Speculations on the Microbiology Laboratory of the Future

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Changes in the availability of skilled laboratory personnel, new technologies, and the financial environment will all influence the practice of diagnostic microbiology in the near and more distant future. Because of the special expertise needed for the accurate identification of anaerobic bacteria, the ability to diagnose anaerobic infections may decline as a consequence of these changes. Physicians should anticipate a difficult time in the years between the loss of expertise in traditional methods and development of reliable and accurate molecular assays.

Several converging factors will have major impacts on diagnostic microbiology laboratory testing in the near future, defined as the next 5 years, and in the more distant future [1]. The ideas expressed in the present essay are opinions only, based on my own experience and the thoughts of others in the field. Five content areas are addressed: (1) testing and directing personnel, (2) laboratory space issues, (3) instrumentation, (4) test menus, and (5) the impact of the previous factors on laboratory service and health care delivery.

Several years ago, a sample of >500 infectious diseases specialists responded to a questionnaire with their thoughts about their primary testing laboratory with regard to quality and service [2, 3]. They indicated a high level of satisfaction with their laboratories, particularly those directed by board-certified microbiologists, either American Board of Medical Microbiology or American Board of Pathology with a Microbiology specialty. The ability to talk to technologists and directors, the availability of special tests, and rapid turnaround time for results were listed as key satisfiers. The increasingly common laboratory response to the continuing fiscal crisis in health care in the United States, consisting of consolidating services and reducing staff, promises to erode the very factors that infectious diseases physicians find most valuable for their practice [4]. This year, partly on the basis of information presented by Peterson et al. [4], the Infectious Diseases Society of America published a position paper advocating the retention of on-site microbiology laboratories wherever possible [5]. The realities of the near future speak directly to these concerns.

The unprecedented national emergency precipitated by the deliberate release of anthrax spore-laden mail in early October 2001 underscored the importance of the relationship between infectious disease specialists and their microbiology laboratory. In none of the 23 documented cases of symptomatic infection did the primary laboratory require >1 day to report the presumptive presence of *Bacillus anthracis*, despite their never having seen a case of anthrax before. In at least 1 case, this rapid and accurate response was attributed directly to the interaction between the clinician and the microbiologists [6].

In microbiology today, more than most other diagnostic laboratory disciplines, the ability to arrive at the correct and clinically relevant result is dependent on the skill of the clinical laboratory scientist (CLS). The ability to quickly narrow down the options and arrive at a microorganism identification is grounded in subjective criteria, such as smell and color, and experience. Even though instrumentation has greatly enhanced susceptibility testing and identifications, instrument results must be constantly compared with “gut” feelings and...
phenotypic patterns established through years of practice [7]. The average age of a CLS at Stanford University Medical Center laboratory is >55 years. Within the next 10 years, more than half the laboratory workforce in the United States will retire. The accumulated expertise of these senior workers will not be replaced. A forecast by the American Society for Clinical Pathology (ASCP) shows 4000 new positions being created in laboratories each year for the next 10 years because of new testing modalities (cytogenetics and molecular diagnostics), 5300 retirements in each of those years, and only ~4900 new CLSs entering the field each year, leaving a shortfall of ~4400 workers per year (ASCP) [8]. Without the experienced technologists to train these newcomers and with the increasing tendency to work short-staffed, microbiology knowledge will surely be lost. Staffing shortages are already a reality in microbiology laboratories. Carey and Sewell queried 86 laboratories representing a cross-section of the United States. Only 31% of these laboratories had no vacancies at the time of the questionnaire; 37% of the positions had been unfilled for >6 months, and only 25% had been filled within 3 months (R. Carey and D. Sewell, personal communication). Even with potential renewed interest in diagnostic microbiology careers because of the excitement generated by bioterrorism and its continuing threat, it will take at least 6 years before new microbiologists are working on the bench.

Besides the dwindling workforce, the remaining personnel often suffer ergonomic injury. Pipetting, working within an anaerobic chamber, vortex-mixing small microcentrifuge tubes, and numerous manual tasks take their toll on both an aging workforce and an increasingly diverse one. Our large instruments and devices were not well designed for small, slight Asian American bodies.

Directors of microbiology laboratories are aging, too. The stress of making decisions on the basis of financial and not patient-centered criteria, the need to learn new financial management skills, the difficulty of learning and implementing new highly complex molecular tests, and, in some cases, lack of computer skills, have resulted in disillusionment and depression. In parallel, integration of laboratory services and downsizing have contributed to an overall decrease in the numbers of certified and/or experienced microbiology laboratory directors while increasing the workload and responsibilities of those remaining.

The laboratory’s physical environment is also suffering for the near term. Laboratories are either consolidating in new, distant locations, central to the several facilities served, or new technologies are being crammed into existing space that was not designed for the purpose more than a decade ago, when laboratories were renovated the last time. Despite the promises of manufacturers, molecular testing requires that sample handling be kept separate from nucleic acid amplification, to avoid contamination [9]. This is extremely difficult in laboratories designed in earlier times. The ability to bring new tests on board is often limited by space constraints and so, in some cases, new tests take precedence over older technology. The anaerobic chamber, which requires a relatively large section of bench-top space, may be abandoned in favor of a Qiagen birobot or an automated nucleic acid–amplification instrument. Although the federal government earmarked new funding for bioterrorism preparedness, the money is being spent on increased airline security, commercial research and development of rapid detection systems, and upgrading the capabilities of public health laboratories. In other words, local diagnostic laboratories have not benefited from this enhanced funding.

Instruments used in the bacteriology/mycology sections of diagnostic microbiology are still commonly limited to those used for blood cultures and new broth-based mycobacterial cultures and those used for antimicrobial susceptibility and bacterial and yeast identifications. Fewer anaerobic blood cultures are being collected these days, partially in response to the decreased incidence of anaerobic sepsis coincident with the use of more broadly effective antibiotics [10, 11]. The failure to detect some anaerobic bacteremias could ultimately lead to both a cryptic rise in drug resistance among anaerobic bacteria and increasing numbers of treatment failures.

Classical bacteriology and mycology are still heavily dependent on microscopes and the skills of those using them. A few new instruments, such as those that perform real-time PCR (LightCycler; Roche Diagnostics), cellular fatty acid methyl ester analysis (MDI), or ribotyping (Riboprinter; Qualicon), are found in only a limited number of laboratories, primarily major commercial laboratories or research-oriented academic centers. Virology laboratories, in contrast, are rapidly automating. Numerous new methods for infectious disease immunologic testing, gene sequencing, nucleic acid extraction and amplification, and real-time PCR are populating virology and recently renamed molecular diagnosis laboratories across the United States.

Some technological advances have been aimed at enhancing bacterial detection. Several such tests in common use in clinical laboratories include rapid membrane-based enzyme immunoassays for detection of Clostridium difficile toxins A and B in feces, nucleic acid amplification methods for detecting Chlamydia trachomatis and Neisseria gonorrhoeae in genitourinary specimens, commercial microbroth dilution panels for yeast susceptibility testing, and DNA probes for Streptococcus pneumoniae and Legionella pneumophila serogroup 1 in urine (NOW tests; Binax). Tests commercially available but not yet in widespread use can rapidly identify from pure cultures those Staphylococcus aureus that express the mecA gene (BBL Crystal; BD Microbiology Products, Velogene; ID Biomedical, and Denka Seiken), enterococci that express vanA and vanB genes (in development from Velogene), and, directly in patient specimens,
fluorescent in situ hybridization assays for *S. aureus* and *S. pneumoniae* [12]. Laboratories specializing in oral flora are using such assays for the identification of the agents of periodontal disease in gingival scrapings [13, 14]. Kits for DNA sequencing are available, too, and this approach will become the preferred method for identifying anaerobic bacteria, coryneform rods, and nonfermenting gram-negative bacilli within the next 5 years (MicroSeq; Applied Biosystems).

Given the scenario described, what will be the impact on physicians’ use of the laboratory? It will be more difficult to receive unofficial information about patients’ isolates. Laboratory workers will not have the skills to make educated guesses on the basis of experience, and specialists will not be available on off-shift hours. Critical decisions will be made increasingly without microbiology laboratory input, driving more defensive and broad-spectrum antimicrobial choices for empiric therapies. In some cases, either because of transport to a distant facility or limited staffing, final results will be delayed beyond clinical relevance, and the true etiology of some infectious processes may not be known. Loss of Gram’s-stain reading expertise and declining budgets may lead to lack of recognition of some serious anaerobic infections.

What about the distant future? My predictions are for fewer highly skilled CSLs and for more generalists and fewer CSLs altogether. In response, there will be more point-of-care testing and more automation, especially front-end sample-handling instruments to help with the ergonomic problems of existing staff and the future projections of decreasing numbers of personnel. Microbiology laboratory directors will be skilled in molecular methods but lacking in classical microbiology training. Gram’s-stain interpretive abilities will diminish. There will be more specialty-trained pathologists and fewer PhD microbiologists. Those directors who survive the near-term environment will be more financially savvy, basing administrative decisions on cost-effectiveness and evidence-based medicine.

I predict that the technological revolution will bring benefits as well as hardships. Although experienced Gram’s-stain interpreters will be fewer, laboratories will be able to use real-time digital graphics image capture to send slide images to an expert at a distant site for interpretation. This same image can be easily included in the laboratory report, which will be instantly accessible to the physician at any location by use of a handheld device with wireless internet connectivity. Identification of anaerobic bacteria in particular, whether in a smear prepared from the original specimen or an isolated colony, will benefit from experienced observers.

The detection of etiologic agents of infection will be primarily by molecular means in the distant future. For those organisms whose presence does not automatically indicate causation of the infectious process, combinations of tests for human genomic responses to infection and agent detection will aid diagnoses. For example, approximately one-half of *Clostridium perfringens* isolated from blood are transient and not associated with infection [15, 16]. By looking for the up-regulation of ribosomal response to clostridial infection, using genomic dense oligonucleotide microarrays, a laboratory will quickly discriminate between agents causing infection and agents recovered serendipitously in part because of the exquisite sensitivity of amplified molecular methods [17, 18]. Syndrome-based detection panels will be used for rapid disease diagnosis.

Although the detection of mechanisms of antimicrobial resistance will still be difficult, new modalities of infection prevention and treatment will also be technology driven. Antimicrobial activities that do not lead so directly to increased resistance, such as interfering with the initial adherence of the microbe to the appropriate host tissue without affecting the organism itself, will be designed and tested in virtual assays, allowing huge diversity in development and sparing animal testing. Advances in information technology will allow immediate and global access to patient status and laboratory results for all physicians treating a patient. Patients can safely travel or change health care providers, and their records will be available, protected from inappropriate use by sophisticated biological security devices.

Finally, I would like to believe that sufficient resources will be allocated to health care and that those resources will actually be targeted for real aspects of patient care: medicines, instruments and technologies, physical environment, caregivers, and technical personnel, rather than layers of bureaucratic administration and highly paid outside consultants. In the ideal future, physicians and other patient care providers and laboratory workers will work together as teams, respecting and acknowledging each other’s special skills and contributions to the common goal of better health for all.

References


