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THE STATE AND MEDICAL RESEARCH*

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At no time has the position been more favourable than to-day for appreciating Harvey's greatness as an investigator or for acknowledging the extraordinary position he holds as a leader of medical science. More and more men are endeavouring to follow his example, and the revolutionary changes in medicine during the past sixty years have only increased the appreciation of his foresight and skill.

Many still living have seen this revolutionary phase of modern medicine and surgery in its entirety—the introduction of new methods of prevention, diagnosis, and treatment of disease, the enormous increase in hospital accommodation, the initiation and development of clinical laboratories and radiological departments, and the transformation and multiplication of the public health services. Most medical men will agree that the main cause of these developments is the great increase of knowledge in medical science acquired in the past sixty or seventy years as the result of investigation. People began to realize that health and disease are not conditions conferred upon man for humble acceptance, but that a certain method (Harvey's method) of acquiring knowledge is at hand, and that by this knowledge disease can be combated and death itself warded off. More men and women entered the field of investigation, and knowledge accumulated more rapidly. Success bred success. A spirit of optimism as regards the acquisition of good health and the elimination of ill-health pervaded the mind of civilized man.

It cannot be denied that in this country, and even more so in the United States of America, the increase in scientific research has had no special intellectual basis so far as the public, even the enlightened public, is concerned. Research has been found to deliver the goods in these countries often enough to deserve special encouragement. This was not the case in Germany, where for a hundred years or more it had been accepted that teaching in medicine should be done by those who could extend or had extended the boundaries of knowledge by research. It is true that great medical discoveries were made in the past century in countries other than Germany, but in such cases the researches which led to these discoveries were made by men of genius working independently and often under uncongenial conditions. Germany, on the other hand, had an academic atmosphere saturated with the research spirit. Whatever may be the present or future state of medical and other science

in Germany, we ought to remember with appreciation this enlightened attitude, which flourished at a time when medical research breathed but feebly in other countries. Nor, in these earlier times, was the outlook utilitarian. A time came, however, when it was apparent that medical research could and did forge weapons to fight disease. The discovery of antiseptics, antitoxins, and salvarsan left no doubt on this point. It came to be realized that medical and other research was not an interest of a few curious people with a special aptitude for discovering facts which seemed to have but little bearing on life. Wise men, both in public life and in industry, saw that scientific research was the life-blood of modern existence, that it was a means of providing easily the needs of mankind and the knowledge necessary for healthy existence under modern conditions. As might be expected, the earlier disinterested German attitude was first affected by the practical issues, and organized research there received even a greater fillip. Industrial leaders in Germany and in the United States of America also soon grasped the significance of research applied to industry, and found that throwing a sprat of expenditure on research to catch a mackerel of large profit was good business.

It has sometimes been said that it took the great war to make this country realize the importance of scientific research, and it is true that the Department of Scientific and Industrial Research was only set up in 1915, largely as the result of the urgent demands of war. The Medical Research Committee, however, was initiated in 1913. Practically all its activities until 1919 were directed to the solution of medical problems related to war, and right well did it justify itself.

The Endowment of Research

During the present century there have been two rapid developments in medical research activity running side by side, the one in this country and the other in the United States: the former organized and to a large extent financed by the State, the latter richly endowed and controlled by private interests. Each movement has already produced a good harvest, but the crops differ in many respects. It can at least be said that the American record of medical research during the past twenty years has been a very fine one. There is good reason to believe that in America the State intends in the near future greatly to supplement private endowment for medical research, and the recent

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Nuffield scheme started at Oxford is possibly an indication that private individuals here will in future regard the endowment of such research as more worthy of support than in the past.

Financial aid, either from the State or from private endowment, is an essential to research. Money cannot, of course, buy discoveries, certainly not great discoveries, in the same way as it can buy manual labour; but it can offer freedom from the need for earning a living by ordinary work, and afford to those with the necessary ability the means to devote their lives to research. Until recent times, scientific discovery in this country has depended only too often on the haphazard distribution of wealth. Sometimes, as in the case of Darwin, private means have allowed leisure for experiment and contemplation. Sometimes a private society, such as the Royal Institution, has endowed men like Humphry Davy and Faraday in the same way as Trinity College, Cambridge, subsidized Newton. If these men had been completely without financial resources, and dependent for their living on ordinary labour, there can be no reasonable doubt that the particular discoveries associated with their names would not have been made by them.

On the other hand, the limitations of finance to ensure additions to knowledge are equally undoubted. Some of the best work has been done by men labouring under conditions of extreme simplicity. Would, for instance, the work of Claude Bernard and Pasteur have been better had they received abundant financial support early in their lives? It is true that when their work was more or less finished both these men were given adequate laboratory facilities, but for most of their active lives, when they were making their great discoveries, they worked under very poor conditions. The Harveys, the Claude Bernards, and the Pasteurs of this world will make discoveries under the most meagre circumstances, and, beyond a minimum of amenities, increased finance and improved facilities may not aid their output—may, indeed, detract from it.

These instances from past history, where men given slight but real opportunity have made discoveries of the first order, have imbued us all with the thought that many a genius for research must have been lost to the world by lack of such opportunity, and there is a determination that in future finance will not be the preventing factor. Nothing is more clear than that the mental outlook and ability to discover are present throughout all grades of society. Whether this ability is equally distributed is not so sure. In any case, the real discoverer is a rarity in all classes of society, and it must be the object of civilized communities to find these individuals and give them the means of freely carrying out their activities. As a class, those who choose research for their life's work are unworldly in the sense that they are content with a relatively low standard of living as compared with what they could often obtain in other walks of life. It is generally true that the more able the investigator the less are his demands on life's amenities. Even so, however, there is a limit to this, and the scientific genius when found must be given his chance and not be expected to use up all his time and energy fending for a living. In addition to these men there are a larger number who, although not men of genius, work out the rich veins discovered by their leaders. These men must also be looked after and given facilities for their work.

This, then, was the great justification in this country for State support for research, since private endowment was completely inadequate. Everybody will be agreed up

to this point. In the absence of private endowment State support assures the opportunity and offers a means of livelihood to potential investigators who could not otherwise direct their activities to medical research. On the other hand, it is certain that State endowment of medical research must be associated with State control. According to general experience, such control is often repressive and is accompanied by bureaucratic methods and all that these imply. The words "control" and "bureaucracy" have a disagreeable sound in all ears, but more particularly in the ears of those searching after truth by experiment, when success depends upon freedom to work quietly. One of the main objects of this discourse is to show how State control of medical research can be brought about and be compatible with freedom to the investigator. Another object is to explain the manner in which State funds are used for the purpose of promoting discovery in medicine.

The Medical Research Council

It is now twenty-five years since the Government decided to promote medical research by setting up the Medical Research Committee under the National Health Insurance Joint Commission to administer funds provided by the National Health Insurance Act of 1911. This arrangement was terminated in 1920 when the Medical Research Council received its present title and constitution. From this time funds for its work began to be provided direct from the Treasury in the form of a Parliamentary grant-in-aid, and the Council became subject to the general direction of the new Committee of Privy Council for Medical Research, with the Lord President of the Council as Chairman.

Of the present eleven members of the Council, eight are men chosen for their scientific and medical qualifications in the various fields of medical science. Every scientific member must not only have the approval before election of the Lord President of the Council but also that of the President of the Royal Society. Only two members are politicians in the sense that one must be a representative of the House of Lords and the other of the House of Commons. At present the remaining member, the treasurer, is a distinguished banker. With a body of this nature it will be seen that direct political influence is not likely to affect their decisions. It might then be said that, although direct political influence is obviated by the constitution of the Council, some such influence might still be exerted through the secretariat and permanent officials. To meet this the Secretary of the Council is elected by the Council itself—that is, by the scientific majority of the members. The Secretary of the Council is also Secretary of the Committee of Privy Council for Medical Research. There are, in other words, no administrative officials or machinery standing between the Medical Research Council and the Lord President of the Council. So far as constitution and powers are concerned, every action has been taken to see that the Council consists mainly of a group of experts in medical research with full authority to use and control the public money placed at its disposal, independently of all other bodies.

A question that often arises calls for consideration here. Some will doubt whether it is good for medical science that any group of men, such as constitute the Medical Research Council, should be in a position to act almost as dictators in a whole branch of scientific study. It may be argued that, however able, they are apt to become for the time being a body of official interpreters of the truth and, if they are wrong, to misdirect the lines of investigation and

even the interpretation of results so as to interfere with the development of truth. The first answer is that a sure safeguard against the continuation of biased views by an authoritative body is the constant change of personnel of the Council, whose individual term of office is four years. It is, however, a most important question, and its importance is made particularly evident when medical men occasionally appeal to the Council, not for financial support so much as for moral backing of their particular views and a pontifical declaration in favour of their special solutions of problems of health and disease. It is obvious that the Council must never become a backer of any speculative views. In forwarding research the Council must clearly use its discretion, and it can only act to the best of its judgment in this most difficult enterprise.

For the most part, good work is financially supported, but occasionally other work of a more uncertain nature is given the benefit of the doubt and assisted until its true value is seen; but whether the work be good or otherwise, the results obtained, and the views expressed thereon, are those of the individual investigators and not of the Council.

There always have been, and there probably always will be, mistakes in the appraisal of some investigators and their work—cases where relatively poor workers stand, especially in the eyes of their near colleagues, on a pedestal of distinction, and the much more serious case where the first-class discoverer and his work go unrecognized. After all, it is not so long since Lister passed through ten years of criticism and obloquy before the value of antiseptics was accepted. The Medical Research Council can do something to prevent the recurrence of an incident of this kind by asking other workers to repeat the investigation which is criticized; but that is not enough, and it is necessary for all medical men, especially those not engaged in research, to be guarded in their criticisms of the discoveries of others. The critical mind is useful, however, especially when it is associated with the power of discovery. A long experience of scientific research has taught me that only seldom are the facts of a discovery wrong; but the interpretation of these facts, and especially the first interpretation, is often wrong.

This question of the appraisal of new discoveries, especially when they are of a nature which requires much time and careful inquiry for repetition, is clearly one of great difficulty. Nor, so far as the individual worker is concerned, does the matter end always with the establishment of the correctness of the discovery itself, especially if it is one of great importance, and even Harvey's reputation as a clinician was anything but raised by his discovery of the circulation of the blood. Wrong personal judgments and false values are always liable to be met with in the research field, and this is one of the strains which individual workers must expect to experience. At least it will be clear that the estimation of the relative value of discoveries and their discoveries is one of great importance. To the Medical Research Council, all of whose actions in promoting research are a reflection of its judgment of men and their investigations. In my experience more mistakes of judgment are due to benevolence than to harshness, so far as the Medical Research Council is concerned.

Advisory Committees

A brief description of the mechanism and some of the general principles guiding the actions of the Medical Research Council may now be given, because there are probably many medical men interested in research who have no idea of these facts.

For general guidance, as regards much of the detailed work, the Council relies on the advice of committees specially set up to cover a large part of the field of medical science. Here, as in the formation of the Council itself, and indeed as in every problem of medical research, the question of personnel holds the key to the situation. Every person should be chosen primarily because of his capacity to aid investigation. Representation either of territory or of learned societies must be absolutely subsidiary to the main purpose of research itself. Territorial and representative interests are out of place in these committees; detailed technical knowledge and sound judgment alone are essential. Representation on committees must, if possible, be confined to representation of research in different parts of the special field of investigation, and it is always wise to have a number of active workers as well as those with past experience of research in any body whose duty it is to plan, initiate, and guide investigation into unknown territory.

The Medical Research Council has twenty-seven such committees. In addition, the Industrial Health Research Board, an important subsidiary of the Medical Research Council, receives advice and guidance from those committees whose work is primarily associated with problems of industry. Some of these committees are appointed conjointly with other bodies. All the services of the members of committees are given voluntarily, and magnificent work has been done by them. Their advice and help are absolutely essential for the work of the Medical Research Council.

Finance

Now a few words as to the finance of the Medical Research Council. Its present annual grant from the State is £195,000, having increased to this sum from about £50,000 which it received at the time of its institution as the Medical Research Committee twenty-five years ago. The block grant is considered every five years, a method which has its advantages and disadvantages. It has the advantage of allowing the Council to plan ahead with some feeling of security. It has the disadvantage of having to provide suddenly for expensive research, often at the request of other Government departments, out of a fixed income, and so curtailing the ordinary programme. It tends to lead to periods of expansion followed by periods of penury. The present time is one of penury. One year of penury in five is probably good, as it gives an opportunity for reviewing research programmes more closely and cutting out any dead wood that tends to occur. In addition to its public funds, the Council is in a position to help in the disposal of private endowments for medical research, and to do this either by directly controlling such funds or by giving advice to others who themselves hold the money. Private funds held by the Council for disposal as interest or capital amount to over £100,000, and, in addition, it receives annual sums of money for special purposes from the Rockefeller Foundation, the Dental Board, the Leverhulme Trustees, the British Empire Cancer Campaign, and the Halley Stewart Trustees amounting to £12,000. Altogether the sum at the disposal of the Council at the present time amounts to about £220,000 per annum.

There has recently been some public criticism, both in the Press and in Parliament, about the small amount of financial support provided by the State for medical research. It has been said that it is a curious anomaly that only £195,000 per annum is provided by the Government for research on disease which costs the country from 200 to 300 million pounds annually, since it is mainly by

research that the Government can hope to reduce the vast amount of sickness and the expenditure it involves. Whereas it is undoubted that much more financial provision is required for medical research, there is no reasonable doubt that in course of time this money will be forthcoming. The Treasury naturally demands that every request for an increase in research expenditure must be justified.

There are three main directions in which the Council disposes of the money. In the first place, the National Institute for Medical Research at Hampstead and Mill Hill has been established. Secondly, a rapidly growing number of research units, both clinical and laboratory, and whole-time workers at various centres in London and elsewhere are maintained. In the third place, grants are given to individual workers for specific pieces of research at many of the universities and hospitals throughout the country.

The National Institute for Medical Research

This organization was set up with the idea of doing large-scale and long-distance work requiring investigation by teams, and of a nature not suitable for university or hospital laboratories. Here, under the direction of Sir Henry Dale, the work is done in two main divisions: physiology, pharmacology, and biochemistry on the one hand, and experimental pathology and bacteriology on the other. An active subdivision of the former is endocrinology; while subdivisions of the latter include protistology and microscopy and physical methods. In addition to the above there is a Department of Biological Standards, the personnel of which is small, since every member of the staff of the National Institute is expected to contribute to this important part of the work when his special knowledge of a particular problem is regarded as essential.

The work of the National Institute has always reached the highest standard, and to recall its many triumphs would be a pleasant task, but it may be well to dwell on one aspect of it only—of particular interest to the practising doctor—which it has taken in its stride. I refer to the biological standardization of drugs.

Standardization of Biological Substances

Here it can be claimed without cavil that the National Institute has led the world and, both nationally and internationally, has rendered a great practical service to mankind. Here have been devised, are held, and are distributed standards required by the British Government for the purpose of the Therapeutic Substances Act, others for the Health Organization of the League of Nations, and some made necessary by the inclusion in the *British Pharmacopoeia* of biological assays for certain remedies. The following standards are held at the National Institute:

Antitoxins and Antisera: Tetanus antitoxin; diphtheria antitoxin; gas-gangrene antitoxin—(a) *perfringens*, (b) *Vibrio septique*. (c) *oedematis*; staphylococcus antitoxin; anti-dysentery serum (Shiga); anti-pneumococcus serum, Types I and II. **Drugs:** Digitalis, ouabain, strophanthin, arsphenamine, neoarsphenamine, and sulpharsphenamine. **Vitamins:** Vitamins A, B, C, and D. **Hormones:** Insulin; pituitary (posterior lobe); oestrus-producing hormones—(a) hydroxyketonic form (oestrone), (b) benzoate form (oestradiol monobenzoate); male sex hormone (androsterone); corpus luteum hormone (progesterone).

Recently additional standards have been adopted by the Health Section of the League of Nations for four of the active principles of the anterior pituitary gland, and these will be prepared and stored at the National Institute.

In addition, the Medical Research Council maintains at the Lister Institute the National Collection of Type Cultures of Micro-organisms, so that, at any time, any doctor in the world can obtain for a nominal sum a specimen culture of almost any type of micro-organism. The value of this service is shown by the fact that 5,000 such applications were made last year. In a similar way medical men and research workers can obtain standard bacterial suspensions and sera for the diagnosis of enteric, dysenteric, brucella, and meningococcal infections from the Standards Department maintained at the pathological laboratory of Oxford University by the Medical Research Council. It will be obvious to anybody interested in the subject of biological standards that this work necessitates continuous research in the maintenance of standards, in the search for new standards, and in helping towards a solution the innumerable problems which arise during their use.

Research Units and External Staff Workers

The second line of policy is the placing of units of research in different institutions. This plan has shown great developments in recent years, and its progress is limited only by finance and personnel—that is to say, the Council is desirous of promoting further development along these lines, as it considers this is one of the most effective methods of aiding research. When such a unit is set up in any place the Council makes itself responsible for the payment of salaries and the actual cost of the research. It expects the university or hospital, however, to provide accommodation and ordinary services, and in the case of hospitals the provision of beds and nursing facilities. To ensure the success of each unit the most crucial point is the choice of a suitable director, who becomes a member of the Council's whole-time staff. Every encouragement is given by the Council to ensure that the unit is regarded with pride by its hosts, and each unit is considered to form an integral part of the hospital or university where it is placed. The following units have been established by the Council:

(1) The department of clinical research at University College Hospital; (2) the neurological research unit at the National Hospital for Diseases of the Nervous System; (3) the department of research in puerperal infections at Queen Charlotte's Hospital (with the aid of (a) the Rockefeller Foundation and (b) the Pilgrim Trust); (4) the department of bacterial chemistry at the Bland-Sutton Institute of Pathology and Courtauld Institute of Biochemistry, Middlesex Hospital, with the help of the Leverhulme and Halley-Stewart Trustees; (5) nutritional units (a) at the Lister Institute and (b) at the Dunn Nutritional Laboratories, Cambridge; (6) a unit of clinical research at Guy's Hospital; (7) a unit of research on mental defect at the Royal Eastern Counties Institution, Colchester; (8) a unit of research in experimental and clinical surgery at Edinburgh University and the Royal Infirmary, Edinburgh; (9) a department of statistics at the London School of Hygiene and Tropical Medicine; (10) a unit of industrial psychology at Cambridge University. Other members of the staff of the Medical Research Council are seeded in other universities and hospitals, each an expert in his own line and acting as a central stimulus to those around.

The influence of this policy on medical research in individual universities, hospitals, and medical schools is great. In some cases the appointments have been too recent to reach their maximum effectiveness, but in some of the older-established units the work has been first-class and is known throughout the world. There are still many important gaps in this programme, and the expansion of the policy will undoubtedly continue.

Research Grants

Now as regards the third part of the Council's policy—the giving of personal and expenses grants to aid research by individuals. The personal grants are temporary, and are usually limited to three years. This rule is, however, not always applied, and, so far as the Council can help, it is not allowed to end promising and successful research. In making these grants the initiative nearly always rests with the head of a laboratory or hospital in favour of some individual worker, or with the worker himself. The success of the application depends upon the individual and his choice of subject, and the kind of help, when given, varies greatly. Sometimes personal grants for whole-time or part-time work are made; sometimes money is provided for research expenses; and occasionally, in the case of more established workers, for technical assistance. It is in this part of the Council's activities that the various committees are most helpful.

It is difficult to appraise the real value of this policy. It is the side of the Council's work of which most is heard, for every grantee is expected to refer in his publications to help he has received from the Council. A review of scientific and clinical journals soon reveals, therefore, the number and nature of these grants, and it is commonly found in many particular journals that a large part of the work published has been financed from this source. On the other hand, there is undoubtedly some wastage, which is probably not surprising, since at any time about three hundred separate investigations are being thus supported.

One point ought to be realized by those interested in applications for research grants. The Council provides money to individuals and not to institutions. The reason for this is obvious, because the Council considers it essential to control the choice of the individual worker and the type of investigation. Much trouble and much criticism of the Council's activities have arisen through non-appreciation of this rule. When, therefore, institutions, such as universities or hospitals, are planning a scheme of medical research which they cannot completely finance it is desirable, if they wish for financial support, that they should consult the Council in the early stages and before the personnel are appointed. Needless to say, its advice is entirely disinterested, and help in such cases is gladly given.

After a personal or expenses grant is once made every individual is given the fullest freedom to develop his problem. He is encouraged to keep in touch with other investigators studying allied subjects, and it is the duty of the secretary to help in every way. Apart from sending in a short statement each year to be grafted into the annual report of the Council, and the return of vouchers for expenses, the grantee has absolute freedom, and his work is generally allowed to continue for three years unless for some special reason. By this time the average worker has had his chance, and, if at all successful, he qualifies either for a further grant or for one of the many fellowships established in the country, or is definitely placed in a post allowing research facilities. By this means also many young clinicians are given an opportunity both for research and to establish themselves. This interest of the Council in providing personal and expenses grants must not be viewed too narrowly in terms of discovery, but its influence as a recruiting field and as an educative process must also be taken into account.

There is one other activity of the Medical Research Council which touches this College closely and about

which it is desirable to speak. I refer to its policy of awarding travelling fellowships in research. The greater number of these are generously financed by the Rockefeller Foundation of New York, and others are paid out of the Council's private endowments. In all cases the award is at the full discretion of the Council, and each year many applications for these fellowships are received from young medical men with excellent medical and scientific records. A large number of the prominent young medical men in this country—both in clinical and in laboratory work—will be found among the past holders of travelling research fellowships.

Research for Government Departments

This part of the work is rapidly growing, and only its great importance justifies the large expenditure of the Council's resources on these investigations. Questions of health and disease in all their aspects are assuming greater prominence in the view of Government departments, and since many of these problems demand investigation and expert advice the Medical Research Council is often called upon for assistance.

It is useless to deny that the attitude of the Council towards the problems presented varies greatly, and all are not greeted with enthusiasm. Most of them require from the investigators answers which offer a practical solution of difficulties. If an effective answer to any problem can be foreseen the probability is that the work required is more of a routine nature and for that reason itself the inquiry may be unattractive. If the problem is more difficult and no immediate solution can be foreseen, the fact that an early answer is expected may make the task irksome to the investigator.

On the other hand, some of the problems raised by Government departments are greatly welcomed by the Medical Research Council because they offer entry into fields of opportunity where a rich harvest can certainly be obtained. One of these, in which the Council has gladly taken on large responsibility, is that of tropical medical research at the request of the Colonial Office. Already it has sent a number of trained workers into different parts of the tropical Empire to study various problems, and the opportunities are so great that it has also embarked on a scheme for training young men in research in tropical diseases. Quite recently it has also appointed a small number of experts to direct and co-ordinate a large nutritional survey in many colonial territories.

It is impossible, however, to deal adequately here with this aspect of the Council's work, but it can be assumed that most Government departments call on the Council for help and advice, and such calls often involve large-scale research. This phase of activity is removed from the public eye, but its value is none the less very great, and promises to be even greater in the future.

Research Supported by the Council

A few words now on the actual research supported by the Council. On the whole, although there are many exceptions, it will be seen that the Council's initiative in research is largely confined to the work of its permanent staff, while as regards grants (personal and expenses) the initiative lies with the investigators. This is a crude way of expressing the situation, because the permanent staff themselves have wide liberty of action in planning their investigations, and the initiative of the Council is only apparent

in the choice of the personnel, which depends on the merits of each member and on the subject he represents.

The Council seldom chooses particular diseases for investigation, though here again there are exceptions, and any promising line is followed up as a special problem when it offers itself. Generally the choice is of a broader nature, so as to include a group of diseases or a type of treatment of wide application or a system of physiological control. For instance, in the early days of the National Institute for Medical Research the Council decided to encourage specially the study of virus disease. A staff of workers was appointed, with Sir Patrick Laidlaw as leader. More recently the Council decided to extend its interests in endocrinology, and appointed Dr. Parkes to lead this work. Other able investigators were chosen as the undertaking developed, and now there is an energetic team at the National Institute investigating endocrinological problems from all angles and also working in close harmony with most of those engaged in research on this subject, both from a laboratory and a clinical aspect, throughout the country. The most recent decision of the Medical Research Council to develop the field of chemotherapy on a much larger scale than anything previously seen here is now well known. The reasons for this decision have received wide publicity, and I shall not discuss the matter further.

These, then, are some examples of the kind of initiative in research shown by the Council. In a sense, however, all its appointments to the permanent staff, whether at Hampstead or in different parts of the country, are examples of initiation of specific research. Posts have been made for suitable men in the subject to be stimulated, and not men appointed to established posts.

Nothing has yet been said specifically about the desire to encourage clinical research by the setting up of clinical units. It is well known that this is one of the main objects of the Council. This programme is being slowly but steadily developed. As men suitable for appointment to posts of this nature appear, more units will be set up. If clinical research is to enter into its kingdom, success in its early enterprises must be obtained, and this can only happen if first-class investigators are appointed to these posts.

It will thus be seen how it comes about that the Medical Research Council has not usually adopted the practice of making an organized attack on special diseases except when the problem has developed as part of a larger and more general investigation. It has not, for instance, made a mass attack on such important diseases as rheumatism in its many forms and cancer, although, of course, in both instances it supports a good deal of research by different individuals. It considers that it would be relatively unprofitable to spend the large part of its total resources necessary for the adequate study of these diseases at the expense of other work. Extensive *ad hoc* research on a disease like rheumatism, however important as a practical problem, is apt to be unprofitable until the master key of its aetiology or some other essential fact has been disclosed. This master key is just as likely to be discovered by the use of the experimental method over a wide field as by the direct study of a particular disease where the experimental method is hardly available at present. Much is heard about the value of team work nowadays, and far be it from me to decry this method of investigation. But the success of team work depends either on brilliant leadership or on the working out of a special line of inquiry, and this latter is usually supplied by the observation of one

individual. There is no great difficulty in arranging team work; the difficulty is to find the outstanding individual discoverer—the Harvey—to blaze the trail.

Criticism is often made of the type of medical research supported by the Medical Research Council. Sometimes it is said that this work is generally too academic and includes too many problems of biochemistry, biophysics, and physiology. These critics take the view that much more money should be devoted to clinical research and direct attack on disease. The opposing school say that more money ought to be used for the support of fundamental research and that all major discoveries in medicine come from disinterested research in fundamental medical science. The fact is, however, there is no royal road to discovery in medicine, and all we know is that the experimental method used by Harvey with such brilliant results is still the sure method for acquiring knowledge and “searching out Nature.”

The Physiological Aspect of Disease

Claude Bernard took the view that all experimental medicine was applied physiology—a view which was killed at the time and for many years after by the success of the investigations of his fellow-countryman Pasteur, of Koch, and of the army of bacteriologists who followed them. When all disease came to be regarded as due to the invasion of the body by some form of *materies morbi*, the body itself was either forgotten completely or attention was mainly confined to the blood and its immunological powers. In more recent times the Claude Bernard point of view has received wider acceptance. The sooner the investigator recognizes the truth of both the physiological and the invasive bases of disease and the close interaction of these factors, the quicker will be the advance of medicine. Defence of the body against invasion by pathogenic micro-organisms represents a physiological process, and there ought to be no dividing-line between the two aspects of the subject for the wise investigator.

My predecessor, the late Sir Walter Fletcher, whose wisdom in guiding the policy and action of the Medical Research Council for the first nineteen years was exceptionally great, was strongly imbued with the Claude Bernard point of view, and played no small part in encouraging the revival of this philosophic outlook on medical research. It requires wise interpretation and tends to mislead those of narrow orthodox outlook who think of physiology in terms of the textbook. Yet there is nothing more prominently established in modern times than the success in discovery which has followed the extension of interest by the physiologist into that aspect of a problem which concerns a function going wrong—that is, its pathology. Again and again we have seen points of major physiological interest established by work on the pathological side. What would we know at present about such things as vitamins B₁, C, and D, insulin, thyroxine, cortin, liver and stomach active principles of pernicious anaemia, if experimental research had not been directed to the abnormal? Yet all these are physiological substances of the first order. Who can doubt that the physiology of the eye would be greatly extended by a knowledge of glaucoma, of the blood vessels by a knowledge of the cause or causes of hyperpiesis, of the heart by a knowledge of the causes of auricular fibrillation, of the kidneys by a knowledge of albuminuria, of the alimentary tract by a knowledge of gastric and duodenal ulcer, appendicitis, and colitis? It is probably no exaggeration to say that it is no more unlikely that a

physiological truth will come out of an experimental study of a pathological condition than that a fact of pathological significance will result from a purely physiological study. Every man working on a problem from either angle ought to be familiar with the other aspect. There has too long been a divorce between the two subjects, although this is tending to diminish. In recent years the Medical Research Council has endeavoured to help this situation by offering studentships to highly qualified young men to enter the field of experimental pathology as well as clinical investigation. The best qualification for such men is undoubtedly a good training in physiology, and physiologists in general would find a greater opportunity for essential discovery if they realized that a study of abnormality of function often offers the key to the elucidation of the normal process. Harvey himself did not confine his observations to one aspect of his problem. When necessary he called up evidence from every branch then known of physiology, pathology, and clinical medicine to support his argument.

The Future of Medical Research

And now, what can be said of the future? Short of a catastrophic change which may upset or even destroy national life, the future of medical discovery is bright. Past experience shows that, whatever problem concerning the body can be formulated by the human mind, there is a possibility of a solution or partial solution to it being obtained. There is thus no doubt that more and more knowledge will be obtained, giving control, both preventive and curative, of disease. The limiting factor in this progress will always be the men of genius available who make the first-class discoveries, but it is probable that with the spread of educational opportunities to poorer people more of these men will present themselves. The money available for medical research will increase, and financial obstacles will almost certainly be removed as the work develops now that the State has put its hands to the plough. No insurmountable difficulty may be expected in the direction of finance if the situation is handled wisely.

The difficulty I foresee is not that of obtaining knowledge but of its application to human needs. Curative remedies as they appear will, as in the past, undoubtedly be generally taken up by the medical profession. Much of the new knowledge to be gained, however, may concern the prevention of disease, especially the prevention of chronic and degenerative conditions, including cardiovascular disease, rheumatism, and pulmonary disease. The adoption and application of this knowledge will generally depend on the degree of education and wisdom of individuals. In some cases it will involve Government action. Without an enlightened public opinion the average individual will do nothing to save himself or herself, and the State even less. If we are to continue as a successful democracy, dependent on public opinion for action, this must be guided suitably and quickly in problems of health as in other matters.

It seems to me that one of the most important functions of this Royal College in the future will be to lead public opinion and to guide State departments, especially in matters of preventive medicine. The Royal College of Physicians is an ideal body for giving guidance and to press for action, if such be needed, in cases where scientific discovery has supplied new knowledge of importance to public health. Its independence and freedom from political relations, and the high and honourable standing

of its Fellows, would give its edicts an unassailable power.

I have now completed my task of giving a bird's-eye view of the modern movement of State support for medical research. It would be idle to pretend that the State or any other body could do much more in this matter than supply facilities to assist generally, and guide the natural genius of the country in studying problems relating to health and disease. Much remains to be done to improve and develop the movement, but, bearing in mind the limitations of any such enterprise, it will probably be agreed that the entry of the State into this field of discovery has been both stimulating and fruitful.

SOME ASPECTS OF RECENT WORK ON THE BACTERIOLOGY OF RHEUMATISM*

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Reviews of the rheumatism problem appear with a regularity which is certainly not in keeping with the rate of advance of our knowledge of the subject, for rheumatism in its diverse forms presents an aetiological problem which is among the most difficult that medicine now faces. Consideration of its complexity suggests that entirely new conceptions of the host-parasite relationship may have to be evoked before the observed clinical, pathological, bacteriological, and serological results can be resolved into a comprehensive pattern.

For present purposes it is proposed to discuss the more recent work in its bacteriological and serological aspects, picking out certain salient and significant observations for more detailed consideration. As a starting-point the now well-known phenomenon of throat infection with *Streptococcus haemolyticus* followed by a latent period, which in turn succeeded by an attack or relapse of acute rheumatism, will be considered. (Schlesinger, 1930; Collis, 1931; Sheldon, 1931; Coburn, 1931.)

Each phase has received careful study by Coburn (1932, 1935, 1936). The initial throat infection is often of very mild type, causing a slight rise of temperature, and in many cases it is overlooked by the patient. The presence or absence of tonsils does not affect the outcome, since a pharyngitis or nasopharyngitis clinically recognized as a feverish cold may be the starting-point for the rheumatic attack. Coburn and Pauli (1935d) have studied the characteristics of those strains which may be effective in producing a rheumatic relapse in susceptible subjects, contrasting them with strains which are non-effective in this respect. The effective strains were characterized by the capacity to produce strong erythrogenic toxins and haemolysins, and were in fact indistinguishable from scarlatinal strains. Those strains lacking in exotoxin production, although of human Group A and culturally similar to the effective strains, were not associated with rheumatic relapse. The toxins produced were not regarded as causative of the rheumatic lesions. On the contrary, a very low incidence of Dick-positive reactions was found among rheumatic children, and the erythrogenic toxin is

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