annoying incident of bacteriological practice. It was the chance coincidence of three conditions which made its occurrence on a particular plate in 1929 the starting point of a discovery of first-rate importance. (1) The contaminating spore was that of one particular mould species, *Penicillium notatum*; (2) the culture on the plate was that of a staphylococcus, susceptible to the restraining effect of an antibacterial agent which this mould produced; and (3), most important of all, the worker concerned was Professor Alexander Fleming, with the eye of a medical naturalist, alert to detect the unusual phenomenon of a kind of halo round the spot where the mould colony grew, free from colonies of the staphylococcus which grew abundantly over the rest of the plate. Sir Alexander Fleming, as you know, picked off the mould colony and cultivated it in a broth, and found that the broth contained an antibacterial agent which he named penicillin. Then, as happened with Minkowski and the pancreatic hormone, neither Fleming nor anyone else for some years could hold out any hope of the chemical isolation or even of a substantial purification of penicillin, to say nothing of its eventual production in a form and in a quantity enabling its therapeutic possibilities to be critically tested. Such a possibility had in fact been practically written off the account and almost forgotten until, like Banting and Best with insulin, Sir Howard Florey and his chemical collaborators took it up with determined energy and with brilliant and resourceful enterprise; and now the research chemists and the organized therapeutic industry of half the world have combined to exploit and develop this gift of an alert opportunism and to make it a practical reality for human need. And the chemists have isolated several penicillins, determined their constitutions, and even made one of them by synthesis. And this success has had value not merely for its own sake, it has opened up a most hopeful vista of other and perhaps equally important discoveries in the same field, streptomycin, chloromycetin, and others yet to come.

Of course there are plenty of other instances to be found of opportunity coming to an attentive worker in research through what we have to regard as chance or accident; and, apart from the many which could be collected, there must be innumerable cases which will never be recognized because no record of them has been preserved. I hope, however, that my choice of a subject and citation of examples will not bring me under the suspicion of suggesting that accident is the principal factor of success in research of any kind, or of medical research in particular. Accidents of the kind which we have been discussing do not, in fact, happen to the merely fanciful speculator who waits on chance to provide him with inspiration. They come rather to him who, while continuously busy with the work of research, does not close his attention from matters outside this principal aim and immediate objective but keeps it alert to what unexpected observation may have to offer. I certainly do not believe that any research work of permanent value is done, or any discovery of importance soundly established, without a great deal of hard, systematic, and conscientious work.

Then I should not like to be misunderstood as suggesting that mankind would have been left in permanent ignorance of any of the items of scientific knowledge, great and small, which I have cited through default of the accidents which were in fact associated with their discovery. If Archimedes' bath had failed to overflow, or the falling apple to catch Newton's attention, the principles which they gave to the world would not have remained hidden for ever, and probably not for long. We know in fact that Hooke, Wren, and Halley were actually competing in speculation about an inverse-square law of gravity and the moon's orbit without being able to calculate the relation;

and that it was the news, indeed, of such an approach to its independent discovery which acted as a stimulus to Newton, leading him to publish at last what he had known in principle and worked upon intermittently for over 20 years. We cannot be so certain in other cases, but it does not seem likely that the effects of removing the pancreas, or of injecting a suprarenal extract into a vein, would have remained very long unknown even if von Mering had not called on Minkowski to perform the one for another purpose, or if Oliver had not goaded a reluctant and sceptical Schäfer into trying the other. Incidents of the kind which I have described may greatly advance the date of a discovery or may associate it with the name of a particular investigator, but I do not believe that they will ever produce discoveries which would not eventually be made without them. They may provide, however, touches of highlight in the varied landscape of science, of decoration to its solid building, or of light relief to the more serious drama of its normal and logical advancement. And if they have thus lent something of life and colour and everyday interest to an hour of talk about medical research they have helped me to achieve a large part of my intention.

THE PROBLEMS OF CLINICAL RESEARCH

BY

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First-class clinical research has been and is being done by men busily engaged in practice. For examples in my own generation I think of J. W. Brown's work on congenital heart disease, Cookson on thyrotoxicosis, or Sheldon on haemochromatosis. In a delightful article called "Clinical Research with a Notebook" Alvarez (1946) has illustrated the good research work done by what he calls small-town doctors. The man in practice has the best opportunity of carrying out clinical research in depth, the intimate and prolonged study of people to learn what happens to individuals with certain constitutions or chronic diseases. If in the rest of this article I refer to clinical research by whole-time workers in hospitals or institutes it is not that I forget these facts but rather that I am addressing myself to those who wish to make clinical research their career or major interest and to those who should provide the facilities for them. I must ask to be excused, likewise, for quoting examples from the work of my own department.

Simon Flexner (1939) said that one of the essentials for successful clinical research was the power of the researcher to command his time for the patients, from whom the research problems are derived, and for the laboratory, in which those problems are investigated. No man in a busy practice can command his time, and for this reason great men like Richard Bright have found it impossible to continue clinical research when they have made a name in practice. The young man who wishes to engage in clinical research in this country should usually work whole-time in a hospital or a research institute. The opportunities for this type of employment have been greatly enlarged by the increased funds which are now at the disposal of the University Grants Committee and the Medical Research Council. Nevertheless, whereas medical practice may be regarded as a stairway, in which the opportunities do not diminish as a man advances in years, the academic and research

career will always be like a pyramid, with more room at the bottom than at the top.

A Recurrent Suggestion

Running through discussions on the new health service like a strand in a rope there is the recurrent suggestion that improved organization of medical care and the formation of regional boards will lead to better facilities for clinical research. One hopes this will be true, but there are reasons for not being too sanguine. There is an immediate danger that senior clinical research workers will be overwhelmed with administration and that juniors will be tempted away by the high salaries of young consultants. There will be obvious gains if notes are better codified and if we can register sickness as exactly as we can register the number of people in the country, their births, marriages, and deaths. The burden of filling in forms is so heavy, however, that I hope our statisticians will not try to do too much at once. A vast amount of time and labour can easily be spent on records, and research of this kind needs to be carefully planned and costed if it is to yield an adequate return. Democracy begins at the grass roots, and more willing co-operation will probably be obtained if the regions are given specific tasks, as in the notification of jaundice in Region IV during the war. This, however, is social medicine rather than clinical research in the ordinary sense.

There is likely to be increased concentration of cases in special centres, like the centres for head injuries, chest diseases, and gastric complaints which were started under the E.M.S. in the war. On a short-term basis this undoubtedly leads to technical advances, particularly when physicians and surgeons work together on common problems, but it is like farming for cash crops and the output soon seems to dwindle. Moreover, the advances are almost entirely technological and self-limited, unless the centres are designed as research units, as Colebrook's burns unit and some of the malaria research units were. Pupils of mine who have worked in units which were primarily designed for research on a single disease have nevertheless spoken of their anxiety to get back to general medicine after a time to refresh their minds. Special clinics for asthma, rheumatism, and anaemia tend to develop a routine, and research fades into the background. Just as the best farming is mixed farming, so the best clinical research is likely to be done in general hospitals, particularly those which are so fortunate as to be associated with university scientific departments. The chief stimulus to clinical research in the new health service will probably be the creation of more full-time specialists. Much has been done by such men under the old regime, as, for example, Avery Jones on gastro-duodenal ulceration, Banks on cerebrospinal fever, and Anderson and his colleagues on pneumonia.

How clinical research units or institutes should best be organized is still not settled. In university departments research must usually be combined with teaching. I have been convinced by my own experience, and that of other clinical researchers and whole-time teachers in this country and America, that it is not possible to research or teach on other people's patients and that whole-time academic workers and part-time consultants do not mix. I know that the rational answer is that the practising clinicians should "feed" the academicians, but owing to the loyalties and antagonisms which develop among groups of human beings this rational solution does not work. Whole-time and part-time clinicians are much better friends if they work in separate compartments. The clinical research workers must control their own group of patients. It is this necessity to

combine research with the treatment of patients which differentiates clinical research from all other forms of medical research and poses problems to which there are as yet no generally accepted answers.

Size of the Research Unit

The first problem is how large a clinical research unit should be. Sir Thomas Lewis believed that the number of beds in a university department of medicine should be small—20 or 30. I worked for eight years with a department having only 21 beds, and I am sure Lewis was wrong. Lewis's own small research unit was superimposed on a much larger whole-time general medical unit, with which he worked in a particularly happy association. The total number of beds was in fact over 50. Lewis talked vaguely about a pool, but whereas one can pool ships and merchant seamen in wartime (even then there are complaints) one cannot shuttle patients about in this way. Our fellow-countrymen are sensible of the needs of clinical teaching and research, but they will not tolerate the conception of patients as clinical material which can be moved hither and thither at our convenience. The physician who is in practice acquires obligations to his patients and their general practitioners which make it hardly possible for him to hand them over to the care of another. Yet without complete control clinical research may be frustrated. On the other hand, the conclusion of any research project such as the study of special diets in hepatitis or the treatment of rheumatoid arthritis by the induction of jaundice leaves a responsibility for a large number of chronically ill patients which cannot be summarily abrogated. Just as the practising physician cannot hand over cases for research without qualms, so the clinical research worker cannot expect his colleagues to look after patients he has tired of. Finally, senior clinical research assistants must have the opportunity at times of exercising major clinical responsibility. If they do not, they will move at an early age to another post. Constant changes of staff on this account crippled the research of the London University professorial units in the inter-war years. In the language of the cinema, the professor was degraded from director to continuity girl. All this means that the unit must contain four or five times as many beds as are theoretically necessary for research.

Latterly I have been working with a total of 45 beds in two units, unfortunately geographically separate, of 21 and 24 beds respectively. The smaller unit has been used for acute illnesses, complicated cases, and clinical research. The larger unit has been used for routine work, for cases requiring protracted treatment, and for neurology. There has been little undergraduate teaching. These 45 beds, with their associated out-patient and follow-up clinics, have provided the background for a staff of six senior colleagues and a further six juniors of registrar status. With such a staff it is possible for all members of the department to have short periods of concentrated clinical work and longer periods when they have adequate leisure for research. No one is ever responsible for the supervision of more than 21 beds, but this is quite enough for one man to look after when investigation and research are being carried out at high pressure. We have plans for a unified department of 64 beds, and I believe that a unit of 50 to 100 beds, subdivided on functional lines and with a staff large enough to allow of alternation between research and routine clinical work, should provide the best solution of this difficult problem (Gardner and Witts, 1946).

The great danger in a unit of this size is the tendency to fritter. The world of medicine is so full of interesting and distracting things that we are tempted to diffuse our energies

over all of them instead of concentrating on one problem. It is this tendency which has made the words "clinical research" and "clinical pathology" an offence in the nostrils of the preclinicians, who regard us as expensive butterflies rather than worker bees. This is at bottom a difference of philosophies. One school teaches that every patient must be regarded as nature's experiment from which something new can be learned. All mysterious and bizarre cases, particularly if they affect the bones or the endocrines, are inevitably classified as professorial cases. The other school teaches that the clinical researcher must at all costs narrow his field of vision and draw an absolute distinction between research and the routine practice of medicine. I am sure that this is right. Once we give way to the temptation of following every interesting problem that presents itself at the bedside we shall be like the centipede counting its legs. In the ward one must constantly put a blind eye to the telescope. I am adamant on the rule that you can't research on all the diseases all the time.

Training

The next question is that of training. The key word in clinical research is clinical. The clinical scientist must be a properly trained clinician or no hospital committee will give him charge of beds. Nothing is more disastrous than for a man to take up clinical research and find himself in the thirties without a proper label, recognized neither as clinician nor as scientist. In the United Kingdom the clinical label is the M.R.C.P., preferably taken three years after qualification, after say two years in house appointments and a year working for the M.D. From the beginning, therefore, the clinical researcher is handicapped in comparison with the researcher in the basic sciences, who can begin a research career immediately after qualification. But a clinical training will not make a man a researcher—in fact, in some ways it unfits him by encouraging a superficial, know-all attitude. A man cannot get far in clinical research to-day without some special knowledge of experimental pathology or chemistry or physics or statistics. He must have another string to his bow. There is little doubt that at this stage of his career a man should spend a year in a non-clinical department, not merely to refresh his basic knowledge but even more to learn how problems can be isolated and how knowledge can be advanced by patient work and by learning to take one step after another. Technical equipment can be picked up by the way. What cannot be picked up is faith in the scientific method, in the value of experiment, in the ability to master technical procedures, in the necessity to concentrate on one purpose. All this is so different from the atmosphere of a busy ward, where many tasks must be carried out simultaneously and where judgments must be made and acted on immediately, that it is hard for a man to acquire a real faith in the scientific method without a period of isolation from patients.

Clinical research is inevitably a compromise between the desire to practise medicine and the desire to advance knowledge. As such it makes the clinical researcher suspect to the practising physician as well as to the pure scientist. With some of my colleagues it is an article of faith that a clinical scientist cannot be a good doctor. This is really a rather foolish controversy, but it is the sort of thing that happens when practising clinicians who are individualists work alongside clinical research workers who should be team-workers. I will merely turn the argument and say that the clinical scientist need have no false shame about asking for advice, whereas I have known honorary physicians who would have cut off their right hands rather than sign a request for consultation from a more expert colleague. The practising clinician should be superior in

manual dexterity, though the clinical scientist can, if he wishes, concentrate on one technique or operation. The only charge which requires an answer is that the clinical scientist studies diseases while the practising clinician treats patients. If research should lead to neglect of the patient as an individual, then indeed the head of the department would be open to serious criticism. A genuine affection for patients is a prerequisite for a man in such a position.

Technical Problems

The technical problems of clinical research at the present time are those of research in general and of clinical research in particular. They depend partly on specialization of knowledge and partly on the need for workers, equipment, and buildings on a lavish scale. Within the narrow field of haematology there are now particular groups which talk a language that is almost incomprehensible to other haematologists. The workers on the rhesus factor, on blood coagulation, and on the macrocytic anaemias have each developed a body of data and hypotheses which needs a man's whole attention to keep up with. It is difficult if not impossible to make further progress in these subjects without a special knowledge of genetics, physics, or chemistry.

Here we meet one of the logical problems which face the clinical research worker who by luck or good management gets in on the ground floor, as it were, at the beginning of some new advance. Good examples in recent years are the effects of vitamin K and dicoumarol on blood coagulation, and the rhesus factor. As soon as a new idea like this is out of the bag the laboratories of the world, particularly its western hemisphere, are after it like a pack of hounds. The pace of advance is breath-taking. Pretty soon our clinical scientist must decide whether he is going to dedicate his life to a single pursuit, as Price-Jones dedicated himself to the measurement of red cell diameters and Ponder to their lysis, or whether he is going to remain the unspecialized researcher. This is a difficult and an individual decision. My own view is that just as the key word in clinical research is *clinical*, so the proper contribution of the clinical scientist is that of the *holist*. Once research gets down to fundamental problems of chemical structure or enzymology or radioactivity it is probably better handed over to people trained primarily in those subjects. At this level the clinical research worker may act as one member of a team, but he can rarely get far under his own power.

What is quite certain is that it is unwise for the man with a clinical training to start researching in a rapidly moving subject unless he really does get in on the ground floor. It is different, of course, if the entry to the subject is restricted by shortage of supplies, as in the case of penicillin and streptomycin, and he is one of the favoured ones who is asked for clinical trials. I have known a number of promising men who have had a good line of their own and yet have never been able to resist the fatal attraction of new discoveries and have fluttered off to them like moths to a candle. The usual result is a repetitive article in one of the journals, not infrequently there is a coldness on the part of the original discoverer, and sooner or later people, remembering his own particular subject, begin to ask, "I wonder why X never got on with so-and-so; he seemed to have the ball at his feet a few years ago."

The Law of Diminishing Returns

It is difficult to see any end to research in the basic sciences; certainly the sky is no longer the limit. The field of clinical observation, however, is subject to the law of diminishing returns. The descriptions of the signs,

symptoms, and morbid anatomical appearances of disease made in the first fifty years of the nineteenth century were more numerous and striking than those which have been made in the twentieth. Apart from coronary thrombosis and subarachnoid haemorrhage, it is difficult to think of any important diseases which have been discovered with the unaided senses at the bedside and the necropsy table in our generation. It is still possible to paint fresh pictures of disease in the tropics and in industry, but so far as ordinary clinical work is concerned the methods of Bright and Addison have yielded their harvest and only a few ears like temporal arteritis and bronchial adenoma remain for the gleaners. The recent advance has come from the application of the techniques of microbiology, chemistry, and physics. As a general rule it is unwise for the whole-time clinical research worker to take up projects which demand personal supervision of large numbers of patients. That kind of work is much better done by the full-time specialist (Avery Jones, 1948). Just as the full-time specialist cannot afford to get too far away from the bedside, so the academic physician or clinical scientist cannot afford to be too long away from the laboratory.

For clinical research to be profitable it must follow the sequence of observation, hypothesis, experiment. Experiment may be carried out in man or animals. The difference between the clinical scientist and the experimental pathologist in the use of animal experiment is hard to define, but it is nevertheless real. It depends on the fact that the clinical scientist is in close contact with patients and therefore tends to use animal experiment, and indeed all other scientific techniques, for the solution of immediate problems. Just as medicine is the mother of the sciences, so to-day those sciences are continually making fresh contributions to the support of medicine. There is a never-ending task in adapting new techniques and discoveries to the solution of clinical problems. The application of induced radioactivity and radar to the study of disease in man is the latest example of this process.

Experiment in Man

As new drugs are discovered they require trial in man, and the same applies to techniques as diverse as the punch card and the electro-encephalogram. Pharmacological experiment in man has given us new substitutes for morphine and new treatments for insomnia, epilepsy, and migraine. Similar studies may well lead us to the control of other common mental ills such as anxiety and impotence, depression and brooding. There is much to be done in psychiatry, genetics, social and industrial medicine, and demography. Many forms of rheumatism, and some aspects of the allergic and the psychosomatic diseases, can at present be studied only in the human subject. Our lack of progress in the control of these diseases and of mental disorders in general nevertheless emphasizes the difficulty of studying disease in man without the aid of animal experiment. How easy it is to aver that mental ideas or states can be converted into physical disease processes as they can be converted into phobias or hysterical paralyses, but how difficult it is to prove it or to demonstrate the mechanism! This is certainly a field which no one but the clinical researcher can enter at the present moment. The reason work has not got much beyond the descriptive or speculative stage is because of its extraordinary difficulty. Nevertheless, the work of Selye on the alarm reaction, Wolff and Wolf on pain, Lewis on urticaria, and Macfarlane on fibrinolysis does suggest some methods of attack.

Deliberate experiment in man is a relatively recent development, and I should like to say something about the

ethical problem. I have had practical experience of therapeutic trials in pernicious anaemia, of exposure of human volunteers to T.N.T. and to mepacrine, and of the induction of infective hepatitis in man. Each of these experiences has occasionally caused the most lively apprehension. There is no evidence that anyone died or became permanently ill as a result of the numerous successful transmissions of jaundice to human volunteers during the war, yet this method of approach has for all intents and purposes been abandoned. It is not just that the volunteer is sometimes an unstable person who may swing violently from co-operation to antagonism: the plain fact is that few researchers would willingly inoculate themselves with jaundice, and it is an absolute rule of clinical research that one should never do to others what one would not do to oneself. Once break this rule and one is on the slippery slope that led so many Nazis to the abyss. Moreover, it is a moot point whether a healthy citizen is within his legal rights in volunteering for a dangerous experiment, any more than he has a right to bequeath his body. Certainly, the complications as regards inquests and sickness and life insurance are formidable. For all these reasons dangerous experiments on healthy researchers or volunteers are rarely wise in peacetime.

Therapeutic trials and investigations on sick people are on a different footing, for every treatment is an experiment and every potent remedy is dangerous. Nevertheless, here also one must stick to the rule of doing as one would be done by. All of us know surgeons, physicians, and investigators who have got a reputation for ruthlessness. This was never a good thing, and it is probable that it will be anathema in the new health service and under the present egalitarian regime. Even such relatively safe procedures as the deliberate provocation of attacks of angina or epilepsy, or the study of the failing heart by catheterization and angiography, have come in for lively criticism. The only justification for experiments on patients is that the information cannot be obtained from animals and that it is likely to be of benefit to the patient and his fellow-sufferers.

Mackenzie and Lewis both held that the study of symptoms in man would be as profitable as the study of physical signs and post-mortem appearances in the nineteenth century. So far it has proved unproductive. Indeed, I believe that they did English clinical science something of a disservice, and that the great weakness of our clinical research, in surgery even more than in medicine, is its failure to turn instinctively to animal experiment. The work of Himsworth on hepatitis or of my own co-workers on macrocytic anaemia is the type of procedure we should encourage. The problem, a clinical problem, arises in the ward and it is studied under simplified conditions in the experimental animal. Perhaps at this point I should confess my opinion that clinical science is essentially an applied science and therefore clinical research should be practical. Too great a concentration on the human subject leads to work which may be elegant but which gives a poor return for the talent and effort devoted to it. Much of the work which has been done on renal function and on the peripheral circulation in man seems to me to come into this category. One feels *a priori* that this is not the right approach to the prevention and treatment of nephritis or vascular disease.

The happy warrior, of course, is the man who, like Adrian, is equally at home with human or animal experiment and who uses each for the purpose for which it is most appropriate. So let me make it clear that I am not trying to advise the clinical researcher to work on animals rather than men, but that I am emphasizing the importance of the experimental method. In the address I have previously quoted, which was given on the foundation of the Nuffield

Clinical Chairs in Oxford, Flexner said that the key to achievement lies in the laboratory. It is not merely that the laboratory contains instruments of precision and that work can be carried out on animals; but the laboratory implies experiment. Above all, laboratory experiment means that fixed times and days are consecrated to research, and there is not the same danger of allowing research to be swamped by routine or to be relegated to the evening hours when the real work of the day has been done, as so often happens in clinical research.

Conclusion

The power to command one's time—that is the root of the matter. Unless clinical research is strongly buttressed by the laboratory and the experimental method it may be swept away and submerged by the oncoming tide of hospital organization. I am prepared to interpret the concept of the experimental method broadly, and I accept the view that there may be valuable psychological and sociological techniques which differ from the classical methods of experiment. All I wish to emphasize is the need of time and space for the pursuit of knowledge in the field of clinical medicine. The university clinical departments were diverted from research to teaching after the first world war, and there is a real risk that they may be diverted to regional organization after the second. If the new health service makes excessive demands on the universities for technical and administrative help clinical research will suffer. There are too many people in influential positions in this country who act as if they believe that clinical research is useful as an intelligence test to decide whether a man is energetic and clever enough to be appointed to a chair or the staff of a hospital, but that it should not engage his time thereafter. The fact that a single clinical scientist like Colebrook can do more for the relief of suffering in obstetrical and surgical emergencies than a hundred practising specialists or administrators makes little impression. What one misses in the United Kingdom, in contrast to the United States, is an abiding faith in clinical research as the most important business in which a hospital can be engaged. Until that belief becomes more widespread we may have an efficient apparatus for the treatment of disease by orthodox methods, but we shall never in the literal sense of the words have a health service.

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The Council of the Faculty of Ophthalmologists has reported that the Ophthalmic Subcommittee of the Negotiating Committee met representatives of the Ministry of Health on two occasions to consider the fees for the testing of sight under the Supplementary Service. As a result of these negotiations the Ministry agreed to the payment of £1 11s. 6d. per case, on the condition that the work would be carried out on premises and with equipment provided by the ophthalmic medical practitioner. The question of general-practitioner ophthalmologists caused some difficulty, and the fee was fixed on the understanding that not less than 95% of the work would be carried out by ophthalmologists of specialist status. The Ministry agreed that specialist status should include any doctor who held an ophthalmic diploma, even though he might be engaged in general practice. The remuneration of medical officers carrying out refractions in hospital has also been considered by the council, which has reiterated its opinion that the Supplementary Service should not be carried out in hospital, and has agreed that remuneration for refraction work in hospital should be on a sessional rate, based on the Spens Report. It has been decided to take the matter up with the Ministry of Health, together with various other points, including the establishment of the ophthalmic subcommittees of the regional boards, the position of the dispensing opticians in hospitals, and the employment of refracting opticians in hospitals.

MEDICAL RESEARCH IN THE LABORATORY

BY

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In attempting to present a picture of medical research in the laboratory as it is understood to-day it is very difficult to define the limits of the field. There was a time not so very long ago when an institute for laboratory medical research could be considered reasonably complete if there were adequate representation within it of pharmacology, pathology, and bacteriology. Now, on the other hand, we are approaching, if indeed we have not already reached, a state of affairs in which any sort of scientific discipline may be called upon to contribute to the solution of a medical problem.

The trend of development may be illustrated by what has happened at the National Institute for Medical Research. The Medical Research Council has always taken the broadest view of the range of activities which should be embraced by medical research. Nevertheless, when the National Institute for Medical Research was opened in 1920, with the avowed intention that it should house the principal scientific activities of the Council, only three groups of experimental laboratories were set up; these were laboratories for physiology and pharmacology, pathology and bacteriology, and applied physiology.

It is true that from the first the scope of the activities included under these headings was very wide; within the division of physiology and pharmacology, for instance, the work ranged from synthetic organic chemistry to pure physiology. Nevertheless, the picture was a very different one from that presented by the National Institute for Medical Research to-day, in which most branches of scientific work are represented and in which more and more importance is attached to those branches which at first sight have the least immediate contact with practical medicine.

The great developments which have taken place in the laboratory branches of medical research during the past thirty years, and which are reflected in the history of institutions such as the National Institute for Medical Research, are of course the result of development in branches of natural science other than those earlier recognized as being of direct importance to medicine, and of the growing realization of the closeness with which these other branches impinge upon medical and biological problems. It is within the period mentioned that biochemistry has emerged from its origin as a branch of physiology and has come to occupy its present status as an independent scientific discipline; it is also within this period, and particularly within the last few years of it, that the applications of various branches of physics to biological and medical research work have shown themselves to be of such outstanding importance.

It is notorious that the medical student often tends to doubt the importance and indeed the necessity for the instruction in the so-called basic sciences which he receives in the early part of his training. It remains difficult for the qualified medical man, unless he happens also to have been a serious student of some branch of science, to realize how closely dependent on scientific research work are the advances in practical medicine which are of immediate interest to him. It may therefore be worth while to reflect briefly on this question and to recall some examples of the way in which medicine is assisted by scientific work in the laboratory.