# The Impact of Emerging New Diagnostic Laboratory Techniques on Clinical Infectious Diseases

*Written by Phil Vinall*

Along with a futuristic view, Franklin R. Cockerill, MD, Mayo Clinic, Rochester, Minnesota, USA, presented a technical and historical review of current diagnostic methods for infectious diseases. His presentation focused on new testing methods, including nucleic acid sequencing, polymerase chain reaction (PCR), and mass spectrometry, and the effects of this technology on healthcare outcomes.

Dr. Cockerill discussed important turning points in diagnostic testing in the last 50 years. At the top of his list were technological advancements for detection and quantification of HIV such as an immunoassay for saliva testing and flow cytometry for detecting and quantitating CD4 cells, the main target of HIV. Flow cytometry allows simultaneous multiparametric analysis of the physical and/or chemical characteristics of up to thousands of particles per second. Breakthroughs in PCR and sequencing enable the quantification of HIV and the detection of HIV resistance. PCR can amplify a small amount of template DNA (or RNA) into large quantities in a few hours.

Real-time PCR was number 2 on the list. Instead of being able to detect RNA and DNA at the end point, real time allows this detection while it is occurring. It offers the advantages of having reduced labor requirements (complete automation is now possible) and a high throughput, as well as being inexpensive, sensitive and specific, and fast (minutes instead of days). There is a decreased potential for contamination while allowing for qualitative, quantitative, and mutation analyses. It has recently been used for anthrax identification.

Number 3 was real-time PCR/microarrays, which can be used to identify possible methicillin-resistant *Staphylococcus aureus* (MRSA) and acute viral epidemics such as SARS.

Mass spectrometry, number 4 on the list, is an analytical technique used to determine masses of particles, and the elemental composition of a sample or molecule, and for elucidating the chemical structures of molecules such as peptides and other chemical compounds. The matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) is a protein mass spectrometry that can be used for the identification of microorganisms such as bacteria or fungi (Figure 1). Species diagnoses by this procedure are much faster, more accurate, and cheaper than other procedures based on immunological or biochemical tests.

Nucleic acid sequencing was number 5. It is being used for detection of HIV resistance mutations, and bacterial and fungal identification. The next-generation genomic sequencing devices will allow for massive parallel sequencing. Their use will include the detection of microbiomes, German Shiga (produces *Escherichia coli* gastroenteritis and hemolytic–uremic syndrome), and low-frequency HIV quasispecies.

Except for flow cytometry, the developers of all of these breakthroughs have been recognized with Nobel Prizes. Such methods have provided considerably faster and more accurate means for diagnosis of pathogens traditionally isolated and identified by cultivation and in some cases have provided the first means for identification and quantification of pathogens, particularly viruses.

Society is confronted with a difficult poor economy, diminished basic research funding, a focus on gene discovery/patents versus technology development/patents, reimbursement issues, and increasing compliance requirements. However, Dr. Cockerill believes these issues can be overcome. The acute issues are patients' poor access to medical care, worsening reimbursement that will require improved efficiency and lower-cost

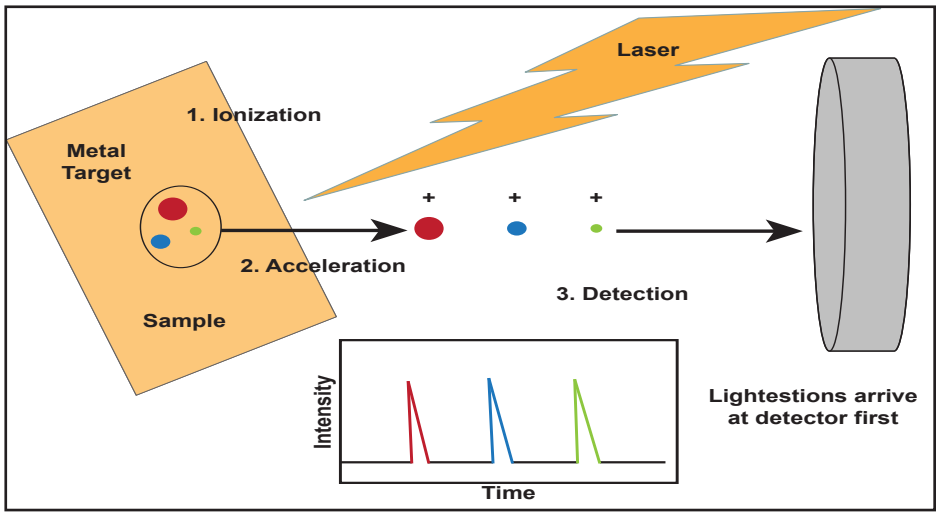
Official Peer-Reviewed Highlights From the

ICAAC 2012

52nd ICAAC – Sept. 9-12 – San Francisco

diagnostics, and the overutilization of diagnostic services. He sees the recent Supreme Court decision that prevents the patenting of naturally occurring phenomena as having a positive impact on innovation in laboratory medicine; instead of focusing dollars on patenting genes, capital will be directed to the development of new testing platforms (target capture/enhancement, small molecule detection [phenotypes]) and mobile testing units, the evolving application of basic technology (next-generation sequencing, automation, and compartmentalization), and the advent of informatics as evidence that even bigger breakthroughs will occur in the future.

**Figure 1. Mass Spectrometry.**




Reproduced courtesy of R. Patel, MD, Mayo Clinic, with permission from F.R. Cockerill, MD.

Consumer-oriented testing and the possibility of futuristic tricorders, automated and continuous artificial data integration and interpretation, and automated testing algorithms and formularies suggest that there will be new opportunities for healthcare delivery. The ability to miniaturize technology, improvements in specimen preparation and data analysis, smartphone transmission, and devices with minimal energy requirements herald the arrival of tricorders for disease detection. Qualcomm is offering a $10 million prize to the first group who develops such a device. Besides being lightweight and small, the tricorder must have the ability to detect anemia, urinary tract infections, diabetes, strep throat, sleep apnea, melanoma screen, chronic obstructive pulmonary disease, abnormalities in a metabolic panel, hypo- and hyperthyroidism, and the absence of disease.

Point-of-patient testing by the patient, miniaturization and portability of standard testing platforms, and integrated reporting transitioning to integrated data interpretation are key features for future patient care. Mayo Clinic has developed a patient self-swabbing procedure for throats that is just as effective as having a physician perform the procedure.

Increasing amounts of patient data mean that information integration, informed ordering, and integrated reporting/interpretation fed into a computer system are areas in need of improvement. Doing so may enable real-time integrated interpretation at the bedside.

Dr. Cockerill stressed the importance of thinking outside the box to meet future needs.