. 8 this army had shrunk to 20,000 sick and disheartened men. Most of the losses were due to illness; and typhus, dysentery, pneumonia, and enteric fevers were the active agents. In 1813 Napoleon started his new campaign once more with 500,000 men. By the time he had to fight the Allies at Leipzig his force was reduced to 170,000, his losses being 105,000 battle casualties and 219,000 by disease. In the Crimean War France sent 309,000 soldiers to Russia, and at one period 200,000 of them were in hospital—50,000 because of wounds, 150,000 because of disease. Many other examples of a similar or even worse nature could be given.

No wonder Zinsser wrote in his book *Rats, Lice, and History*: "And typhus, with its brothers and sisters—plague, cholera, typhoid, dysentery—has decided more campaigns than Caesar, Hannibal, Napoleon, and all the inspector-generals of history. The epidemics get the blame for defeat, the generals the credit for victory. It ought to be the other way round."

An Outstanding Achievement

It may be too early to exult, because there is still the great menace of malaria to be faced by the armies of the Far East, especially in Burma, and this disease may well settle the campaign. Up to the present, however, the health record of the British Navy, Army, and Air Force has been so good that it must be considered to be one of the outstanding achievements of the war. Even the Eighth Army, during its three years in Egypt, Libya, and Tunisia, where it has been fighting under conditions ideal for the development of dysentery, typhoid, cholera, small-pox, and typhus, has been remarkably free from these deadly diseases. The incidence of typhus, tetanus, typhoid, cholera, and small-pox has been almost negligible.

Protection by inoculation was given to the troops, before leaving this country, against typhoid and paratyphoid fever

cholera, small-pox, tetanus, and yellow fever. This protection has proved most effective. We now know, for instance, how much greater protection has been afforded to our own troops by typhoid vaccination as compared with that of the Italians and Germans. This was reflected especially in the high endemic rate of these diseases among the Italian and German prisoners in our hands as compared with that among our own men who were prisoners of the Italians. When the Italian and German prisoners were inoculated with our vaccine, typhoid fever ceased abruptly and the endemic level remained low thereafter. It is undoubted that our T.A.B. vaccine made from strains rich in the Vi antigen has proved much more effective than the Italian vaccine made from non-virulent strains. It will be remembered that the Vi antigen was a discovery of a British research worker.

In the case of tetanus, although it is only fair to say that a high incidence of this was not expected in the Western Desert, active immunization by tetanus toxoid has also worked well. The incidence among British troops in the Middle East was 0.013%, whereas in the South African force, in which active immunization had not been carried out, the incidence of tetanus was 0.16%, or twelve times as great.

The incidence of dysentery, even in the fly-swarming area of the Western Desert, has also remained relatively low among British troops, and those who have been affected have reacted well to recently discovered drugs. The incidence of dysentery among enemy troops, on the other hand, has been much higher, and it is said that a part at least of our success at El Alamein was due to the enfeeblement of both Germans and Italians by widespread dysentery.

All honour must be paid to the medical services of the Navy, Army, and Air Force for their successful achievements in maintaining the health and efficiency of the Services under fighting conditions, and credit is also due to the Ministries of Health and of Food and to the medical services of this country for the high standard of health—higher even than it has ever been in peacetime—of the general population. Having paid this tribute, I regard it as a duty to remind you that these health results, both in the Services and among civilians, during war have a more fundamental cause than the administration and practice of medical men. I refer, of course, to the work of those engaged in medical research, who have provided the knowledge for the maintenance of health and the methods for preventing and for curing the deadly diseases of war. So far as I am aware, in the public references made to the subject of health and disease in wartime no credit has been given and no reference has been made to this magnificent achievement of scientific research. The work of Government Departments (Service and civil), of medical men (Service or civil), and of nursing staff in controlling disease can only be as good as knowledge allows it to be, and this knowledge has come, and can only come, by medical research. I suggest

that medical scientists have served this country and its fighting Services well, and in counting our blessings let us not forget the enormous debt of gratitude we owe to this small but almost unknown body of men and women, scattered about in the research institutes, universities, and hospitals, who, by devoting their lives to the search for new knowledge, have forged the weapons which have proved so effective for the maintenance and restoration of health in wartime.

The Medical Research Council

In the course of my further remarks it will be necessary for me to refer often to the Medical Research Council, and it may be well to explain what this body is. Although it is an institution of the State, financed by the Government, it is not a large self-contained Department like the Ministry of Health and other Government Departments. The Council itself is a small body which meets once a month, and is made up for the most part of men of great experience in different branches of medical science, changing partially each year. It has a small administrative staff and a larger, though still small, permanent research staff. As its object is to help and co-ordinate medical research generally, much of the work with which it is associated is done in the universities and hospitals of the country, including those of this city, by the professors, lecturers, and medical men on the staffs of these institutions When, therefore, I talk about the Medical Research Council, this is simply a short way of referring to the organized medical research of most of those engaged professionally in this country in such labours. Any success it attains or has attained can only be regarded as a reflection of our general standard of medical research, and must largely depend also on the maintenance of the good will and active co-operation of these investigators.

Even in peacetime a large proportion of the medical research in Britain is in one way or another associated with the Medical Research Council. In war the natural trend of events makes this association closer. The reason for this is obvious. Most men engaged in research want to direct their energies to the solution of problems that benefit the war effort. A body like the Medical Research Council, working closely with the Services and other Government Departments, is more aware of the immediate problems requiring investigation. In these times, therefore, either research workers ask the Council for advice on important problems or else the Council approaches suitable workers for their help. Working committees are formed of groups of investigators in each subject, so that each worker can be kept informed of the investigations of others and the researches can be co-ordinated. About 40 research committees on different war problems have been formed, and these cover a large part of the field of medical science. Representatives of the Services are members of all war committees. It must be emphasized that the initiative for action often comes from outside the Medical Research Council.

In peacetime the Medical Research Council does not finance research work which is exclusively of interest to the fighting Services, but from the outbreak of the present war this policy was changed, and all the resources, both of personnel and of finance, were made available for the solution of Service problems. A great reorientation of research took place, fundamental work of a long-term nature being largely replaced by investigations of a short *ad hoc* nature with immediate practical objectives. However, even in wartime, some fundamental research has continued, partly because it is not possible to place every individual worker on a war problem, and partly because some practical problems of war are always arising which can only be solved by a study of the basic principles of medical science.

Under normal peacetime conditions the Medical Research Council has no administrative duties outside the promotion and carrying out of research. On the whole this is a most salutary rule, although it has its drawbacks. For instance, it might happen that great delay in the application of new medical discoveries to the public service would be shortened if the discoverers had some say in administration. On the other hand, if a research department normally undertook administrative duties outside research it would often lead to great friction with the large administrative departments. Nor has it yet proved possible to obtain and retain the best research workers in an administrative department. These men want to work with their own kith and kin in an atmosphere of freedom, and they will not become a subsidiary part of a large administrative machine.

The general attitude of politicians and Government officials to all scientific men is that they must be "on tap" and not "on top"—*vide* the *Times*. Some scientists say they would not object to this position if there was any evidence that their superior administrators knew when, where, and how to turn on the tap and how to make use of the beverage (not "Beveridge") when they had got it.

If, then, a research department is outside the administrative sphere, it is obvious that it must always be prepared, when asked, to advise other Government Departments on technical matters within its competence, either by supplying information or by making the necessary investigations. As I shall show later, the advisory functions of the Medical Research Council have increased greatly during the war and a number of important actions of Government have been guided by the Council. In addition, even before the outbreak of war the pressure of events forced the Medical Research Council to break its rule and to take on administrative duties, and some of these instances will be mentioned not only because they have been very effective but also because they have filled important gaps in medical service and will probably have to continue in some form or other after the war.

No success could have been obtained had not very close and friendly relations been established in recent years between the Ministry of Health and the Medical Research Council. First let me say a few words about a new service known as the "Emergency Public Health Laboratory Service."

The Emergency Public Health Laboratory Service

The history of the establishment of this service is one of great interest, which will no doubt be told in full some day. It began with discussions between the Medical Research Council and the Committee of Imperial Defence, and more particularly with its secretary, Sir Maurice (now Lord) Hankey, who on this and many other occasions was a tower of strength and a most powerful supporter of scientific projects. The result was that a committee of the Cabinet asked the Council (with the blessing of the Ministry of Health) to organize and prepare for the establishment of this new service, to be ready on the outbreak of war. Laboratories were selected all over the country (mostly in public schools and universities), apparatus was purchased and stored, transport was arranged, and bacteriologists were chosen to take up their duties on receiving instructions. Immediately on the outbreak of war the laboratories were ready, with complete staff and equipment. Fifteen new laboratories were started and 28 other working laboratories were brought into the scheme, and these are still functioning as one compact service.

It is not possible to disclose all the reasons for this new service, but it will be obvious that one good reason was the expectation that large-scale bombing of industrial centres would necessitate mass movement of the population, and that this, together with the interference with water and other supplies, might well result in epidemics. The fact that there have been no major epidemics during the war and that, indeed, the epidemiological health of the country has been better than in peacetime is at least partially due to this network of laboratories. It has been the constant endeavour of the staff to catch such epidemics at the beginning and, by co-operating with local health authorities, to find and eliminate the cause, and deal with the situation vigorously. By detecting the cause and eliminating it by segregation or otherwise, by determining the methods of spread and dealing with these by inoculation or other means, their efforts have been very successful. Let me give one of many examples of how this service works in dealing with an outbreak of infectious disease.

This is an excellent example of co-ordinated laboratory and field work. The occurrence of several scattered cases of typhoid fever in a certain county was investigated by one of the Emergency Laboratories, and the opinion was formed that the infecting agent had probably been carried by milk. Although most of the patients had been supplied from different dairies, all these dairies had drawn some of their milk from a particular wholesale depot. Inquiry showed that the milk coming into this depot was derived from four

different sources. One of these, a group of farms in another county, came especially under suspicion, but inspection of each of the farms failed to reveal the presence of anyone with a history of typhoid fever. The quest for the original source of infection was thus held up for the time being. One point, however, was established: the strains of typhoid bacilli isolated from the patients were referred to a specialist attached to the headquarters of the Service, who found that all these strains belonged to a single bacteriophage type, D4, which had not previously been encountered in Britain. This left little doubt that all the patients had been infected from the same original source.

Months elapsed before a further group of cases occurred, this time in a different part of the county from that in which the first outbreak took place. It was found that the dairy supplying the patients had received milk from the same wholesale depot as before, and again the organisms isolated from the cases belonged to the D4 type. The clue to the puzzle was provided later, when a single case of typhoid fever occurred in the other county from which some of the depot's milk supply came. Inquiry into the source of infection in this case showed that the patient had until recently been employed as a milkman at one of the farms of the group that had been under suspicion a year earlier. A full investigation at this farm led to the discovery that the owner, although his medical history had not given rise to suspicion on the former occasion, was in fact a chronic typhoid carrier. It could therefore be concluded that, through faulty personal hygiene, he had occasionally infected the milk which he had been sending to the wholesale depot. Thus the co-operation of several laboratories with each other and with field investigators led finally to the detection of the distant source responsible for the outbreaks.

Blood Transfusion Service

The prime movers in the promotion of the Blood Transfusion Service, now so active and successful throughout the country, were a group of pathologists who independently came to the Council a year before the outbreak of war (indeed, immediately after the Munich episode) because they needed some official backing and a central organization to carry out their ideas.

The Council limited its own activities to the establishment and running of the four London blood transfusion depots, to the erection of plasma freeze-drying plant, and to helping the Navy, Army, Air Force, and Emergency Medical Service in their own efforts to supply blood or its products for transfusion, either by advice or investigation or by providing additional supplies. The spin-freeze-drying plant, for which the Wellcome Foundation supplied £20,000, is a fine example of ingenuity and skill. It is capable of drying 5,000 bottles of plasma a week (each bottle containing the blood plasma of three donors). It actually dries 2,500 bottles a week, and of these 800 bottles are for the Navy, 800 for the Army, and the remainder are distributed according to demand (Navy, Army, Air Force, and civilian). In addition the staff of this service have carried out a great deal of research on blood compatibility and incompatibility, and have certainly improved the quality of the transfusion products. There has been a fine

spirit of co-operation among all workers, both civil and Service, in this important project, and the country owes a debt of gratitude to them for providing both the civil population and the Forces with the vast amounts of material for transfusion that have been forthcoming. The lives of thousands of wounded Service men and civilians have been saved by transfusion in this war, and it is to be hoped that an organization of a similar nature, to cover the needs of the whole country, will remain in peacetime.

Pooling and Dispersal of Biological Immunizing Products

On behalf and at the request of the Government, the Medical Research Council made arrangements before the war for the pooling and distribution of emergency immunological agents to meet the partial needs of the fighting Services and the anticipated requirements of the civil population. By undertaking the provision of large stocks of such agents as tetanus antitoxin, gas-gangrene antitoxin, diphtheria toxoid, and various vaccines such as typhoid-paratyphoid, typhus vaccines, and other sera, and acting as a central distributing agency, it is obvious that much expense was saved to the country, properly controlled distribution was obtained, a strict eye was kept on the potency and general excellence of the products, and new discoveries of importance were quickly brought into use in their preparation.

Registration and Allocation of Pathologists

In addition to these services the Medical Research Council set up a committee in 1938 to keep a register of and to allocate pathologists to war emergency duties. This committee has filled a most important gap in the medical services, and its very success in arranging for the supply of competent pathologists to the civil and military hospitals, both here and abroad, and also for that of laboratory assistants at a time when there is but a limited supply of such people, has hidden the difficulties of the task and even its very existence.

Advisory Functions of the M.R.C. in War

It may be well now to refer briefly to some of the more important instances in which organized medical research has been called on during the war to give advice to various Government Departments. Sometimes this advice could be given immediately on the basis of present knowledge, but often a considerable amount of *ad hoc* research had to be carried out to obtain the necessary information.

Food and Nutrition

Research workers on nutrition have had the satisfaction of seeing the adoption during wartime of some of the teachings on nutrition that they have been urging during the past 20 years or more. Among those worthy of mention are the increased consumption of milk by infants and children and by pregnant and nursing mothers, also the increased consumption of potatoes and other vegetables, and the change of bread made from white flour to flour of higher

extraction. It would, however, be idle to think that all these changes took place because it was thought that they would be nutritionally advantageous. This was probably the reason in the case of milk, but the economic and supply factors were the paramount causes in the bread and vegetable changes. It is, however, no good quibbling over the reasons; the fact is, the changes have been made and the country's health has improved accordingly.

The Medical Research Council took a strong line over the bread question almost from the beginning of the war, and published memoranda on the need for adopting an 85% extracted flour with a minimum of fibre and a maximum of wheat germ, vitamin B complex, and iron, together with additional calcium carbonate. With the excellent co-operation of the workers in the Cereals Division of the Ministry of Food, test loaves were made and detailed specifications of the desirable bread were issued. These were ultimately adopted by the Ministry, except that they halved the proposed amount of calcium carbonate. This was a pity, because the basis of this advice was most carefully considered and the proposals were unanimously made, both by scientists and by clinicians consulted by the Council. Some further improvement in the calcium content of bread has been recently made by the addition of 2 lb. of dried separated milk to 280 lb. of flour. The need for adding vitamins A and D to all margarine was also strongly pressed.

One of the paramount difficulties of mass feeding under conditions of control and restriction has been to find the best means of dealing with exceptions, such as are presented by invalids and those requiring special food. Action in this respect has been taken by the Ministries of Food and of Health on the advice of a special committee set up by the Medical Research Council known as the Food Rationing (Special Diets) Advisory Committee. Besides meeting the nutritional needs of those really requiring special consideration, this committee has to deal with people—only a small proportion of the whole, but a large number *in toto*—who think they are ill or who are full of special fads and fancies. All kinds of diseases have been catered for—diabetes, tuberculosis, steatorrhoea, dyspepsia, fevers and other acute illnesses—and the consensus of opinion is that the scheme has worked well. All individual cases, on special grounds, were considered by members of the committee and received careful attention. Any criticism there has been is largely due to misunderstanding of the problem to be faced. The view of the committee is that special feeding arrangements, in time of restriction, can only be made which aim at the rapid return of sick people to work or the retention at work of those chronically ill. It would be easy and natural to be kind to all sick and old people and give them the best of everything, but what they got in this way would clearly be at the expense of healthy people who have to carry on the work of the country and who must be kept healthy. Decisions were therefore made strictly on medical and scientific grounds with these objects in view, and compassionate grounds were not allowed to influence their advice. With very few exceptions, the medical men of the country have played their part well under difficult circumstances. Taking into account the great difficulties met with in rationing in the last war because of the claims of invalids, it cannot be considered that the labours of this committee have been in vain.

Drugs

On the whole the country has been well served with supplies of essential drugs. In the last war the Medical Research Council

learned its lesson in the case of arsphenamine (salvarsan), an essential substance for the treatment of syphilis discovered by Ehrlich and supplied to us entirely by Germany. There were hardly any stocks in this country at the outbreak of the last war, and since none could be imported it fell to the Medical Research Committee (now Council) to arrange both for the study of its preparation and for large-scale manufacture. The inexplicable toxicity of some batches of the drug greatly added to the difficulty of supply. Even to this day all new batches of arsphenamine and its products are tested biologically before sale. Well before the present war, with the approval of the Committee of Imperial Defence, the Council initiated a movement which ensured that all essential foreign drugs not previously made in this country should be manufactured here if war broke out. A list of these drugs was drawn up and the Association of British Chemical Manufacturers was invited to divide the task of studying their preparation and manufacture among different firms, and so the position was secured. Except in the case of mepacrine (the German atebrin), the needs of which suddenly became enormous because of the loss of the world's main source of quinine when Japan took the Dutch East Indies, these arrangements have worked satisfactorily and, so far as supplies are concerned, no sick person has gone without the proper treatment for his condition.

As regards drugs in general, the Therapeutic Requirements Committee of the Medical Research Council has advised the Ministries of Health and of Supply on allocations when shortages of drugs were apparent, and have suggested substitutes. They also classified all drugs in categories of relative importance, so that these Ministries knew beforehand how essential each substance was in treatment and how urgent or otherwise it was that imports should be maintained or increased.

It would be possible to spend much time on this question of advice given by the Medical Research Council during war, but I must limit myself to the brief mention of two other instances. The Care of Shipwrecked Personnel Committee has advised the Navy and Ministry of War Transport on the care of shipwrecked sailors. Much research had to be carried out on the many problems raised. Most of these experiments had to be made on human beings, and it may be of interest to add that for part of this work conscientious objectors volunteered their services and cheerfully suffered a good deal of discomfort. One notable decision was made by this committee—namely, that water supplies were far more important than food supplies to shipwrecked sailors—and action was taken accordingly.

When the incidence of tuberculosis greatly increased early in the war, the Ministry of Health asked the Council to study this subject, giving its members the widest terms of reference. The committee set up to do this work not only designed a new mass-radiography apparatus, which will shortly be in general use, and tested it on thousands of workmen and others, but also drew up a scheme for the care and treatment of tuberculous people, which was accepted by the Government and formed the basis for legislation. This was no mean achievement, and will have great repercussions on the incidence of this disease in the near future.

I have given an account of these co-operative developments of wartime because they seem to me to illustrate how a research body and administrative Government Departments should work together, and how fruitful and rapid such co-operation can be. If only this system could be continued and extended we should hear much less about the frustration of science.

Nevertheless, I should be sorry if I gave the impression that all liaison work of this nature has been as successful as the instances described. Much has been said and written during the war about the failure of Government Departments to make use of scientific help. Great improvement seems to have taken place in this respect, especially in the physical, chemical, and engineering sciences, but there are still many sad failures and delays to bring the fruits of medical science into the war effort. These are generally due to human frailties and not to wrong machinery.

Medical Research for the Fighting Services

Much of the research work previously mentioned has been concerned primarily with civil life under war conditions and only secondarily with the Services. I should like to refer briefly now to war work with greater implications to the Services and less, but still often substantial, advantage for the civil population. This has fallen into two main groups: first, work of a clinical and pathological nature on such problems as wounds, burns, fractures, infection of damaged tissues, traumatic shock, blood transfusion, and brain and nerve injuries; secondly, the study of the best means of increasing the efficiency, safety, and comfort of fighting personnel. This latter group calls for investigation mainly by physiologists and psychologists.

As regards the work centring round wounds and injuries, the two main problems are those of traumatic shock and infection, which are the factors determining death. If shock and infection can be avoided or treated satisfactorily, modern surgery can ensure recovery after the severest mutilation. Briefly, the research work on traumatic shock has been disappointing in spite of the greatest efforts both here and in America, and no doubt also in enemy countries. Between the two wars practically no advance in fundamental knowledge of the subject took place and nothing comparable to the discovery of blood transfusion that came in the last war. Methods of transfusion of blood and its products have, of course, improved and their use has been greatly extended, but we have little or no more knowledge of the pathological process of shock, and there are still many instances of shock developing and proving fatal in spite of blood transfusion. Confusion has been introduced into the study of shock by the difficulty of defining the condition, and some research workers have been more iconoclastic than constructive in their teachings. Histamine as the curative agent, accepted in the last war, has been generally repudiated. The histamine hypothesis served its

purpose well, for it was mainly instrumental in introducing the practice of treating shock by blood transfusion. A small beam of light on the subject of traumatic shock has recently appeared from a neighbouring university, but whether it will wax or wane in strength only the future can tell.

In the case of infection, both general and wound infection, quite another story must be told; it represents the greatest medical advance of the war, and will be of inestimable value to mankind at all times.

A Great Medical Advance

The astounding advance in recent years in combating generalized blood infection by chemotherapeutic drugs is so well known as to require but little emphasis. Deadly diseases like streptococcal septicaemias, cerebrospinal fever, and pneumonias have had their lethal effects greatly reduced by the sulphonamide derivatives. Great progress has been made on this subject, even during the war, and newer and better sulphonamide drugs, which are both more effective in their action and less toxic to the patient, have been discovered. The field of action is also being extended, and now includes excellent curative effects of the more insoluble products, sulphaguanidine and succinyl sulphathiazole, in bacillary dysenteries and probably even in the diarrhoeas of infants and young children, which account for so many deaths in this country.

Recent reports from Britain and from the U.S.A. all bear witness to the remarkable curative effects of penicillin. The great difficulties of making this substance on a large scale are gradually being overcome, but it will probably be some time before it is an easily acquirable remedy. Penicillin has important effects even in staphylococcal septicaemia, a condition which previously has not responded to treatment even with the sulphonamide drugs. In a large series of such cases in the U.S.A. treated by penicillin, previously nearly always fatal, the mortality rate came down to 20%. In chronic bone infections also, which have previously resisted all treatment for months or years, the curative effect of penicillin has proved to be very great. Penicillin has the advantage of curing infections by many sulphonamide-resisting micro-organisms. Almost every week new fields in which penicillin is effective come to light.

So far I have mentioned the use of these bacteriostatic drugs given systemically, but mention must also be made of a very important development of the war—namely, the successful local treatment of infected wounds and injuries. Many will remember that the vast experience of the last war indicated that treatment of wounds by antiseptics was regarded generally as a failure. Medical research in this war is coming to the opposite conclusion, and we are now, by the use of these substances, in the position of having much greater control of wound sepsis. The same applies to burns and industrial injuries. Lister would have been interested in this turn of the wheel.

The recent success of local treatment depends on the discovery of new antiseptics—the sulphonamides, especially sulphanilamide and sulphathiazole ; also penicillin, propamidine, and the amino-acridine compounds, of which proflavine (2:8-diamino-acridine) is the best-known. Almost as important in the success attained in this field is better knowledge of how to use antiseptics.

It is interesting to note that, except for the sulphonamides and in this case, also, their early clinical establishment depended largely on British research), the development of these drugs and the knowledge of their antiseptic properties in wounds has been mainly done in this country. Much of the success obtained in this recent work has depended on discoveries related to the right way of applying them, and this side of the problem still needs extending. What is required is low solubility, which allows a small but effective concentration, together with long persistent action. These conditions have been obtained with the sulphonamides, proflavine, and propamidine, which are applied to the wounds in solid or semi-solid form and allowed to act over long periods. Penicillin, while very strongly bacteriostatic, has the drawback of being too rapidly absorbed and requires constant application, but recent work indicates that it may be possible in the future to use preparations which, while themselves inactive, slowly dissociate, with the liberation of active penicillin.

Generally speaking, the advance in the treatment of infection by systemic, alimentary, and local methods has been amazing, and it looks as if, apart from virus infection, the back of this important problem is broken. The value of recent medical research in this field, both to man and to animal, cannot be exaggerated, and a victory over disease has been won which, in terms of saving life, will in a short time far surpass the losses caused even by such events as world wars.

Nothing can be more important than that the medical man, both Service and civilian, should realize his responsibility in keeping abreast of this rapid development in treating infection, both local and generalized, by these drugs. It is unpleasant to be constantly reminded that gonorrhoea is on the increase in this country, at a time when doctors have at their disposal a drug which, some experts declare, will cure 90% of such cases in three days' treatment. It is of interest to note that sulphonamide-resistant gonorrhoea cases, which, although relatively few in number, are a real social burden, can be cured in two days by penicillin.

Research on Fighting Personnel

One of the most remarkable developments of the war, which has been largely in the hands of medical scientists, has had nothing to do with the study of clinical conditions, but has been concerned with the maintenance of the safety, efficiency, and comfort of fighting personnel. With the vast mechanization of combat the tendency has been to centre most interest on

instruments of war and to leave the men who had to use such instruments to get on as well as they could. Many machines were not only intricate in their nature but placed the individuals working them in such unnatural conditions that it was impossible to retain their efficiency and often, indeed, their judgment or consciousness. Many instruments of war demand the highest skill and intelligence. An aircraft, a tank, or a submarine with crews whose surroundings have lowered or deprived them of this intelligence is not much use. Again, all such instruments must be so designed as to allow the men to work them in comfort. Personnel must also be chosen who have the best natural aptitude for working them. The growing importance of these and many related problems has resulted in the setting up of three committees—the Flying Personnel Research Committee, the Military Personnel Research Committee, and the Royal Naval Personnel Research Committee. The first of these was started by the Air Ministry a year before the outbreak of war, and the Military Personnel Research Committee and the Royal Naval Personnel Research Committee are committees of the Medical Research Council, upon which the Army and Navy respectively are strongly represented, appointed during the war. Each main committee has a number of working subcommittees to investigate special problems. While it would be wrong to give the impression that this line of research is entirely novel, it is true to say that the war has tended to emphasize its importance and to crystallize the point of view of the primary need for looking after the interests of the fighting man in relation to his weapon and his environment. Both lack of time and the necessity for war secrecy prevent me from dealing with this particular aspect of war research in any detail, but probably I can best give you an idea of the work and the kind of problems to be studied by referring briefly to some of the abnormal conditions an air crew have to withstand and yet retain the fullest intelligence. As an aircraft ascends the atmosphere becomes rarified and the pressure of oxygen diminishes. Ascending from sea level, aviators breathing ordinarily would become unconscious at an altitude of 16,000 feet, and they therefore require oxygen supplied to them from cylinders and delivered to their lungs through masks well before this height is reached. Even breathing pure oxygen in this way, they would become unconscious at about 42,000 feet, and above this height must breathe it under pressure, and, since the lungs would refuse to work if the pressure were applied only through their mouths, it is necessary that the oxygen should be supplied under more complicated conditions. But oxygen is not given simply to retain consciousness in the airmen. Consciousness may well be retained, but the crew may lose their intelligence and judgment. An individual who is only partially supplied with oxygen is rather like a drunken man, and not only does not realize his incompetency but also resents being told this fact. Such a mental condition can have almost unbelievable effects on

behaviour, and you may have heard stories from time to time of such incidents. One such case was related recently by Dr. Bryan Matthews, who is head of the Physiology Laboratory of the Royal Air Force. While at a great height the pilot announced to the crew through the intercommunication set that he was about to land. He thereupon guided his plane gently along the upper surface of a cloud. Descending rapidly through the cloud he then proceeded to tell the crew to get out and began to do so himself. Fortunately the navigator understood what was happening and rapidly seized the controls. There is no place for amusing episodes of this kind in an aircraft, and not only is the efficient supply of oxygen a matter of first-class importance in aviation but the varied conditions to be met make it a difficult problem to ensure this.

In addition to the provision of oxygen supplies for aviators, there are a number of other important conditions from which they have to be protected. When an aircraft turns in the air the crew and plane itself are subjected to an increase in gravitational effect. This may be 3, 4, 5, 6, or more times ordinary gravity, according to the speed of the aircraft and curvature of the turn. At about 5 g. blood is driven from his retina and he develops the condition of "black-out"—i.e., he is momentarily blind. At about 6 g. he becomes unconscious, again only temporarily, but during these few seconds he may have covered much space and, since he may be turning to avoid action or chasing an enemy plane, it is of the greatest importance that his wits and eyesight should be perfect during the turn. The problem therefore is to provide the airman with such conditions that his threshold for blacking-out is high, and yet it must not be higher than that which the aircraft will stand. Full consciousness would be no consolation if the aircraft broke up. Another trouble aviators have to meet at high altitude is due to the nitrogen dissolved in their blood coming out of solution and forming bubbles. These cause intense pain in joints and muscles, which may pass on to collapse and unconsciousness; and the condition is known as "bends." It is now known that "bends" can be mitigated by washing out the nitrogen from the tissues before ascent.

You will see that these problems require much research, and it is the object of the physiologist to arrange his investigations so that as performance of aircraft becomes greater so also must the airman be kept provided with better means to increase his own powers of control. So far the physiologist has responded to all calls, and improvement in aircraft performance has been accompanied by equal powers of control. Submarines and tanks also have their own problems, and much work has been done to promote the efficiency of their crews under the many different conditions which may arise. It would be possible to give many other examples of investigations on personnel necessary in wartime—clothing to meet the extremes of heat and cold as met with in Persia or on an Arctic convoy respectively, the best diet for normal and extreme conditions, food for

special purposes like commando operations, conditions for optimum vision in the dark. Probably I have said enough to show that this kind of research on fighting personnel is of very great importance.

Conclusion

I have now given a general survey of medical research activities during the war. I regret that, for obvious reasons, I have not been able to include in it an account of many of the more interesting discoveries that have been made, but most of these will come to light in course of time. The advance of medical science, both before and during the war, has been fantastic.

This lectureship has been instituted in memory of a man whose outstanding quality was to apply scientific knowledge to the service of man. The work I have attempted to describe is exactly of this nature, and I am sure it would meet with his approval when I express the wish that this lecture be regarded as a tribute to all those engaged on medical research in this country. Sitting as I do at the centre of all these activities I am in a position to say that this body of men and women—pathologists, bacteriologists, physiologists, biochemists, pharmacologists, and clinicians—deserve well of their country for the unsurpassed quality of their work, for their devotion to its performance, and for their complete unselfishness in carrying out their allotted tasks.

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