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MEDICINE'S CHALLENGE TO THE EDUCATOR*

BY

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An invitation to speak on the problems of medical education in Britain that would be of interest in the United States is one that offers much freedom of choice. Some would choose to display how most of our doctors, particularly the more energetic and talented, are being submerged by uncontrolled growth of committees; and they would discuss how this strange phenomenon has come about, and perhaps how it could be controlled. Others would take the registrar problem, with its temporary interruption in the flow of men through the training posts. Related to this would be the disparity between numbers of permanent posts in the National Health Service and of those being trained to fill them, and the effect of the monopoly created by the National Health Service on recruitment to medicine. Or he might wish to show how the universities can best utilize their new-found freedom to provide a better curriculum, thanks to the new wisdom of the General Medical Council. All these subjects require more study than I have been able to give, and to do justice to each would require a separate essay. Besides, some of these problems, though not the first and the last, are largely administrative, and therefore of restricted interest to our colleagues abroad.

I propose, therefore, to interpret the invitation liberally and to take three issues that affect our attitude to medicine and the teaching of medicine. These three are, firstly, the issue of instruction versus education; secondly, the importance of the proper use of words; and, lastly, the growing importance of population studies in clinical research. I have to confess that these are three old hobby-horses of mine. But I always find the ride exhilarating, and can only hope you may do so too.

Instruction versus Education

My own introduction to the conflict between education and instruction took place during my undergraduate days at Cambridge. One of my friends, who was a teacher of English, pointed out to me that medical students were not being educated; they were being instructed. He explained that education was a training of the mind; that in education a student is set to work in his own time; and the chief function of his teacher is to appraise his efforts, to cure him of bad mental habits, and to encourage him in good ones. He explained to me that this was what was done in the arts faculties of our ancient universities, where a man attended lectures for not more than two hours a day and spent the rest of his time preparing work for his tutor to criticize. The process of instruction, on the other hand,

was a process of forced feeding, in which nothing was required of the student except to memorize and to reproduce what he remembered. In such a process the student was required to know the conclusions but not necessarily the evidence on which these were based.

It was clear to me that he was right, and this became even clearer to me in the clinical years, when many teachers did not themselves know what the evidence was or where it could be found. We students were receiving not education but instruction. We went to so many lectures and classes and had so many textbooks to read that we learned things by sheer memory. And we learned the conclusions, not how these had been arrived at. The contrast was all the more striking because between the preclinical and clinical parts of the medical course proper it had been my privilege to take Part II of the Natural Sciences Tripos in Physiology. That was true education under a brilliant collection of teachers—Langley, Barcroft, Adrian, W. B. Hardy, Hopkins, Roughton, Hartridge, Marshall, and others. We had very few lectures, all very much to the point and highly critical, and we were expected to read the more important original papers. I personally owe most to Joseph Barcroft, who not only inspired us in his lectures and practical classes but who also made us write essays for him once a week. There were but four of us. It is not difficult to imagine what a contrast there was between this thrilling intellectual exercise and the dreary grind of instruction of the medical course proper.

My first point is therefore this, that in any branch of university education, including medical education, we should aim at using the methods of education rather than instruction. We must teach the student how to collect the facts, to verify them, to assign a value to them, and how to draw conclusions from them and test those conclusions; in short, how to form a judgment. As Karl Pearson said, "the true aim of the teacher should be to impart an appreciation of method rather than a knowledge of facts," for method is remembered when facts have been forgotten, and method can be used in a new situation where there are no, or too few, facts. The student learns how to learn and can go on acquiring knowledge for the rest of his life.

To obtain some insight into the effect of instruction as opposed to education on a sensitive mind, may I quote Charles Darwin's experiences as a medical student in Edinburgh University in 1825: "The instruction at Edinburgh was altogether by Lectures, and these were intolerably dull, with the exception of those on chemistry by Hope; but to my mind there are no advantages and many disadvantages in lectures compared with reading. Dr. Duncan's lectures on Materia

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Medica at 8 o'clock on a winter's morning are something fearful to remember. Dr. Munro made his lectures on human anatomy as dull, as he was himself, and the subject disgusted me. It has proved one of the greatest evils in my life that I was not urged to practise dissection, for I should soon have got over my disgust; and the practice would have been invaluable for all my future work." In medicine the great difficulty in using the educational approach used to be the small number of teachers and the wide range of subject-matter to be covered. Logistics determined the didactic approach by lectures and large practical classes. This still holds in countries like India, Germany, and elsewhere.

Two Difficulties

In the United States and in Britain two developments have made the educational approach possible—namely, a great increase in staffing of medical schools, and a great development of postgraduate education. The obstacles in our way are now different. They are two. In the first place, knowledge is growing apace. And since man is only one of a very large number of living creatures having many features in common, and since it is believed that ultimately physico-chemical behaviour will be shown to be at the root of all biological behaviour, there is almost no piece of natural knowledge that may not be turned to account in medicine. Our first difficulty is then what limits to set to the fields of knowledge in which to practise the educational method. Our second difficulty is how to teach, whether by lectures, seminars, ward clinics, out-patient clinics, discussion groups, or their variants. My own view is that the ground covered and the precise method used are of less importance than the attitude of mind of the teacher himself.

A true educator must have certain innate characters. He must be intelligent and thoughtful; he must be interested in the material he is using for teaching, and in the minds of those taught. He is more likely to have the right attitude if he has come into close contact himself with a great teacher. Finally, he must be able to detach himself from the ever-increasing pressure of modern life, which tends to crush all individuality from him. Let me quote Fridtjof Nansen, who began life as a zoologist, spent three years of his life drifting across the North Polar ice, one of it with a single companion, and who ended his life as the greatest humanitarian of this century: "The first great thing is to find yourself, and for that you need solitude and contemplation, at least sometimes. I tell you deliverance will not come from the rushing noisy centres of civilization. It will come from the lonely places."

Proper Use of Words

I now come to my second topic, the need for the correct use of language. Of the various points I have to try to make to you I would myself regard this as the most important because the most neglected. The function of language is the transfer of information not only from the mind of one individual to that of another but also, what is often overlooked, to transfer information from one part to another of a single individual's mind. It would seem self-evident that the information that is transferred must be accurate if the action taken is to be closely related to the information received. Electronics, servo-mechanisms, cybernetics, and their amazing products, the automatic machines of great power, versatility, and accuracy; guided missiles; and the like have made us familiar with the importance of transmitting accurate information in order to obtain precise and predictable performance. It is a continuing

source of wonder to me that we doctors are so little concerned with the accurate transmission of information within our own minds, and between other minds and ours.

The chief source of inaccuracy in the transfer of information is, I think, the use of technical jargon. On another occasion, in your country, I devoted a little time to the way in which scientists nowadays fence off their subject with technical terms, so that those who have not first learned the language of the specialty cannot understand what the author is trying to say. Those of us who teach and work in the field of cardiovascular diseases are not entirely blameless in this matter. This is, if you like, a manifestation of the growth of nationalism in science, just as the move to teach in Erse, in Welsh, in Afrikaans, and other tongues is one example of the growth of nationalism within the general cultural life of the British Commonwealth. This is important. Nevertheless, I will say no more of it. I want to deal rather with two other aspects—namely, the transfer of information from the mind of the patient to that of the doctor, and from one part of the doctor's mind to another.

In taking a history of the patient's illness I teach my students that they are eliciting an account of the patient's experience. They must use the patient's own words, provided always that both the patient and the doctor are sure that the information conveyed in these words is so far as possible accurate and unequivocal. They must never use terms, like "chesty," which means nothing at all. Nor must they use technical terms, such as anginal pain, or asthma, bronchitis, haemoptysis, or haematemesis, because these are not terms descriptive of experience but are terms that attempt to interpret that experience. Used by the patient, they are often used wrongly, as also indeed they are sometimes by the doctor, who, in using them, prematurely comes to a conclusion. To my mind a good history is one that is expressed entirely in words that are as simple and well known to us as the words used to describe events in the old and new testaments of the Bible. And I suspect we would all agree that a good history is perhaps the most important part of the evidence that takes us to an understanding of our patient's disability.

I always feel I have great difficulty in persuading my colleagues of the importance of what I have just related, but I have even greater difficulty with the next—namely, the errors that we make our own minds commit by the use of technical terms. To illustrate my point I would ask you to consider four examples from cardiovascular and related pathology—namely, shock, arteriosclerosis, bronchospasm, and hypertension.

"Shock"

Shock was a name that came to be used to describe a failure of the circulation, quite distinct from failure of the heart. It became a problem of first importance in the first world war because so many wounded soldiers died presenting this clinical picture. Many distinguished scientists devoted themselves to it, notably Cannon from your side and Bayliss from ours. And the conclusion that emerged from that war was that shock was a traumatic toxæmia produced by the effects of vaso-active substances like histamine released from the injured muscles. It needed the genius of your Dr. Alfred Blalock and the experience of the second world war to show that this was not so, and to show that this clinical picture was not an entity. It was shown that, arising from war wounds, the clinical condition was usually due to loss of blood but could also be due to infection, loss of plasma (as in burns), loss of other body fluids, or due to the vasovagal or fainting attack.

Now, why Cannon, Bayliss, and other distinguished physiologists went wrong was because they were not clinicians familiar with the variety of circumstances in which this clinical picture called shock could arise. They assumed that because the same word was used, therefore the circumstances leading to the final picture were the same; and because in some cases they could exclude the

obvious cause, loss of blood, they assumed that there must be another and more important cause that must operate in all cases. The history of our understanding of traumatic shock is to my mind a most illuminating one. Cannon and Bayliss were most distinguished scientists with a deep insight into the phenomena with which they were dealing. There were few subjects they touched that they did not illuminate. The error came because information was not fully or accurately transmitted in their minds, but was transmitted in the form of a technical term. It is the kind of error that is easily committed where the mind tries to grapple with a problem with which it is not fully and deeply familiar. And too often and to too many of us understanding is limited by the concept consciously or unconsciously conjured up by the technical term to express it.

"Arteriosclerosis"

My second example is arteriosclerosis. As a student this term confused me utterly, and the confusion was worse confounded by its being sometimes used as almost synonymous with hypertension. Cowdrey's book on arteriosclerosis first showed me the light. It became apparent to me that the distinguished authors were equally confused and were talking about different things. In fact, it became apparent that a large number of conditions affecting different coats and different sizes of vessels were there considered, and indeed E. T. Bell said so.

Nowadays our own specialty runs hotfoot to find the reason why increasing numbers of males in the richer countries die young because their coronary arteries become occluded. This is generally described as the problem of atherosclerosis. Now, this term was introduced by Marchand, in a paper given in 1904 to the German Medical Congress, to include both the fatty proliferative nodular change in the intima characteristic of atheroma and the other degenerative, cellular, and calcific changes of intima and media included in the term arteriosclerosis. His paper was indeed entitled "Über Arteriosclerose." He proposed the term not as an alternative to atheroma, but as an alternative to arteriosclerosis, including lesions of both intima and media, but emphasizing the importance of the intimal fatty change. Atherosclerosis is currently used by most to signify atheroma, which is purely an intimal lesion and is the proper term to describe the coronary lesion that produces ischaemia. Others, however, used it, as it should be used, in Marchand's sense. In fact, I have seen a leading pathologist in this field show a group such as this how atherosclerosis might produce a coronary artery that was wider than normal or one that was narrower. To my rather sceptical eye it seemed that in the first the chief change was in the media, in the second in the intima.

A great deal of wealth and a great deal of man-hours of work are now being invested in this arresting problem. I am tempted to wonder whether the greatest hindrance to our understanding of myocardial infarction lies in the term atherosclerosis. And I wonder if a careful and critical review of the types of arterial change that occur in disease, and their bearing on coronary occlusion, is not the first step that will have to be taken before we reach our goal. As I tried to illustrate by the history of shock, the kind of misconception that technical jargon conjures up is one of the most potent causes, and certainly the most insidious cause, of erroneous conclusion. Many of the distinguished scientists now invading this field of arterial diseases, and particularly ischaemic heart disease, are unfortunately not themselves deeply conversant with the clinical and pathological facts. I often wonder if they really understand what they are seeking to explain, and whether they know how much and how little the term atherosclerosis really means. Or are they being misled as Cannon and Bayliss were by a technical term?

"Bronchospasm"

My third example is bronchospasm. This clearly implies to my mind, and I think to most, that contraction of their

muscular walls has greatly narrowed the bronchi. For some years it has been a common practice, even among skilled chest physicians in my country, to describe the association of difficult breathing with rales and rhonchi as bronchospasm. A few years ago I was concerned in a therapeutic trial on the effects of a certain drug on status asthmaticus. As the results came to be set out several of the distinguished doctors wished to refer to the bronchial obstruction that characterizes this state as bronchospasm. This seemed to me to be an intellectual lapse that is characteristic of the age. As every experienced pathologist knows, the characteristic feature of the post-mortem appearances of the lungs in status asthmaticus is the swelling of the bronchial mucosa, and the blocking of the lumen by mucus and other material. To describe this by a term signifying smooth-muscle contraction is surely to reveal a mind that has lost all pretence of being an instrument of precision.

"Hypertension"

My fourth example is hypertension. I will just say this, that the introduction of this technical term, its evolution into the concept of essential hypertension as a disease entity, and the necessity of defining normal blood pressure and hypertension, represent a sequence of events that the readers of Wilfred Trotter's (1941) essays on "The place of general ideas in medicine" and "Has the intellect a function?" will recognize as inevitable. But, as I mentioned earlier, they have made it very difficult for the average doctor to understand the nature of so-called essential hypertension.

Importance of Population Studies in Clinical Research

I would like to leave this rather damaging assessment of a common behaviour of the mind of many who actually lead in medicine to-day and proceed to consider the new importance being given, particularly in Britain, to the study of selected populations with the object of identifying the factors concerned in producing disease and the effects of treatment.

In recent years clinical science has been dominated by what the late Sir James Spence described as phenomenology; that is to say, the application of the methods of physiology and biochemistry to the search for causal sequences in the individual patient. This method has been quite invaluable in showing how the various organs work in disease and what happens when they fail. It has also been invaluable in demonstrating the precise action of drugs which act quickly. Nevertheless, there is no doubt that a great deal of unnecessary effort is put into this form of investigation. I remember the editor of a well-known journal telling me that he had had 53 papers submitted to him in one year on the effects of exercise on the cardiac output in mitral stenosis. Moreover, invaluable as this method is in its proper sphere, it can tell us next to nothing about the genetic and environmental factors producing disease nor how to prevent it or control it. Thus the physiological approach has enabled us to understand the symptoms and signs and electrocardiographic changes in coronary heart disease and assess the effects of vaso-active drugs on exercise tolerance. But it is virtually useless in identifying or measuring the effects of genetic and environmental factors in producing myocardial infarction, or the effects of treatment in preventing recurrence or prolonging life. In other words, the physiological approach is of little value in the prevention or control of disease.

The study of populations to assess the influence of genetic and environmental factors began with Francis Galton, the cousin of Charles Darwin, in his studies in inheritance in man. Galton (1889) found that there were two kinds of inheritance, that of alternative characters such as blue or brown eyes, and that of blended or graded characters such as height. The former type of inheritance was later explained by Mendel's work as representing the effects of single genes, distributed in allelomorph pairs and behaving as dominants or recessives. The latter type of inheritance is believed to be polygenic—that is, to repre-

sent the sum of many genes, each of which probably behaves in Mendelian fashion. Hamilton, Roberts, Sowry, and I (1954), and Miall and Oldham (1955, 1957) have shown, using extensions of Galton's method, that blood pressure is also inherited as a graded character over the whole range. In the field of cardiovascular disease this method has thus shown that the distinction between so-called normal blood pressure and essential hypertension is nothing else but an artifact and that in the production of levels of blood pressure ordinarily termed essential hypertension genetic factors are important but not exclusive; environmental factors as yet unidentified are probably also concerned.

The aim of this method is to study populations that are alike in every respect except for the variable studied. Because of the complexity of factors concerned and the impossibility of assessing and controlling them all, this means the study of large numbers, with the expectation that the influence of these uncontrolled factors will be the same in the two populations, the differences thus representing the influence of the variable factor. This was achieved by us by measuring blood pressure under the same circumstances in three populations—a sample of the general population, the first-degree relatives of subjects with normal blood pressure, and the first-degree relatives of subjects with so-called essential hypertension. The second essential is to be able to measure a character or to assess the presence or absence of a peculiarity with some precision in the population studied. Finally, there is the mathematical analysis which may need to employ devices for allowing for sex, as Galton had to in his study of height, and allowing for sex and age, as we did in blood pressure. May I just mention an aside here, and say that the most important point is the careful planning of the experiment and collection of data. There is a tendency now to under-emphasize the reliability of the data and their suitability for mathematical treatment. As L. J. Henderson once said of a distinguished colleague, "his mathematical ingenuity is such that he can provide a formula for any set of data, however erroneous."

Much use is being made of the epidemiological method to try to identify the genetic and environmental factors concerned in producing coronary heart disease. There are two major difficulties—namely, the identification of coronary disease with precision in the kind of population samples that need to be compared, and the difficulty of obtaining two populations alike in all respects but one. Thus the higher-income groups in Western countries in which ischaemic heart disease is more prevalent usually differ from the lower-income groups in which the disease is less prevalent in at least four factors: the composition of their diet, their consumption of tobacco, their mental life, and the exercise taken. Nevertheless, I cannot help thinking that a correct choice of groups and a more precise index of prevalence, morbidity, and mortality will ultimately lead to the truth.

Assessing the Effects of Therapy

The other great function of the scientific study of populations is to assess the effects of therapy. The method known in Britain as the controlled therapeutic trial, and developed particularly by Bradford Hill (1951), had its roots in biological assay on the one hand and the testing of chemical manures on the other. Curiously enough, the dominant parent of the controlled clinical trial is the method perfected by R. A. Fisher and his colleagues for the testing of chemical manures, and developed theoretically in Fisher's (1951) "Design of Experiments," for the two methods are used to assess differences in behaviour over weeks, months, and years. Thus development of these two techniques showed how it was possible to measure reasonably accurately the effects produced by altering a single environmental factor, or even two or more environmental factors, despite the variability common to all biological systems.

The principles for such a trial are relatively simple. In the first place, the group of patients for study must be

defined as exactly as possible, the reasons for selecting some patients and rejecting others. Secondly, a method must be adopted for allocating about equal numbers of patients at random to the two treatment groups to be compared. Note that allocation of alternate patients to the two groups and allocation by day of admission to hospital are not acceptable, since both give the doctor an opportunity of influencing selection and therefore introducing bias. The two groups selected are then each treated according to the therapies to be compared, by the same doctors in the same institutions, both doctors and patients being, if possible, ignorant of the precise therapy used. The results are finally compared, using objective criteria and eliminating observer error wherever practicable.

I might illustrate the usefulness of the controlled therapeutic trial by contrasting our knowledge of the effects of sympathectomy on the course of hypertensive disease, and the knowledge gained by trial of the anti-tuberculosis drugs. Now, it is an unfortunate fact that, despite the many thousands of patients subjected to sympathectomy by most skilful surgeons, it is still unknown whether this operation affected the prognosis in hypertension, if so how much, and in what groups of patients. Many series of patients were followed and the results analysed and published. But to the best of my knowledge there was not a single series with adequate controls selected at the same time and with the same criteria as the operated group and followed by the same doctors. The control groups were either series such as the well-known one of Keith, Wagener, and Barker at the Mayo Clinic, or patients seen at the same hospital as those selected for surgery but rejected for, or refusing, operation. It is thus quite impossible to judge whether observed differences in mortality were due to treatment or due to initial differences between the groups.

M.R.C. Trial of Anti-tuberculosis Drugs

We may contrast this with the Medical Research Council's therapeutic trial of anti-tuberculosis drugs. The story begins in 1946, when the M.R.C. obtained a small amount of streptomycin to assess its usefulness. Quickly a committee was assembled and a trial arranged (M.R.C., 1948). Six hospitals participated. Patients with acute progressive bilateral tuberculosis of presumably recent origin bacteriologically proved, unsuitable for collapse therapy, aged 15 to 30 years, were selected for study. About one-half (52) were allocated bed rest only, the other half (55) were allocated bed rest and streptomycin. The allocation was made strictly at random. After six months' and one year's treatment the results were compared objectively. At six months in the streptomycin-treated group 69% had improved and 7% were dead, as compared with 33% improved and 27% dead in the control group. At one year the streptomycin-treated group showed improvement in 56% and death in 22%, as compared with improvement in 31% and death in 46% of the controls. By the time this trial had been completed a new anti-tuberculosis drug was available—namely, para-aminosalicylic acid (P.A.S.). The Medical Research Council (1950) therefore decided that this should be tried in the same way as streptomycin. The results with P.A.S. seemed less good than with streptomycin, but much the best results were used with the two drugs in combination.

By the time the trial with P.A.S. was completed another anti-tuberculosis remedy had appeared and had passed with great distinction all the preliminary tests. It was isonicotinic acid hydrazide, hereafter referred to as isoniazid. A new trial was therefore planned by the same Medical Research Council Committee, using very much the same methods but with these differences: (1) The scope of the trial was greatly enlarged; no fewer than 39 hospitals collaborated; (2) the variety of cases included was increased. Thus the following criteria were adopted. The sputum must be positive, and the bacilli must not be streptomycin- or P.A.S.-resistant at the beginning of treatment. The patient should not have had more than 15 g. of streptomycin nor 300 g. of P.A.S. during the previous three months. The patient must not be

undergoing collapse therapy. The records from the proposed patients were examined centrally and the cases classified into three main groups and seven subgroups and allocated at random to the two methods of treatment to be compared. (3) Reports of progress were received at one month, two months, three months, and six months from the beginning of the trial.

The speed with which this trial achieved its objective is one of its most impressive features. In February, 1952, preliminary announcements were made in the American press indicating the effects of isoniazid on clinical tuberculosis. The Medical Research Council trial was initiated the same month and treatment begun on March 29, 1952. The preliminary report of the trial was published the same year (M.R.C., 1952), and it established that isoniazid alone was not superior to a combination of streptomycin and P.A.S. During this time 173 patients had been treated with 200 mg. of isoniazid daily, and 158 with 1 g. of streptomycin plus 20 g. of P.A.S. daily. Improvement in general condition was rather better on isoniazid alone, but radiological changes did better on the combination. Acquisition of bacterial resistance to isoniazid was a severe problem, and occurred in 11% of cases at the end of the first month, 52% at the end of the second month, and no less than 71% at the end of the third month. The trial was therefore modified to compare the results of 1 g. of streptomycin daily plus 200 mg. of isoniazid daily with those of streptomycin and P.A.S. It was concluded that the degree of radiographic improvement was essentially the same on streptomycin and isoniazid as on streptomycin and P.A.S., and better in either than on isoniazid alone. Improvement in general condition and conversion of positive to negative culture were more frequent with streptomycin and isoniazid than with streptomycin and P.A.S. Thus it seemed that a combination of streptomycin and isoniazid was in general the most effective treatment known for pulmonary tuberculosis.

In this account I have omitted many details of method and of the knowledge achieved, and I would refer those interested to the article by the late Dr. Marc Daniels (1951), to whose personal qualities so much of this success was due. But I do want to say that I cannot conceive how so much and so exact a knowledge of the relative efficacies of these drugs could have been got so quickly and with so little expenditure of human life and suffering in any other way. Imagine the fate of the tuberculous patients if these drugs had been prescribed without plan or purpose and their assessment left to "clinical judgment." When I reflect on this I am amazed, stupefied, and I confess rather horrified that some of my colleagues, of unquestioned integrity and of no mean intelligence, adopt the attitude they do to controlled therapeutic trials.

I would also like to add that the controlled clinical trial is to my mind the most important new method introduced into clinical science in recent years. It should not only tell us what drugs can do, but if only the practical details can be overcome it could tell us, for example, whether or not overindulgence in fat, or in a particular kind of fat, is a contributing factor in the pathogenesis of ischaemic heart disease. Patients must be treated, and it would seem only sensible that treatment should be designed so that the results shall add to knowledge and help us in the prevention and control of disease, so long as the trial is not against the best interests of the patients.

REFERENCES

- Daniels, M. (1951). *Brit. med. Bull.*, **7**, 320.
 Fisher, R. A. (1951). *The Design of Experiments*, 6th ed. Oliver and Boyd, Edinburgh.
 Galton, F. (1889). *Natural Inheritance*. Macmillan, London.
 Hamilton, M., Pickering, G. W., Roberts, J. A. Fraser, and Scowry, G. S. C. (1954). *Clin. Sci.*, **13**, 273.
 Hill, A. Bradford (1951). *Brit. med. Bull.*, **7**, 278.
 Medical Research Council (1948). *Brit. med. J.*, **2**, 769.
 — (1950). *Ibid.*, **2**, 1073.
 — (1952). *Ibid.*, **2**, 735.
 Miall, W. E., and Oldham, P. D. (1955). *Clin. Sci.*, **14**, 459.
 — (1957). *Acta genet. (Basel)*, **7**, 114.
 Trotter, W. (1941). *The Collected Papers of Wilfred Trotter*. Oxford Univ. Press, London.

SERUM GLUTAMIC OXALACETIC TRANSAMINASE IN ACUTE MYOCARDIAL INFARCTION

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The estimation of glutamic oxalacetic transaminase in serum (S.G.O.T.) as an aid in the diagnosis of acute myocardial infarction was first introduced into clinical practice by LaDue, Wróblewski, and Karmen in 1954. Since then a fairly extensive literature, most of it American, has developed. Particularly comprehensive papers are those of Chinsky *et al.* (1956), Ostrow *et al.* (1956), Kattus *et al.* (1957), and Ratner and Sacks (1957).

The enzyme is widely distributed in the tissues, and high concentrations are present in cardiac and skeletal muscle and in brain, liver, and kidney. It is liberated into the blood on the death of cells of these organs. It is also present in erythrocytes, so that when samples of blood are collected for its estimation, haemolysis must be avoided and the serum or plasma separated as soon as possible. The enzyme will retain its activity for two weeks if the serum is stored at 0–5° C. (LaDue and Wróblewski, 1955). Its concentration can be estimated by the spectrophotometric method of Karmen *et al.* (1955) or by the colorimetric method of Reitman and Frankel (1957).

The level of S.G.O.T. activity in normal controls varies from 5 to 40 units per ml. of serum, with a mean of approximately 21 units (Wróblewski and LaDue, 1955; Kattus *et al.*, 1956). In a normal person the level does not vary by more than 10 units from day to day and is independent of time of day, meals, or previous exercise (Chinsky *et al.*, 1956).

Agress *et al.* (1955) showed that graded experimental infarction in dogs was associated in all cases with increase in S.G.O.T. Infarction of as little as 10%, and possibly less, of the total myocardium produced a significant rise in S.G.O.T. and there was a linear correlation between the peak S.G.O.T. level and the amount of infarction at necropsy. Nydick *et al.* (1957) found that there was no rise in S.G.O.T. in experimental myocardial ischaemia in dogs unless myocardial necrosis had occurred. The rise in S.G.O.T. begins within three hours after infarction, attains a peak in 9 to 23 hours, and returns to normal in three to six days. Agress *et al.* (1956), in other experiments, made the useful observation that if pericarditis was produced by sand, talc, or bacterial infections the S.G.O.T. would rise only if the underlying heart muscle was involved in the injury.

Since the enzyme is widely distributed in the body it was realized early that elevation of S.G.O.T. would occur after necrosis of tissues other than heart muscle. In man a rise in S.G.O.T. has been found after necrotic