Modern Methods in Medical Microbiology

Systems and Trends

Edited by James E. Prier, Josephine Bartola,
and Herman Friedman

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Symposium
Keynote Address

Recent and Future Changes in the Clinical Microbiology Laboratory

John C. Sherris

Until 10 or 15 years ago, the only major changes in methodological principles and in the operation of the average clinical microbiology laboratory since the 1920's were the addition of some tests associated with developments in chemotherapy. There had been dramatic changes in diagnostic virology with the introduction of tissue culture techniques, of course, but these applications were generally limited to some larger public health laboratories. Clinical microbiology in most institutions tended to be highly individualistic, favorite and unique procedures abounded, and experience often carried more weight than objectivity. Concepts of quality control, proficiency evaluation, and methodological standardization were seldom applied and were often regarded with suspicion. Training was frequently quite unstructured and many of those performing clinical microbiological procedures in smaller institutions had few qualifications for the task. Many of us in the field at that time looked with some embarrassment at the developments in technology and performance control which were occurring in clinical chemistry, but consoled ourselves with the thought that our own discipline was much more difficult (which it is), required the continuous application of informed judgment (which it does), and was, therefore, perhaps, inappropriate for the application of statistical standards of performance and the use of automated procedures (which it is not). It was with a sense of considerable shock that we learned from the studies of Dr. Morris Schaeffer and his colleagues (1) just how poor

the standards of performance were in many clinical laboratories, and I believe that this was a turning point toward a resurgence of interest in clinical microbiology and the improvement in its practice which has taken place in the past few years.

In the symposium which follows, many of the most important recent technical advances in the field will be covered, as will new and important developments in regulation and training. Therefore, I will address myself mainly to some other areas of advance and change that I believe to be very important, and then will try to look briefly into the future.

There have been several recent important technical developments in the subject, and more may be anticipated at an accelerating rate. Some of these have been concerned with the simplification of existing procedures to make them more readily available to the average laboratory. Under this heading can be considered a variety of kits which permit the easy application of multiple substrate tests and which depend on the extensive use of plastics. Also, kits for a variety of serological tests and spot test methods for rapid biochemical procedures have come into wide use. Each of these procedures has required, or needs, extensive comparative testing with traditional methods to insure an adequate level of accuracy and reproducibility. New methods for detecting early microbial growth and microbial antigens in situ have been developed. New and more sensitive serological techniques have come into use both for detecting immune responses to a variety of microbial pathogens and for demonstrating free antigen in blood or in cerebrospinal fluid, and it seems certain that counter immunoelectrophoretic techniques will play an increasing role in the work of the clinical microbiology laboratory in the future. Technical developments have led to a much greater understanding of infections due to anaerobic organisms and have facilitated their diagnosis and identification. In particular, the introduction of gas chromatography as a diagnostic and identification procedure has simplified, speeded, and improved identification methods. I will not attempt to list all the new technical developments which have occurred, but the above will serve as important examples.

In addition to technical developments, there has been a growing acceptance of the need for methodological standardization of procedures whose results are themselves method dependent. The recognition of this need was first apparent in the case of serological tests for syphilis, and great benefits have resulted from the application of the standardized procedures developed in the Venereal Diseases Research Laboratory. Antimicrobic susceptibility testing is another example where methodological standardization promises to eliminate many of the confusions of the past. The acceptance by the Food and Drug Administration (FDA) (2, 3) and tentatively by the National Committee for Clinical Laboratory Standards (NCCLS) of the same basic diffusion procedure can be expected to yield better interlaboratory repro-

ducibility and a better base line for studies with both new and old antimicrobics in the future. There is need for extension of this approach, particularly to serodiagnostic tests for disease other than syphilis, because the absence of standard or reference procedures continues to encourage much individuality which is often reflected in an inability to relate quantitative data derived in different laboratories. Standardized procedures must be reviewed from time to time and up-dated when new technological or procedural developments render the old ones obsolete. This is best handled by a formal annual or biennial review.

Quality control procedures have now become a routine in most laboratories and are required for those subject to the federal Clinical Laboratories Improvement Act (CLIA). Excellent guides to the application of quality control procedures have been published (4, 5) and the only word of caution needed is that they should not be "overcomplexified" and divert so much of a laboratory's resources that attention to the work itself is impaired. It is to be hoped that performance standards for many commercial media and reagents will become widely adopted and that quality control data on these will be made available by the manufacturers to the individual user so that their own quality assurance programs can be developed on the basis of this knowledge.

Acceptance of both voluntary and mandatory proficiency testing during the past few years has been dramatic and has certainly had beneficial effects on performance, and special credit should be given to the College of American Pathologists for pioneering this approach. Hopefully, by now, almost every laboratory is enrolled in one such proficiency testing scheme. The major function of proficiency testing should be educational because the great majority of laboratories and laboratory workers wish to improve their performance. All evaluation tests should be followed up by a complete analysis of results, the reasons for errors, and recommended procedures for correcting them. Excessive emphasis on regulatory aspects of proficiency testing may be self-defeating by focusing efforts on how to get an acceptable answer to a particular test specimen rather than on how to improve overall quality.

Another development which may certainly be expected to improve standards in clinical microbiology is the wider adoption of registration and certification examinations as a means to identify qualified individuals at various levels of responsibility. The American Board of Medical Microbiology and the National Registry of Microbiologists under the auspices of the American Academy of Microbiology have greatly extended the opportunities in this regard, and their diplomates have now been recognized in a number of federal and state laws and regulations. Hopefully, all those who are qualified but who have not obtained certification or registration by these or other appropriate bodies, such as the American Board of Pathology or the Registry of Medical Technologists of the American Society for Clinical Pathology

(ASCP), will do so, because this increases the ability of the certifying organizations to meet their primary objective of improved standards of performance.

Training in clinical microbiology, particularly at the postdoctoral level, has improved considerably during the past 15 years. Programs were encouraged by the American Academy of Microbiology and several were supported by the National Institutes of Health (NIH). Unfortunately, this source of support has now almost ceased, but several institutions have managed to obtain residency positions specifically for training Ph.D. and M.D. clinical microbiologists. Probably 100 or so clinical microbiologists have passed through these programs into positions of responsibility, and have, in turn, extended training opportunities to others at all levels. At approximately the same time, opportunities for spending up to 2 years training in clinical microbiology have been incorporated in some clinical pathology residencies, and this too is contributing to the pool of well-trained individuals. To supplement these developments, a number of new M.S. programs in clinical or medical microbiology have been developed specifically to provide additional training and education for those who seek technical supervisory positions. These are particularly important programs because the technical supervision has been shown to be the key to good laboratory performance. Hopefully, federal granting agencies will recognize the need for continued support of these programs and there will be some restitution of funds that have been cut off.

There have been great advances in continuing education in clinical microbiology in recent years, as exemplified by this program. The ASCP has been providing a series of workshops and manuals staffed and written by their own members and many by other leading microbiologists. These have been generally excellent. More recently, the Board of Education and Training of the American Society for Microbiology (ASM) has initiated workshops and regional conferences and they too have been highly successful. ASM branches have developed strong clinical sections, and many smaller regional clinical and public health microbiological societies have sprung up in response to the heightened interest in the subject.

Finally, means of scientific communication in the field are improving dramatically. The new ASM *Manual of Clinical Microbiology* (4) is now being supplemented by the ASM *Cumitechs* (6) to provide continuing and up-to-date information and recommendations on technical methods and laboratory procedures. Excellent workshop manuals have been produced by the ASCP Council on Microbiology and many good monographs have recently appeared. In addition, the clinical microbiologists will now have their own *Journal of Clinical Microbiology* through the ASM Publications Office.

Thus, the past few years have been a period of great advance, although much yet remains to be done to improve the quality of work for our patients. At the very least, the framework for a highly effective clinical microbiological service has been developed and further improvements can be expected.

One area of microbiology in which change has been slow to come about on any large scale has been in that of automation and mechanization. Many procedures which are obvious candidates for mechanization are still performed manually, and the time spent in repetitive routine work often deviates effort from the more complicated microbiological problems that can only be resolved by the trained microbiologist. For example, machines for spreading plates under controlled atmospheric conditions are still not available; staining machines are used little; equipment for monitoring growth and for automatic subculture to multiple substrates at night are entirely feasible and test results could be read out automatically. Only now is antimicrobic susceptibility testing being automated and are computers being adapted to information storage and retrieval and quality control in microbiology. The delay in the application of available technology is partly because manufacturers have underestimated the market potential and this, in turn, is partly due to an inherent conservatism among clinical microbiologists which is reflected in a negative response to market surveys for new developments. There is, I believe, little doubt that new developments of this type will become increasingly available and will rapidly find their place in the average laboratory.

Looking further into the future, we can expect more sophisticated and totally new approaches to be adopted in clinical microbiology. For example, the automated measurement of a variety of physicochemical characteristics of microorganisms and their analysis by computer pattern recognition systems seems a likely possibility for rapid identification. Such an approach will probably require the development of new taxonomic criteria and the development of better defined media. Even more sensitive detection or microbial growth and indirect optical methods for quantitation can be anticipated. Susceptibility testing may be at the cellular level and assays will become increasingly specific and accurate through enzymic or radioimmunological techniques. The overall objectives will be toward increasing accuracy and precision and more rapid results, especially for situations of clinical urgency.

It will be very important, as new technical developments are introduced, that we bear in mind continually the ultimate purpose of clinical microbiology which is to develop the means for providing the optimal data required for patient care as reliably and economically as possible and as rapidly as can be achieved in cases of clinical urgency. We should recognize the risk that the production of redundant data may obscure rather than illuminate, and that seeking levels of precision which are clinically irrelevant may enhance costs without value to the patient or the science. The application of judgment, based on knowledge and experience to clinical microbiological work and its interpretation, will continue to remain critical to good performance, and automated systems will extend the capability rather than replace the clinical microbiologist.

Even closer cooperation between the clinical microbiologist and the clinician will be needed in the future as the proportion of immunologically

compromised patients and of opportunistic infections continues to increase. Greater attention to the quality of specimens and to using all available procedures to assess the pathogenic role of organisms in mixed culture will be needed. Rapid diagnosis of opportunistic viral and fungal infections will become more important and in vitro assessment of the effects of combined chemotherapeutics will be more commonly needed. Environmental and epidemiological aspects of microbiology will become an even more important aspect of the work of the clinical microbiologist, and all of this will be facilitated by newer technical developments.

A final word about a neglected area of research—I believe that further effort should be put into evaluations of the effectiveness of the numerous variations in microbiological routines that are employed and of the use to which clinical microbiological data is put in patient care. The results of such studies can guide us as to the most valuable and efficient use of our resources and can help to remove one of the last major areas of subjectivity and contention from the discipline.

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SECTION 1

The Increased Role of Regulatory Agencies in Microbiology