Put It on the Board, 1/14

Call for faster, simpler diagnostic tests for infectious diseases

In a sweeping set of recommendations, the Infectious Diseases Society of America says higher federal funding and an easier regulatory pathway are needed to help encourage the development of tests that will diagnose infections more quickly and accurately.

Speed and simplicity in testing are critical to improving patient care, avoiding unnecessary antibiotic prescribing, and bettering public health, says Angela M. Caliendo, MD, PhD, lead author of the society's policy statement, "Better tests, better care: improved diagnostics for infectious diseases" (*Clin Infect Dis.* 2013; 57 *Suppl* 3:S139–70).

"Getting an answer back quickly is important, and the simpler the test is to perform the more likely it is to reach a broader spectrum of clinicians—whether it's simple enough to be used in the office, or in the ER, or on inpatients, the key is to get a result quickly that allows for a rapid clinical response," Dr. Caliendo says. "Methods that are straightforward would allow testing to be performed in the core laboratory, which would increase access to testing for hospitals that do not have full-service microbiology or molecular diagnostics laboratories."

The need for action to improve infectious-disease diagnostics is great, according to the society's paper. Inappropriate prescribing is partly due to the lack of rapid tests to help physicians identify viral pathogens.

"Giving antibiotics for viral respiratory infections is one of the highest inappropriate uses of antibiotics," notes Dr. Caliendo, a former member of the CAP's Microbiology and Molecular Pathology Resource committees.

Better diagnostics also would help physicians improve targeting of antibiotics and prevent Clostridium difficile infections. The number of C. diff cases rose 200 percent between 1996 and 2009. While it costs money to develop and pay for faster diagnostics, such tests can lead to savings, the authors argue. Rapid testing for methicillin-resistant Staphylococcus aureus, for example, has been found to save nearly $22,000 per patient in health care spending.

Yet the pipeline of infectious-disease laboratory tests is not as full as it could be, says Dr. Caliendo, executive vice chair of the Department of Medicine at Warren Alpert Medical School of Brown University.

"If you look at the number of FDA-cleared assays and the number of different pathogens being targeted, it's not all that great," she says. "Molecular testing has become very popular, but it's still relatively expensive and not all that rapid. We're still grasping for the technology that's really going to be inexpensive and simplify testing to a point where you can get a response in less than an hour."

Until recently, she says, the technology to challenge this hasn't been available. "Now we have the FilmArray test, the GenXpert system, and others that can give us results in an hour, but they're still expensive."

The high cost should come as no surprise given the regulatory obstacles. Near the top of the society's wish list for policy changes is a different approach to diagnostic-test approval.

The FDA's Center for Devices and Radiological Health ought to allow broader use of research- or investigational-use only devices when there are no other diagnostic options. The center also should exempt companies from having to prove all over again that their test is clinically valid when multiple studies for similar products have already been conducted. The FDA also should provide clearer guidance on the development of companion drugs and diagnostics, the authors argue.

"If the process [to put tests through the FDA] were less costly, this could increase the number of tests put forward for regulatory approval," Dr. Caliendo notes.

The IDSA offered dozens of other recommendations it says would speed the pipeline of lab tests.

Several call for more money. The National Institutes of Health should increase funding for diagnostics research through the Small Business Innovation Research program, while Congress should enact a tax credit to cover half of clinical research costs for quick diagnostic tests. Capitol Hill also should fund information technology to help integrate and disseminate infectious diseases data.

Also, Congress and the NIH should clarify conflict-of-interest policies to allow for productive collaborations between diagnostic companies, laboratories, and experts working to meet FDA clinical trial requirements. The Department of Health and Human Services, meanwhile, ought to drop a 2011 proposed rule that would require informed consent for research involving deidentified residual clinical samples. The rule would "severely limit" diagnostic research, the IDSA's policy statement says.

The group recommends that the Centers for Medicare and Medicaid Services simplify the process of creating CPT codes and later including them in the clinical laboratory fee schedule.

In addition, the society's policy statement calls on the CMS to harmonize standards for clinical validation and verification under the Clinical Laboratory Improvement Amendments program with those offered by the CAP, the Clinical and Laboratory Standards Institute, and others. That consistency would encourage wider adoption of new tests.

AMP statement on LDTs

The Association for Molecular Pathology has proposed a new term for laboratory-developed tests and reaffirmed its position that the Clinical Laboratory Improvement Amendments program is the appropriate vehicle through which to oversee them.

In a position statement published in the January issue of the Journal of Molecular Diagnostics, members of the LDT Working Group of the AMP Professional Relations Committee propose the term laboratory-developed procedure, or LDP, to distinguish LDTs from traditional medical devices. They say the new term "better represents the nature of complex laboratory testing" and define it as follows: "a professional service that encompasses and integrates the design, development, validation, verification, and quality systems used in laboratory testing and interpretative reporting in the context of clinical care."

Unlike FDA-regulated medical devices, members of the group write, laboratory tests have a professional interpretive component that offers additional opportunities to enhance care through professional interpretive judgment. "This professional judgment and test performance intersect at the points of design, development, validation, and continued improvement of LDTs," which require a regulatory pathway that acknowledges the difference between traditional medical devices and LDTs and "preserves the role of the laboratory professional."

The CLIA program of the Centers for Medicare and Medicaid Services is the way to oversee LDPs, the AMP says in its statement. To make its regulatory process more transparent, it says, the CMS should update its IT infrastructure to make its registry of labs and their test offerings easily available to the general public and other stakeholders. "Moreover, the registry should make public information about adverse events and other significant problems that have occurred within a particular laboratory," the AMP says.

The working group reaffirmed the AMP's prior position that some exceptionally high-risk tests do require pre-introduction review by a third party. Such LDPs include "those for which methods or other determinants of results lack transparency, or assays for which a skilled laboratory professional cannot independently interpret or assess the validation of the test or its results." Assays that contain black-box algorithms or use proprietary software are examples, the group says, adding that such LDPs typically are offered by a single provider.

Detecting women at risk

Myriad Genetics presented clinical data at the 2013 San Antonio Breast Cancer Symposium in December that showed the myRisk Hereditary Cancer test found 51 percent more patients with a higher risk of hereditary breast and ovarian cancer than did testing for the BRCA1 and BRCA2 genes alone.

MyRisk is a diagnostic test that uses next-generation sequencing to evaluate 25 genes associated with eight hereditary cancers.

This large prospective clinical validation study measured mutations in 25 cancer-causing genes among patients referred for BRCA1/2 testing. Among the 1,951 patients evaluated, 275 patients tested positive for a deleterious mutation with the myRisk test. Testing only for the BRCA1 and BRCA2 genes found 182 of the mutation carriers.

MALDI Biotyper CA cleared

Bruker has been granted FDA 510k clearance to market its MALDI Biotyper CA system in the U.S. for the identification of gram-negative bacterial colonies cultured from human specimens. The system includes the benchtop microflex MALDI-TOF mass spectrometer, software, IVD labeled reagents, a 48-spot MALDI target, and a library of microorganism reference spectra.

Frank Laukien, president and CEO of Bruker, said in a statement that more than 1,000 MALDI Biotyper systems have been sold or leased worldwide.

Robert Jerris, PhD, D(ABMM), director of clinical microbiology at Children’s Healthcare of Atlanta, said in the statement that MALDI-TOF has helped lower health care expenditures at Children’s and has had a positive impact on therapy and infection control.