Papers and Originals

Microbiology as a Medical Discipline*

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In most parts of the world progressively fewer young doctors are making careers for themselves in medical microbiology. In Britain, however, medically qualified recruits are still coming forward, though not evenly throughout the country. These recruits are in great demand, much of the demand coming strongly from parts of the world which have ceased to train any significant number of medical microbiologists. That is the position—a strange and ironical one in many ways. It must raise in our minds the question: Is microbiology a medical discipline? This large question is topical, and of sufficient importance to be worth breaking down for examination in detail.

Clinical Background of Medical Microbiology

Does a medical training provide a doctor with a range of clinical and pathological skills, experiences, insights, and attitudes essential for the good of medical microbiology?

My answer is an affirmative. I had to face this as a real question when a young medical graduate recently offered herself as a recruit for microbiology provided that she was not required to take the clinical appointments needed for full registration or to have experience in morbid anatomy as part of her postgraduate training. As I considered my answer many real situations came to mind. I recalled an incident that occurred over 30 years ago involving two young brothers. The elder was admitted to a surgical unit in a teaching hospital with a diagnosis of suspected appendicular abscess. The signs and symptoms were not conclusive, and the surgeon asked, in a general way, for any help the laboratory could give quickly. The leucocyte count was within normal limits, but the bacteriologist, who had clinical experience in a fever hospital, sat over the water bath with the Widal tubes and soon saw that a significantly high level of typhoid agglutinins was to be the result. Within hours the boy was safely in the fever hospital. He owed his intact abdominal wall to a good surgeon and a good bacteriologist whose training had enough in common to guarantee their effective co-operation for his benefit. Within a week the younger brother was admitted to the typhoid ward of the same fever hospital. The bacteriologist who came to draw blood for the routine samples had seen many acute abdominal emergencies in his days as a house-surgeon. The look of pain on the boy's face, the flexed knee, and the rigid abdomen which the bacteriologist's rapid clinical examination disclosed compelled him to postpone drawing blood in order

to call at once for a surgical opinion. He persuaded his clinical colleague not to tell the consultant surgeon about the boy's brother until a clinical diagnosis was made. The surgeon expressed himself as clear about the need for immediate laparotomy. Even when he was given the family history, along with another unhelpful leucocyte count, he fortunately adhered to his decision and an acutely inflamed appendix with a gangrenous tip was removed. The second boy did not develop typhoid.

Both these brothers owed much to good surgeons but also to the medical training of the bacteriologists who attended them. I agree, of course, that one episode, however dramatic, does not establish a case. But if I cast my mind back over the years I am impressed by the ease with which I can recall other examples of situations in which the bacteriologist was helpful only because he was able to make an essentially medical judgment, drawing upon his own clinical experiences.

I recall the old man with the lesion on the dorsum of his wrist and forearm. The bacteriologist of the hospital to which he was admitted, in an essentially urban industrial town, was invited to sample the lesion to discover if the cause was a virus or a fungus. The patient had been given moderate doses of penicillin for two days without obvious benefit. The bacteriologist, who had an agricultural background and had served a casualty out-patient department in a fishing port, had no hesitation in saying that the diagnosis was an erysipelothrrix infection—this after one look and without even discovering that the patient had recently been shearing sheep and had accidentally pierced the skin of his hand near the site of the lesion. He insisted that the diagnosis was as obvious as it was clinical. He would not aspirate the lesion because the organisms would be found only by culturing a portion of skin excised from near the advancing edge, which was a procedure that would trouble the patient, perhaps admit secondary infection, and add nothing to his own certainty about the diagnosis. The surgeon was a senior man of good judgment, but he needed a little coaching about the difference between erysipelas and erysipelothrrix infection before he agreed to step up the dose of penicillin and wait a few more days for a response, and to refrain from exploding at his bacteriologist's obstinate insistence that the matter was self-evident. The ending was a happy one, but could a non-medical bacteriologist have secured it?

Every clinical bacteriologist worth his keep could recount similar experiences. Their significance is not that they prove superior skill among medically qualified bacteriologists but that they are examples of the way in which a bacteriologist with a good background of clinical and pathological experience can bring something to his work in a rather specialized group of diseases which will be of real and easily recognizable value to his clinical colleagues and the general community he tries to

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serve in a field of preventive medicine. If he has also an acceptable personality the probability is that he will not be one of the many laboratory workers who experience only a continuous frustration over the difficulty of effective communication with clinical colleagues about laboratory matters. If he has a sound clinical and pathological background, in addition to his own specialized knowledge of a relatively unfamiliar field, his clinical friends will soon come to seek him out, even if his laboratory is at the back gate beside the boiler house and the exit for the undertakers' vans.

Microbiological Questions that Need a Medical Answer

Does medical microbiology produce the problems, questions, and situations which are a proper challenge to a medical man?

One of the commonest problems facing medical laboratories at the present time is how to keep an efficient service going with too little space, too small a staff, and rather old-fashioned equipment. Indignation, frustration, and even emigration are distressingly common in consequence of this unfavourable situation. These attitudes are certainly understandable, but they do not provide the only answer, and certainly not the best. Patients have to be served, and epidemics of infection within the community have to be either prevented and controlled, or understood and rationally discussed. It may not be taken for granted that even the second objective is easily attained. One element in keeping a laboratory service going despite difficulties is to make a right assessment of what is being done by the laboratory.

Specimens arrive accompanied by request forms, which often conceal more than they reveal. For efficient work in microbiology the specimen and the request should be seen and judged by a medical man at the earliest possible stage. He should decide what is required in the way of laboratory examination and if further clinical details need to be sought. The examination requested may not be the one most likely to give a positive result. A different specimen might be more useful to examine. Many laboratories, of course, simply have to start off most or all of their specimens on a well-defined routine without awaiting a medical opinion on them, but this is always a second-best procedure. Too often there is failure to realize that a full and sufficient answer could be sent back at once on the basis of an examination of stained films. I see no reason why this should not be done as often as it may be, and usually a quickly given medical opinion is what is needed to deal with genuine bacteriological emergencies. Many specimens reach the laboratory only because for one reason or another side-room work is less commonly done than it should be. If the scrutiny proper to a side-room will yield a sufficient answer for diagnosis and treatment, that should be returned at once. Unnecessary culturing, subculturing, fermentation tests, resistance patterns, serology, and all the rest should not be perpetuated merely to accumulate facts which nobody uses. There are specimens that need every resource of the laboratory, but the greatest obstacle to their receiving it is the brainless multiplication of unnecessary tests. These are usually done simply because it is easier to prescribe them as routine than to think about their necessity.

The kind of selection and discrimination I advocate is increasingly required if laboratory services are to survive, and this selection can be wisely exercised only if there is a medical agreement about what is important and what is irrelevant. The laboratory that must simply do whatever it is asked and report the results is not likely to be a very good one. Laboratories doing medical microbiology owe a great deal to the devoted work both of graduates in science and of technicians. Indeed, medical laboratories could not work without such staff. But the laboratory will still be likely to require a medical director if it serves the kind of doctors I know. For example, I recall

being hard pressed to put a quantitative expression on all antibiotic-sensitivity tests. This was followed by the further suggestion that the concentration of antibiotic in every patient's serum should likewise be added to the information. Why was it wanted? Well, it would sometimes help treatment, wouldn't it? And in a modern teaching hospital surely the records ought to contain this information. Presumably a one-up-man type of student might ask for it. Or a keen registrar might make a thesis out of the mass of otherwise unstudied information. The answer to the proposal had to be that the quantitative information desired would be made available only when there seemed to be a real point in it. Not long after this decision there came a patient whose life, in these pre-methicillin days, depended on finding an antibiotic regimen that would control the penicillin-resistant staphylococcus in his blood-stream. This demanded regular samplings, assays, and conferences, and they were gladly given with a most gratifying result. But for the critical period of five days two experienced medical bacteriologists and two devoted technicians among them gave over 100 hours of time to the material from this one patient, and they examined it at all sorts of odd hours. This is not a unique contribution, but it was possible only because a medically informed selection was able to separate what mattered from what was mere window-dressing.

Apart from preserving laboratory services in a functionally useful form, medical men will often be challenged by the need to interpret the significance of microbiological facts revealed. A report on a specimen listing the names of a great many bacterial species and the sensitivity of each to numerous antibiotics can be confusing rather than helpful. After an outbreak of food-poisoning the isolation of *Salmonella typhimurium* from the intestine of a cook means one thing (not typhoid, it may often have to be explained), but the discovery of *Clostridium welchii* in the same situation has an altogether different significance, though both organisms are causes of food-poisoning. Yet I recall a luckless cook who had been kept off work for six months because, in answer to a specific question, the laboratory reported the presence of *Clostridium welchii* in her faeces. It required much medical argument and explanation to have her allowed back to work; and without it she might never have been allowed to return. The mere presence of microbes is often far less significant than the question whether, in a particular situation, they will be able to multiply and whether they are in a position to be conveyed to a place where they will do harm.

Germs are as individual as humans, and as varied and variable. They need to be accurately interpreted, above all to the partially informed. The clinician who at some stage in his training has done a fine bit of bacteriology for his M.D. thesis is often hard to persuade that what he has truly learned about organism A is of low predictive value about the behaviour of organism B. To sympathize with such personal problems, but not to be ruled by them, often calls for a good deal of background information, needing arguments based on pathology as well as clinical medicine.

When is a disinfectant liable to become a culture medium, and therefore a menace? Is the kitchen staff's latest variation of the catering officer's instructions significant or not? Who is to speak to the white-robed surgeon known to be *en route* from the post-mortem room to the operating theatre, especially as he is also known to be very unlikely to change his white robe before getting on with the next operation? When is cleanliness sufficient and sterilization superfluous? Why is it criminally negligent to use a syringe without a reliable guarantee about its sterility? Is a particular infection one of high or of low communicability? All these are simple examples of questions of a kind that are asked daily in hospitals and laboratories. The true answers need an awareness of the facts of medical, surgical, and public-health practice as well as of microbiology. The wrong answers often produce the equally undesirable contrasted states of unnecessary panic and unjustified confidence, and sometimes

the results are avoidable losses of health or life. A medically trained microbiologist need never go long without meeting a chance to make good use of his medical training.

Medical Training and Scientific Microbiology

Is a medical undergraduate equipped for the study of microbiology as a science in its own right?

Twenty years ago, for one bad reason after another, the training of the medical undergraduate, already rather on the long side, became yet another year longer than was either sensible or necessary. As a result fewer medical undergraduates than previously are now willing to combine a science course with their medical studies. It has always been true that the science of the ordinary medical course did not go very deep at any point, and it has always seemed surprising, therefore, that medical graduates have made as good scientific research workers as they have done. Nevertheless, they were able to be pretty reasonable microbiologists while the subject was in its natural-history phase. After all, they acquired a fair experience of human biology. They were men, also, who had necessarily chosen their profession at a young age, and a capacity to make up one's mind and commit oneself to a long course of study is a good eliminator of the faint-hearted. Moreover, many of them had a good classical education and therefore a capacity to work hard at difficult tasks. This had made up, it might be supposed, for a lack of pure science by development of the powers of endurance combined with some degree of aspiration and some powers of orderly thought and expression. Also, with help, they were not too badly equipped to specialize in a bit of chemistry or mathematics if their work required it. At all events this carried enough of them through.

Microbiology has now advanced from its applied beginnings to medicine, agriculture, and industry, and has fully justified its appearance as a science in its own right. For all that, some of the pioneers of microbiology as a science tend to lament in their candid moments that so high a proportion of the significant contributions, even to the present molecular phase of microbiology, have come from medical microbiologists. Certainly there is an impressive muster of medical microbiologists during the past 20 years among those elected as Fellows of the Royal Society or chosen as Nobel laureates. It may be that what counts is not the scientific content of the preclinical medical course but the basic attitudes of readiness for hard work, of willingness to experiment, of curiosity, aspiration, and even of genuine dedication, which may be seen to grow in some of the rawest medical undergraduates during their strenuous hours of work and play. These qualities are doubtless further developed by early and close contact with the fundamental matters of birth, life, and death, and the acceptance of responsibility for the lives of patients at a relatively young age. The impetus to make progress in knowledge and so to relieve suffering is often suspect, because emotion is no substitute for accurate observation, and a sharp imagination is more useful than a sympathetic nature when it comes to framing a new hypothesis. But, whatever the explanation, there are medical men and women busily and successfully engaged in unravelling protein molecules, in characterizing new globulins, in understanding the intimate biology and physico-chemical structure of cancer cells, genes, phages, viruses, microsomes, and resistance-transfer factors. These proofs of accomplishment show that current medical undergraduate education, for all our doubts about it, does not necessarily deprive those subjected to it of the capacity to be good scientific microbiologists. The same evidence is also another part of the answer to the question whether microbiology offers a proper challenge to a medical man. Evidently it does—and in its pure as well as in its applied aspects.

Training for Medical Microbiology

What is the right kind of education and training for whatever number of medical microbiologists may be required?

Only a brief word need be said about this, but it is timely to express a view because of the current inquiry into all aspects of medical education and the growing shortage of medical microbiologists. Whatever may be the full outcome of all this I hope that we may expect some shortening of the undergraduate period of instruction and some increase in the requirement for clinical experience after graduation and before full registration. Microbiology, like many other specialized disciplines of the medical course, ought to be shown to the student in a relatively short systematic lecture course, combined with practical meetings designed only to ensure that he certainly sees and handles the material he is to read and talk about. Such a course needs to be supplemented by seminars, tutorials, and clinics where small numbers of students learn from a teacher who is emphasizing a point of application to medical practice. There should be no attempt to make any medical undergraduate into a complete microbiologist at that stage. But he should be able to remember that he has had the class. He should be convinced that microbes have reality, individuality, and an application to medicine; and he should know that guesses and approximations to the truth about germs can be dangerous to life as well as tiresome of utterance. He should remember the professor's name and face—some students complain that they have little chance—and, if he has been a bright student, he ought to be seen personally by the professor and assured that there is a possible career for him in the specialty. This assurance, given at the time of the undergraduate's instruction in microbiology, should not be neglected. It can make all the difference to a young man's willingness to consider the specialty as one for which he might be suited. Professors who are never seen and who never say a personal word to even their bright students need not be surprised if none of them seems to wish to work in their departments.

In the period after graduation, which I should hope might be of two years' duration, with four resident posts, each of six months, the aspiring microbiologist ought to be encouraged to include a period in an infectious diseases unit and in a paediatric unit. After full registration he needs a two-year period at least of general apprenticeship training in microbiology and in one other laboratory discipline, followed by a specialized study of microbiology with increasing responsibility. If he can have a year of systematic instruction, as in a course for a diploma in medical microbiology, he may learn more quickly and reliably than by apprenticeship alone. He should be required to investigate problems and shown how to publish the results. He may usefully serve for a year or two overseas; and he ought to write a thesis.

If this brief statement of personal opinions appears to be dogmatic that is because of the need to keep it brief and because at this time, when discussion of medical education is likely to be plentiful, a few dogmatic utterances without too many concessions to other possible views may offer useful beginnings to the general debate.

One of the things that medical microbiologists need to learn is how to communicate with those who have somehow managed to resist the infectious nature of their enthusiasm for the beautiful and fascinating creatures which inhabit their world.

Summary and Conclusion

Outside Britain progressively fewer medical graduates are making careers for themselves in medical microbiology. But the demand for medically qualified microbiologists continues to grow. The contradictions of this situation can be resolved

in only one of two ways: either by recruiting and training more medical microbiologists or by concluding that microbiology is not a medical discipline. If that conclusion was accepted all the work would be done by graduates in science and by technicians.

The present examination of these possibilities concludes that medical graduates have clinical skills and a background of pathology extremely useful in the application of microbiology

to medicine and that this application, to be fully effective, requires what medical graduates have been trained to give. In promoting the advance of microbiology as a science in its own right medical microbiologists have, perhaps surprisingly, played a significant and useful part. Their recruitment and training need systematic thought about methods and objectives as well as some additional effort and imagination. Emphatically it should be continued.

Ischaemic Contracture of Muscle Associated with Carbon Monoxide and Barbiturate Poisoning*

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Ischaemic muscle contracture was first described by von Volkmann in 1881, since when the condition has become generally recognized as a complication of certain injuries in the limbs. In a recent review of Volkmann's ischaemia one of us (Seddon, 1964) referred to cases associated with carbon monoxide and barbiturate poisoning, and this paper contains an account of four of them.

Despite the frequency of carbon monoxide poisoning its association with muscle necrosis is little known. References to it in the literature have been few and scattered.

A detailed description of the muscle changes associated with carbon monoxide poisoning was first given by Larrey (1812). He had the opportunity of examining several cases in troops during the occupation of Berlin by Napoleon in 1806. The soldiers used to heat their quarters by burning coal in open stoves, and the lack of ventilation produced many cases of carbon monoxide poisoning. At necropsy Larrey found brown discoloration of the muscles with softening of the fibres and also skin necrosis over the sacrum and shoulder-blades.

A similar but less precise account of accidental asphyxiation by carbon monoxide in a tavern in Jena is given by Hoffmann (1754); he wrote on the subject in 1740, but we have not had access to this earlier work. Knowledge of the gas, as distinct from carbon dioxide, existed before Priestley described it in 1772 and Dalton deduced its formula in 1808.

The legs of the Jena victims were probably affected by gangrene, similar to that later described by McLean (1911), Briggs (1919), and Fowler (1954).

It might well be thought that muscle necrosis due to carbon monoxide poisoning is rare; however, this is probably by no means so. Petri (1930) suspected that it was not, though he reported only one case; Gunther (1921, 1940) reported nine, three of his own; Hedinger (1948) reported two cases.

Necrosis of muscle, indistinguishable from that caused by traumatic ischaemia, can occur in patients who have taken an overdose of a barbiturate, and in view of the widespread addiction to these drugs this condition may be worthy of wider recognition. We put these two kinds of muscle ischaemia together because, as is explained later, we regard their aetiology as almost identical; in brief, hypoxaemia and external pressure, the latter of a degree that would be tolerable in a normal person.

We are reporting four further cases of ischaemic necrosis of muscle followed by contracture; two followed coal-gas poisoning and two barbiturate overdosage.

Case 1

On 20 September 1952 a man of 30 lost consciousness when about to boil some water on a gas-stove. He was alleged to have burned the dorsum of his left hand and the flexor surface of the right forearm. He was treated for carbon monoxide poisoning and the so-called burns. On recovering consciousness he noted: (1) the fingers of the right hand were flexed—a similar contracture on the left followed about eight weeks later; (2) numbness of the palmar surfaces of the hands and fingers, which subsequently passed off; (3) hardness of the flexor muscles of both forearms, which largely disappeared during the next eight weeks.

The initial treatment was by corrective splints and mobilization; he attended a rehabilitation centre with some further improvement, and then returned to work. However, the contractures became a nuisance and he was admitted to the Royal National Orthopaedic Hospital on 17 February 1953.

Right Upper Limb.—There were two very superficial scars on the flexor surface of the forearm. Excessive sweating was present over the ulnar side of the palm; the radial side and the radial three digits were dry and cold. The brachial pulse was normal and the radial pulse nearly so. There was a flexion contracture of the long flexors of the thumb, and of the index, middle, and ring fingers, so that the fingers could be fully extended only when the wrist was in the neutral position. Hypoaesthesia was present over the middle and distal phalanges on the palmar aspect of the radial three digits. Tinel's sign was positive at the wrist over both median and ulnar nerves.

Left Upper Limb.—The flexor muscles of the forearm were hard, especially about 10 cm. above the wrist on the ulnar side; severe contracture of the long flexors of all the digits was present, so that the finger-tips were about 1.5 cm. from the palm when the wrist was in the neutral position; the thumb was flexed 90° at the interphalangeal joint and 45° at the metacarpophalangeal joint. On flexion of the wrist all but the middle finger could be fully extended. Dorsiflexion of the wrist was limited to 45°, and the hand deviated to the ulnar side. There was also an adduction contracture of the thumb and wasting of all intrinsic muscles of the hand. There was paralysis of the thenar muscles. Hypoaesthesia was present over the palmar surface of the distal two phalanges of the fingers, and Tinel's sign was positive over the median and ulnar nerves at the wrist.

Operation.—Correction of flexion contracture on left side was carried out on 19 February. An arteriogram showed nothing more than slight loss of the fine arterial branches in the distal quarter of the forearm.

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