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Medical microbiology for patient and community[1]

SIR JAMES HOWIE

Before and after Chemotherapy

Forty years ago, when I came into the subject, medical microbiology was already an academic discipline with a respectable history and a distinguished and interesting group of professors and research workers to stimulate its development. But the relevance of the subject to the ordinary work of doctors was still greatly underestimated. The war of 1914-18 provided evidence that bacteriologists had much to contribute to medical and surgical practice; and the great influenza pandemic of 1918 made it clear that there was still much to be learned. The botulism at Loch Maree in 1922 aroused national interest, but the significance of microbes for the public health was correctly appreciated by only a small but devoted group. Too many thought of this aspect of their subject as the rather dull routine testing of many milks and waters—a wrong idea which fades too slowly.

The sulphonamides had still to arrive; and the antibiotics were not to be generally available for another 15 years. Vaccines had not done all that had been expected of them, and there was surprising reluctance to push on with active immunization against diphtheria and tetanus. To the clinical pathologist and to the clinician, bacteriology was an interesting enough part of his work but not one which offered such immediately obvious benefits to patients as did histopathology, chemistry, and haematology. The patient with a streptococcus in the blood was in a bad way; and the finding of tubercle bacilli in the cerebrospinal fluid was a sentence of death. Nothing effective could be done. So the microbiologist in hospital was an aid to diagnosis, and thus respected, but not of much help for treatment and therefore not as often consulted as he would have wished. The bacteriologist's art was not widely understood and much of the academic teaching was hardly calculated to attract the best medical students as recruits to the subject.

Strangely and ironically, it was the development of effective chemotherapy against infections which brought bacteriology to a really important place in hospital. The naive idea that sulphonamides, penicillin, and other drugs would end the need for bacteriologists was soon turned upside down; and what I should rate as an exaggerated, uncritical, and often misplaced deference to the results of antibiotic sensitivity testing soon increased the demand for microbiology and microbiologists. Even so, however, as recently as 20 years ago, I recall that a very good general pathologist asked me to supply him with a table summarizing at a glance the identifying characters of all the microbes which he might meet in the diagnostic work of his laboratory. I asked him if he thought that the possession of such a table would make him a useful microbiologist. He agreed that there was perhaps a little more to it than that but said—inelegantly, as I thought—that if he could 'put the bugs through the hoops', and thus surely and quickly know what they were, he'd doubtless be able to get the rest from a textbook. Histopathology, I gathered, was an art as well as a science, requiring many years of devoted study, and he declined my counter-invitation to supply me with a 'table for telling tumours'. As I say, he was and is a very good general pathologist and we are still friends.

I repeat the story to underline how much more is now expected of a good medical microbiologist. As I see him at work, he first designs the various routine procedures through which most specimens will go, each variety being tested according to its nature. These routine procedures save time and debate but their selection and the precise details of their construction need thought. Their object is to give a reliable result as quickly as possible and to ensure that purely routine specimens requiring only standard tests—at any rate in the first instance—are separated from the smaller number of specimens requiring special treatment of one sort or another. Before he signs reports, whether to authenticate the testing procedure or to offer both a result and comments upon its significance, my kind of microbiologist will at some stage look at the actual tests, the specimen, and the request form. He will surely separate some specimens which will receive either special study or additional tests and about which he may wish to have extended information. When the laboratory findings are established, moreover, the microbiologist may well wish to talk to the sender of the specimen about the significance of what has been learned. In many

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cases, additional specimens are needed, perhaps from relatives, contacts, or material from the patient's environment.

Consultation for the Patient

A very important part of the microbiologist's work is consultation designed to help in the diagnosis and treatment of the individual patient. To make this possible it is important to check whether the patient and the sender of the specimen are unequivocally identified on the request form. If not, the time to settle the question is at once. Reports must not be issued in the vague hope that somehow they will be read by the right person and find their way into the correct notes. I have seen an allegation that in one hospital about one-fifth of laboratory reports failed in one or both of these respects. I also heard tell of a patient whose sputum was unexpectedly found to contain tubercle bacilli but who died without treatment a year later because the report was not seen by the clinician concerned. I have no doubt that strict insistence on the request form's carrying the patient's hospital number and the clinician's identity is fully justified. Reports should not be issued unless they may certainly be sent to the right person and are known to deal with the right specimen and patient; there is an onus on users of the laboratory to see to these details before asking a consultant colleague for help. I think that the more often the clinician and the microbiologist see each other to discuss requests and reports, the better the prospects are that examples of frustrating negligence will be eliminated from request forms.

Often requests carry an element of urgency; and in microbiology I think that personal consultation is always necessary if a worthwhile emergency service is to be given to the patient. The diagnosis and chemotherapy of meningitis is not always straightforward. What the clinician wants is not the result of a culture next day but his laboratory colleague's help and medical advice on the spot. I recall a problem put to me as a matter of urgency by a surgical colleague when he suspected that gas gangrene was developing in a wound after repair of a colostomy. Direct film showed beautiful navicular forms characteristic of *Clostridium septicum* as well as square-ended, capsulated, Gram-positive rods strongly resembling *Clostridium welchii*. In a matter of five minutes, therefore, it was not hard to confirm the surgeon's diagnosis and give advice on chemotherapy and antitoxin treatment. My point is that this kind of help, resting solely on the basis of a direct-film examination, may be given with convincing authority only by a laboratory colleague with clinical understanding; and it is useful only if given at once. So-called emergency services in microbiology which depend upon someone's coming in to put up a culture to be examined next day do not commend themselves to me. Nor do I think it right to ask even the most competent technician or medical trainee to offer on the basis of probability but not certainty what is essentially a clinical opinion and clinical advice. In microbiology, therefore, I always hope that emergencies will be dealt with by the most senior medical microbiologist who is available. And if this means making a strict definition of what is an emergency, I'm greatly in favour of that exercise. An emergency may come at any hour of the day or night. A routine service performed out of normal working hours is not my idea of an emergency.

Ordinary, non-urgent microbiological reports surprisingly often need a good deal of judgment of the laboratory findings in the light of the clinical history and this is seldom adequately presented in the request form. For example, there are circumstances in which quite high agglutination titres against such organisms as *Brucella abortus* and the typhoid bacillus do not warrant a diagnosis of present infection. The findings need to be assessed in the light of the patient's background, previous history, and present illness.

All this kind of consultation needs time and patience. Much of it may be done by telephone if the clinician and microbiologist already know each other well and enjoy a relationship of mutual confidence. With the policy of fewer laboratories serving larger areas, one consequence is that more visits to outlying areas will have to be made often enough to lay such foundations of personal trust and friendship. Without that basis the telephone tends to be a poor instrument of communication and any other method is too slow.

Visits should be made in both directions. Any sensible head of a microbiology laboratory will invite his customers to call on him as often as possible and will arrange open days with a direct invitation and some modest hospitality. Customers should be pressed to say why they ask for certain examinations and what use they make of particular kinds of report. In this way it is truly remarkable how much wasted effort may be eliminated and how many useful services put in its place. As the rising cost of laboratory services cannot be indefinitely accepted rising demand must be contained by a policy of discriminating selection of requests and of tests. Unfortunately, it is extremely hard to measure the consultative work done by a laboratory staff but I have no doubt that laboratories must be well enough staffed to make it possible. Otherwise they will be submerged under a rapidly rising tide of ill-considered requests leading

to diminishingly useful reports, which may not be understood even if read.

Consultation for the Community

For the past nine years I have had the honour to direct the medical and scientific efforts of the Public Health Laboratory Service (PHLS)—an organization created to guard against some ugly possibilities of the war of 1939-45 and continued in existence because it proved how much could be done, by combining epidemiology and microbiology at high enough levels, to improve the understanding and thus the prevention and control of cummunicable diseases. The story of the PHLS has been told many times and I am not to repeat it here. I am glad to note that the government paper on reorganization of the National Health Service (NHS) in England (cmnd 5055, August 1972) gives the assurance that the Service will continue (page 21, para 86, no. 4). But I must explain to clinical pathologists why the Service now undertakes so much work for hospitals. About the early 1960s, as I read the signs, the Service was beginning to be regarded as an invasive growth liable to intrude upon hospitals and devour honest livings.

I am happy to believe that these fears no longer trouble hospital microbiologists. Indeed it has been encouraging to note the local resistance regularly offered to proposals that the PHLS should withdraw from particular laboratories, leaving them to be run wholly as hospital diagnostic services. The PHLS must do enough routine hospital diagnostic work in order continuously to gather information about which infections are prevalent in a sufficient variety of particular localities—for example, cities, ports, country towns, and rural areas. Without that information reliably, regularly, and quickly gathered at first hand, epidemiological studies of communicable disease on a national scale would be impossible. Originally, the PHLS was the laboratory service of Medical Officers of Health (MOsH); but when MOsH lost their hospitals to the NHS the PHLS had to undertake hospital work for the NHS in order to continue to gather basic information without which it could not supply MOsH with the information they needed to fulfil their responsibilities for the control of communicable diseases. It was a difficult time for all—not, however, without good opportunities for useful work but also not without the serious danger that the PHLS might become overcommitted to hospital work and so unable to fulfil its major functions of interpreting the information it collected and promoting the investigative work essential to keep a proper watch on communicable diseases and to offer advice about how to devise ever better methods of preventing them and limiting their spread, whether by appropriate measures of hygiene, active immunization, or well directed chemotherapy.

Work for individual patients in hospital has emotional appeal; the demands grow steadily; and there is a danger that uncritical requests and over-elaborate testing may take up too much time and money. Frequent, sharp, and searching inquisitions are needed to cut out what is not truly useful. It is all too easy to run a particular line of testing to humour a friend, or because it has been done for a long time, or because somebody rated it as a recent advance and wished to write a quick paper and be first in the confirmatory field. In any circumstances, work for patients in hospital makes heavy demands on time, material, and good will. It is clearly essential to ensure both that hospital work is properly done and that the PHLS is not diverted from its main work, namely, to study how infections are spread and how they may be most effectively prevented and controlled. This is now better understood than it once was both by hospital and by PHLS microbiologists.

Epidemiological work in microbiology calls for a high standard of routine bench work; for devising and using typing systems when these can usefully add to knowledge and understanding; and for planning and coordinating field intelligence and the results of field investigations of many different kinds.

Cooperation between PHLS and NHS laboratories has done much to advance the work of each, both for the individual patient and the community. Over 400 NHS laboratories now contribute to the weekly Communicable Disease Report (CDR) and 24 consultant microbiologists employed by regional hospital boards or boards of governors now have honorary status in the PHLS. In other words, PHLS and hospital microbiologists are now engaged upon a joint effort for the health of the community and there is every indication that this collaboration will gain strength by expanding on an informal as well as a formal basis. The Reference and Special Laboratories of the PHLS at Colindale and elsewhere provide a nationwide reference service, extending even into Scotland. No charge is made for this particular part of the service!

The special organization of the PHLS, designed and directed to making epidemiological studies possible and profitable, has yielded many scientific dividends over the 33 years of its existence. They are well documented in our annual and special reports and in over 200 scientific papers which are published each year by the present 78 laboratories of the Service. The PHLS is able to undertake systematic surveillance of certain diseases, for example, influenza, poliomyelitis, and hepatitis in dialysis units, and of certain specific questions, for example, whether new types of pertussis vaccine are acceptable and effective.

Certain outbreaks of infection may be detected at an early stage if a laboratory director observes a sudden increase in the number of isolations of a particular species or serotype—for example of *E. coli*. These isolations may come from hospitals which lie in the areas of different MOsH but which all send their specimens to one PHLS laboratory. In this way the laboratory director may be the first or even the only person to note the presence of an outbreak in a region and to identify its source. Often he has to raise the alert and try to coordinate the efforts of those who have the powers necessary to take the correct steps to stop or limit the spread of infection, for example, by persuading them of the need to regulate admissions or discharges as may be necessary. A good deal of tact as well as energy is often needed to get the right things done in such situations.

Nationwide trials of vaccines and other agents requiring accurate diagnosis of infecting agents by precise laboratory identification of some bacterium or virus would be difficult to organize on an adequate scale without the initiative or support of the PHLS as well as that of the MOsH and their staffs—always willingly given if a good case is presented. Advantages of this kind of approach are not merely the number of observations that may be undertaken during a single epidemic period but the chance of comparing results from different parts of the country and the correlation of different laboratory results with the corresponding clinical and other observations.

New laboratory methods of identification and typing may be tried out quickly and all results may be subjected to critical discussion and analysis at the regular two-monthly meetings of the heads of laboratories. The work of the PHLS is greatly favoured by the relatively small size of our country, by cooperation and tolerance, by the foresight of our founders who planned the Act under which we work, and by the enthusiasm of all our staff of every grade and category. This unique organization for undertaking microbiology both for the patient and the community seems to me to be something which I hope will come to be as well understood at home as it seems to be envied and admired abroad. Whatever clinical pathologists may have said and thought about the PHLS in the past, I hope that this account will now provide a clear definition of its objectives, methods, and philosophy and that they will be judged with charity.

The Future

Having looked back to the past 40 years at the beginning of this lecture, I had better look forward at the end. Current trends and developments may have a profound influence on some aspects of medical microbiology and we had better be prepared for the possibilities.

AUTOMATION AND MECHANICAL AIDS

In serology, automation will clearly be possible, useful, and important. Time and scarce reagents will be saved and accuracy increased if much routine VD and virus serology is concentrated into regional serology centres. These centres will need to be fully associated with consultant virologists and epidemiologists to secure the full benefits of such a plan. The centres will have a training function for their regions. For the rest of microbiology, it is foreseeable that mechanical aids of various kinds are likely to help the work of our present laboratories; but I think that relatively few procedures may be able to be fully automated—at least for a long time.

QUALITY CONTROL

In microbiology we are still feeling our way because our living material is not easy to stabilize or assess with the same accuracy as is possible for the chemical pathologist and haematologist. I think that we must do more work to discover how to prepare, send round, and recover our test materials. I am also sure that we ought to begin to try to measure and define more accurately than we have done before such things in our test material as, for example, the number of viable bacteria, colony size, and reactions on various media, and sensitivity to antibiotics defined as precisely as may be. Antibiotic-sensitivity testing is in particular need of being based on comparisons between unknown organisms and standard cultures of authenticated identity and behaviour issued from a reliable source. A time is surely coming when ways will have to be found of identifying and helping laboratories whose performance clearly needs upgrading.

STANDARD MEDIA AND METHODS

Like all good cooks microbiologists despise precision. 'Cook for a short time in a quick oven' seems to such people better advice than 'heat for 15 min at 300°F'. But I fear that, for economy and efficiency, we are going to be forced by events to define our media and methods far more precisely than in the past; and to accept current 'standards' as the basis of our costings. Whoever can beat the standard in terms of efficiency is a hero and he will be honoured. But those whose methods cost more will have to show whether they also yield some benefit. Their running costs, at all events, will be based on standard media and methods. And why not? People will not be dissuaded from improving upon standard methods, but in the past there has been too little effort to define the basis of

good mystiques. We cannot forever go on being only approximate in our formulations.

USE OF COMPUTERS

Computers are able quickly to retrieve information and rapidly to do sums and correlations which would be too tedious and laborious to attempt without their aid. This is splendid; and we must learn how to use them. To get sense out of them, however, we need to feed sense in. The information must be well organized and the various programs sensibly written. We need to know what is worth working with and what is merely incidental. So we need to define which particular isolates mean, or do not mean, something significant and in which clinical or epidemiological situations. Quality control results and assessments of individual performance by both laboratories and persons will come to be rapidly measurable and we shall have to become accustomed to accepting such methods of studying performance and making full use of the results we produce. The first requirement will be agreement on a form for recording requests and reports. I know that this will not be an easy agreement to reach; but without it we shall make no effective use of computers.

STUDY OF MICROBIAL POPULATIONS

One of the most difficult things is to characterize a mixed population of microbes either accurately or sensibly. Traditional methods are cumbersome and the results are often irrelevant. In the future I suspect that we may come to be looking for evidence of particular kinds of microbial activity, such as specific chemicals, enzymes, metabolites, or genetic material. We may be looking at the broad behaviour of mixed populations and how the balance of various microbial activities can affect things that may be measured and how these activities may throw light on pathological processes and methods of treatment.

VIROLOGY

A full and specialized virological service is costly, difficult, and required at the highest level only in regional and academic laboratories. The ordinary district general hospital laboratory needs a general microbiologist who has a reasonable competence at virus isolation. He should not attempt to grow the most difficult viruses or to titrate sera against all the virus antigens because some of these are very costly and difficult to prepare and must not be wasted. There has been much keeping up with the Joneses in calling for a service in virology. Immediate answers do not influence treatment and the reactions of a good regional virus laboratory should become available quickly enough to serve the real needs of most areas. Methods of transportation and of primary culture before transportation may be usefully explored by peripheral laboratories because some viruses admittedly tend to die on swabs or other uncongenial environments during transport.

MEDICAL RECRUITMENT

Professorial colleagues tend to bemoan the lack of recruits from among their medical students. I am appalled. If what some professors tell me is generally true, personal contact with our students—not to mention the inspiration of our teaching—must surely need revision. Professors must take the trouble personally to tell the promising 10% of each class of students by individual word of mouth communication that they are welcome to call and to discuss how to begin a career in microbiology when the time comes for a decision to be made—perhaps two years after they have taken the class. This—not a general invitation to all and sundry—is what brings in the recruits. This personal word is remembered in the day of doubt when some superb clinical chief has been just one degree too superb. In that moment a would-be consultant clinician may swiftly turn into a potential recruit for the nice professor of microbiology who approved of the student's work in the class and took the trouble to convey his approval in person. This is a simple formula—but surely not too simple to try out. I have used it. I have never been short of recruits.

Do we need medical microbiologists? I am sure that we do. Both in research and in routine work we need to learn how best to employ the skills of technicians, technologists, and graduates in science (and the sooner their gradings and pay scales are made part of one coherent system the better); but assuredly we need the man who has the clinical experience and awareness that allow him to consult on equal terms with clinical colleagues. Without such medically qualified microbiologists we shall lose a priceless advantage which our colleagues in many other countries greatly envy. I know how much I gained from experience of general practice, from house jobs in medicine, surgery, and obstetrics, and from nearly two years in a famous fever hospital in the pre-sulphonamide era. Pneumonia, measles, whooping cough, and diphtheria recall to me the sufferings and deaths of children whose names and faces I still remember, and I would do whatever I thought right to save their successors from such experiences. There is no substitute for such clinical memories. They last a lifetime and they empower quite ordinary mortals to accomplish deeds that surprise even themselves. It would be a bad day for medical microbiology if this source of recruitment ever ceased.

Conclusion

Lectures like this have no possible summary or conclusion. That is one reason why people tend not to read them. This one, I assure readers of this section, is no worse than usual and the separate parts of it are self-contained. In substance it is an attempt to tell general pathologists what I think medical microbiology ought to be and to become if it is properly to serve the patient, the community, and the body of medicine.