It is Time to Supplement Culture with Molecular Diagnostics for Infectious Diseases

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The gold standard for identification of pathogens for infectious diseases till date is culture and culture-based diagnostics have been the mainstay diagnostic tool in the clinical microbiology laboratory due to advantages, including low cost and ability to provide antimicrobial susceptibility testing (AST) for the specific patient's isolate. However, culture-based diagnostics do not capture all pathogens and require an extensive incubation time (days to weeks) and specialized media to allow for microbe growth which may not perfect always for all kinds of bacteria. Furthermore, not all microbial cultures can be grown under laboratory conditions. For example, a study of *Campylobacter* indicated that the culture-based method failed to correctly detect *Campylobacter* in 30% of positive patient stool samples compared to non-cultural methods, including PCR and enzyme immunoassay (EIA). Also, prior use of antibiotics before sampling may affect the growth of bacteria in the culture system and may produce false negative results. On the other hand, molecular methods for identification of microorganisms provide a more rapid result and may be able to identify additional microorganisms that are not detected by culture. As the technology and clinical knowledge for non-culture-based diagnostics have matured, these assays are increasingly incorporated into routine diagnostic laboratories. The molecular biologist plays a key role in determining which assays will be offered to providers within their health care organization, and must understand the scientific basis, assess the technological methods and performance characteristics, and determine the clinical utility of these assays.

Therefore, to meet the requirements for reliable analysis of pathogenic bacteria, including high specificity, high sensitivity, good reproducibility, molecular methods have gradually emerged to supplement the dominant position of culture methods. In recent decades, various rapid, sensitive, and specific molecular methods have been developed. Nucleic acid targeting methods are designed to detect the specific DNA/RNA of pathogens. It is achieved by the hybridization between target nucleic acid sequences and synthetic oligonucleotides. Thus, the species-specific gene of pathogens and virulence genes can be detected through nucleic acid targeting methods. These methods include polymerase chain reaction (PCR)-based methods such as conventional PCR, real-time/quantitative PCR (qPCR), droplet digital PCR (ddPCR), multiplex PCR (mPCR), and other methods such as microarrays, loop-mediated isothermal amplification (LAMP), sequencing. Among these methods real-time PCR has become the standard of diagnosis for many infectious disease emergencies and in some routine diagnostics in either monoplex or multiplex format with resistance gene information. Temptation is also seen for next generation sequencing to identify pathogens with antibiotic resistance gene information in some reference and tertiary hospital laboratories. Clinicians' understanding, communication and education about increasingly complex results and laboratory network coordination are essential in molecular microbiology. Hopefully, these new molecular tests will increase the capability of the diagnostic laboratory to rapidly identify the microbiological etiology of an infection and hence impact on better patient management.