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Q&A

Triangulating Dynamic of Clinical Laboratory Testing

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Over the past 20 years, there has been a continuous shift in decentralizing clinical laboratory testing in the US. Historically, testing was conducted almost exclusively in centralized laboratories in hospitals. However, at present, approximately 53% of testing is performed in hospitals (including some near-patient testing in settings such as critical care and emergency rooms), 34% in commercial clinical laboratories (50% of which is done in Quest Diagnostics and LabCorp), and the remaining in physician office laboratories and other settings as well as directly by consumers using over-the-counter devices. These numbers vary depending on the state. For example, in New York State 368 million tests in chemistry were performed in 2014, 73% of which were processed in hospital laboratories and 23% in independent (commercial) laboratories (data courtesy of Dr. Robert Rej). There are many drivers for this triangulating dynamic shift, including cost reduction, convenience to patients and clinicians, quality improvement (when the frequency of performing a particular test in the hospital laboratory is low), and the use of novel technologies such as nanotechnology, microfluidics, electrical impedance, reflectance, and time-resolved fluorescence, which enabled the miniaturization of devices and the proliferation of point-of-care (POC)[8] testing. Improvement in information technology has been instrumental in the process of decentralizing testing and providing clinicians with patient results; this is, however, not a trivial matter and the cost of the interface is not always justifiable. Regulatory requirements in terms of assuring competency of those performing testing, getting patient laboratory results into the medical records, billing appropriately, and providing patients with their test findings are only few of the challenges of decentralized testing. How is the testing dynamic shift in this $56 billion industry going to evolve over the next 5 and 10 years? What will be the impact of technology, reimbursement, and confidentiality in shaping this shift? Will the movement under healthcare reform toward the metric of "total cost of patient care/patient encounter" drive the demand for greater "actionable information" (more testing to the POC)? To help answer these questions, we invited leaders from clinical laboratories (hospital-based and commercial) and traditional in vitro diagnostic and POC industries to participate in this Q&A.

What are the main advantages of outsourcing laboratory testing from traditional hospital-based testing, if any?

Susan Evans: Economics, skills, and capabilities are the primary factors that impact the decision to outsource. This will vary dramatically based on the hospital and available resources. It is advantageous to outsource tests requiring complexity or skill sets not economically feasible for the hospital to maintain internally or when the testing volumes do not warrant the investment in dedicated human resources or equipment.

Harvey W. Kaufman: Hospital laboratories have the advantage of proximity to the patient and ordering physician. The main advantage of outsourcing laboratory testing to commercial laboratories is to provide testing, typically advanced testing, that the hospital laboratory may not be able to pro-

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[8] Nonstandard abbreviations: POC, point of care; NGS, next generation sequencing; CPOE, computerized physician order entry; MDx, molecular diagnostics; IVD, in vitro diagnostic; ACO, accountable care organization; ICD, international statistical classification of diseases; DTC, direct to consumer; MS, mass spectrometry; FDA, US Food and Drug Administration.

vide. Hospital laboratories are often constrained by space, qualified personnel, and advanced technology. Because commercial laboratories can often provide these capabilities, hospitals rely on them for at least some of their testing needs. In 2014, for example, Quest Diagnostics generated more than $1 billion in revenues (from approximately $7.4 billion in total revenues) associated with testing we performed for hospitals and other commercial laboratories. Finally, cost pressures may encourage more hospitals to outsource some of their operations to entities that can assure high quality standards and lower costs. In 2011, we launched a professional laboratory services business to serve the growing interest of hospitals for assistance in managing or outsourcing their laboratory operations to a specialized provider that can help lower costs while maintaining high levels of quality and innovation for patients.

Charles S. Eby: There are three reasons for referring testing from a hospital clinical laboratory to another laboratory. First, referral is warranted for low-volume tests that are expensive to perform and maintain due to associated capital investment, cost of reagents, external proficiency participation, and maintenance of specialized instruments as well as technologist training and maintenance of competency. Indeed, for some low-volume tests we perform more quality control testing than patient testing. Second, referral may be spurred by unique safety issues such as radioisotope methods or frequent phlebotomy of healthy employees for selected method controls or to establish reference intervals. Third, it is reasonable to refer laboratory-developed testing services for which it would be extremely difficult to initially validate or consistently monitor quality control due to proprietary methodology or rarity of abnormal samples.

Edward R. Ashwood: Outsourcing of laboratory testing has two primary models: (1) a hospital-based laboratory outsources rarely performed tests to a reference laboratory and (2) a hospital outsources its entire laboratory to a commercial laboratory. The latter model has been tried a score of times over the past 30 years to mixed success. Because most hospitals want direct control of their laboratories, I don't see the latter model dramatically increasing in the coming decade. The former model is extensively practiced nationwide. Hospitals need access to a wide variety of tests, some having low demand and complex designs. It is a classic "make vs buy" analysis. Should the hospital invest the resources (i.e., expert personnel, expensive equipment, and laboratory space) for a test or a group of tests so that they can perform them on site? Or, is the test demand so low that outsourcing to a reference laboratory results in lower costs, fastest turnaround times, and access to more expertise (the reference laboratory's professional staff)? Hospital laboratory directors and managers are well served by reviewing both send-out and in-house testing volumes periodically and deciding which send-out tests can be implemented within their laboratories and which in-house test volumes have decreased to the point that performing them no longer makes sense.

Norman Moore: The main advantage is that outsourcing usually saves cost per test. Reference laboratories can more easily batch and run assays to limit technician time and assay expense. However, we are finding that the cost savings on a test level are not balanced by the cost on a patient level in most instances. Outsourcing necessitates a time delay to results, and that can have a direct impact on guiding the physician to the best therapy decisions. Cost may be saved on a per result basis, but if the optimum treatment is not introduced, that may lead to increased length of stay for the patient as well as increased morbidity/mortality. Beyond that, it also leads to significant other issues like increased antibiotic resistance and secondary infections like *Clostridium difficile*. There are tests where timely answers aren't needed, like genetic testing, so reference laboratories may excel in these areas.

How do you see the dynamic shift in testing between hospital-based laboratories, commercial laboratories, and POC in the next 5 and 10 years?

Susan Evans: There will be an interesting ebb and flow between the hospital-based laboratory and the commercial laboratories. To increase test volume and help justify the investment in staff and equipment, hospitals have created outreach programs that have enabled a reduction in outsourcing. At the same time commer-

cial laboratories continue to grow test menus and add new technology, thus increasing the availability of technologically complex and novel assays. We might not see a dramatic change in the next few years but as we look out 5 to 10 years, with an increased focus on predictive and wellness testing, the growth in new tests and new technology has the potential to continue to impact these dynamics, driving more testing to commercial laboratories or alternative testing locations such as clinics, doctors' offices, and pharmacies. The interest in POC continues but the challenges of delivering the quality and comparability of a laboratory-based clinical result remains. Cost and clinical performance are the key drivers. There is the promise that advances in miniaturization and detection technologies will enable the advances necessary for POC systems to expand into additional mainstream applications.

Harvey W. Kaufman: There is a dynamic shift in medical practice. In recent years, a growing number of physician practices have been acquired by hospitals. Laboratory testing that may have been performed by an independent laboratory has consequently been internalized by hospitals. This is an issue that affects patient care because, according to independent reports, hospitals tend to offer testing at higher commercial fees than large independent laboratories. I believe this trend may plateau or even reverse course as commercial payers pressure hospital laboratories to reduce these comparatively higher fees. Many laboratories are confronting personnel shortages. These pressures may be why a number of hospitals are seeking the expertise and services of commercial laboratories to reduce costs of their laboratory operations. Near-patient and POC testing will continue to be an area of interest, particularly for conditions such as for infectious diseases, where patients benefit from a rapid diagnosis.

Another important dynamic is that the need for laboratory testing will grow. As the Baby Boomer population ages, a growing number of people will require laboratory tests as part of their medical care for chronic conditions such as hypertension, diabetes, hyperlipidemia, chronic kidney disease, stroke, and cancer. At the same time, the biopharmaceutical industry will introduce an increasing number of oncology and other novel therapies that rely on genetic biomarkers identified by laboratory tests based on next generation sequencing (NGS) and other innovations. As precision medicine grows, new tests will also provide insights leading to the discovery of new molecules leading to the development of therapies personalized for the individual patient.

Charles S. Eby: Hospitals will continue to consolidate into regional integrated healthcare systems and they will standardize laboratory instrumentation, test methods, menus, reference ranges, laboratory information system and electronic medical record software, and transportation services. These activities will promote consolidation of nonrapid testing for both outpatient and inpatient services by creating economies of scale for routine analytes as well as an expansion of "low volume and/or complex" test menus while improving negotiation positions with national or international reference laboratories for a smaller numbers of esoteric tests. Medical directors will oversee laboratories in multiple hospitals, providing support to a larger and often more varied clinician audience. They will also need to contribute to healthcare system administrators' efforts to control costs through management of laboratory test formularies, clinical decision support strategies at the time of computerized physician order entry (CPOE) test ordering, and patient-specific evaluation of molecular testing in conjunction with genetic counselors. Laboratory medical directors will at best blunt the growth of POC testing by championing clinical utility over convenience as they address an insatiable clinical demand for faster turnaround time for selected chemistry, hematology, and hemostasis tests in emergency and critical care areas.

Edward R. Ashwood: Inexpensive tests are best kept close to the patient to reduce transportation costs. There is rapid growth in more expensive, complicated testing, albeit at very low test volumes. Common clinical laboratory tests have an incremental cost of pennies per test. POC costs are, in general, higher, but the convenience may trump the cost. Rarely ordered tests, regardless of cost, will continue to be referred to commercial laboratories.

Norman Moore: The paradigm for deciding where assays are being performed is starting to shift dramatically. For quite some time, the laboratory has been looked at as a cost center for critical care testing. Now, we see diagnostics better guiding treatment decisions than ever before. To do that, they must be timely and that means bringing them closer to the patient. Therefore, most thought leaders are looking at a shift from commercial laboratories to hospital laboratories and from hospital laboratories to POC.

Technology is also changing so that tests are becoming easier to use while still giving laboratory-quality results. As more tests are CLIA waived, they can be used in far more settings. Hospitals and commercial laboratories may now get the lion's share of testing, but that isn't where patients normally present when they are sick. As tests are more and more available in doctors' offices and urgent care clinics, the shift will continue to increase, especially as the cost of an emergency room visit remains high.

What impact will the association between hospital, POC, and reference laboratory have on the area of nucleic acid testing?

Susan Evans: The promise of routine infectious disease molecular-based testing is now a reality. It is also exciting to see the approval and adoption of easy-to-use POC molecular diagnostics (MDx) tests for detection or confirmation of infectious disease. Whether it is influenza, sexually transmitted diseases, or strep, the physician now has access to rapid direct-detection MDx assays enabling rapid diagnosis and earlier access to treatment. These trends for MDx infectious disease testing will continue as more manufacturers provide "sample-to-result" MDx systems and POC platforms. Hospitals will bring this testing back in house, reducing outsourcing. The story is more complicated for oncology and other nucleic acid–based testing. Tests with sufficient volumes that have been adapted to fully integrated systems can also be brought in house. More complex, multimarker panels, and the explosion of new laboratory-developed tests based on genomic information will be offered and supported by commercial laboratories, major medical centers, and clinical service businesses.

Harvey W. Kaufman: Nucleic acid testing is simply another technology. And like other technologies, advances will make testing simpler and of increasingly higher quality. We may see a progression of testing that moves from the esoteric laboratory to the routine laboratory, and ultimately to the POC test performed near the patient. Indeed, the first nucleic acid test, a test for influenza, was categorized as a CLIA-waived test in early 2015. Tests for emerging infections, such as Ebola virus, are best performed close to the suspected patients and quickly. While there is great interest in immediate test result reporting, many tests do not need to be performed and produce results within minutes to promote favorable outcomes. A more pressing factor may not be the technology but reimbursement policies that influence where tests are performed and if tests are even available.

Charles S. Eby: In the area of infectious pathogen diagnosis, nucleic acid testing is rapidly moving from internal or external special testing areas to on-demand, rapid results requiring minimal technical expertise. This applies particularly to virology. When molecular microbiology testing platforms can simultaneously detect multiple viral and bacterial organisms from clinical samples, the chances of identifying unsuspected or nonpathologic organisms will increase, requiring consultation between microbiologists and clinicians. Whether molecular microbiology testing is performed as POC, near-patient testing, or central laboratory testing will be determined by local and regional logistics rather than the technology. In general, rapid, on-site pharmacogenetic testing lacks clinical utility, but this could change if pharmaceutical companies bring more drugs to market with companion nucleic acid testing diagnostics.

Edward R. Ashwood: The majority of testing with nucleic acid methodology occurs today in reference laboratories. Many of these tests will move into hospital laboratories in the future, especially infectious disease testing. Some tests are amenable to POC methods. Genetic testing requires highly specialized professionals for final interpretation, so a centralized model is best for these tests.

Norman Moore: Genetic testing, such as paternity testing and breast cancer risk markers, is not needed in as timely a fashion as blood glucose or influenza. Therefore, we don't have to worry about timely results and that means commercial/reference laboratories are quite often the place to be for these tests. Since you can have patients self-collecting their specimens, we will be seeing hospitals often removed from this dynamic. We may be seeing this front of medicine move to home kits and Apps that connect to physicians when the need arises.

As healthcare reform advances, how will this change where in vitro diagnostic (IVD) testing is performed (shift between three settings: hospital, commercial labs, and POC [acute care, ambulatory settings, pharmacy, etc.])?

Susan Evans: It is always challenging to predict the future, but the Affordable Care Act, accountable care organizations (ACOs), and other factors will impact where and how much laboratory testing is performed. There will be an increased awareness of the value of laboratory results but also the costs associated with testing. Are we doing too many tests or not enough? Test utilization per patient will be scrutinized and assessed on the basis of delivered value. An important trend will be a shift to wellness and preventative care. The goal of ACOs is to keep members healthy and out of an acute care setting. Many experts believe this will drive an increase in the percentage of testing done in commercial laboratories, specialized clinics, or nontraditional testing locations. Nontraditional decentralized testing will increase the adoption of POC technology while the more centralized testing sites, both hospital and commercial, will be looking for opportunities to efficiently manage increased volumes while reducing costs.

Charles S. Eby: One consequence of healthcare reform will be further reductions in reimbursement for outpatient testing and more limits by insurance companies on what testing is covered based on international statistical classification of diseases (ICD) coding and which labora-

tory will perform the testing. These trends will favor national reference laboratories that are better suited to control costs, electronically interfaced with insurance companies and healthcare providers at the point of service, and provide on-demand expert genetic or laboratory specialty consultations.

Edward R. Ashwood: The shift is complicated by several factors: the number of new tests is expanding rapidly (favoring testing in commercial labs), more patients are being treated in outpatient settings (favoring hospital laboratories and clinic POC testing), and many patients with chronic diseases (e.g., diabetes) are self-testing and using secure patient–physician portals for disease management (favoring POC testing).

Companies like Theranos are predicting that patients will embrace test ordering and specimen collection in pharmacies. This prediction is staking on an outcome similar to the rapid growth of flu vaccination in pharmacies. Around 2009, pharmacies lobbied states to allow pharmacists to administer influenza vaccines. By the 2011–2012 flu season, 3% of vaccinations were performed in pharmacies (4 000 000 of the total 132 100,000 doses distributed. By the 2012–2013 flu season, Walgreen and CVS together accounted for 11 700 000 doses. Although this year's numbers are not yet available, I would not be surprised if more than 10% of vaccinations occurred in pharmacies.

Although direct-to-consumer (DTC) laboratory testing has been unsuccessful in the past, patient attitudes have changed and there appears to be a strong interest in self-directed healthcare. Several laboratory businesses are investing in DTC models (e.g., LabCorp and Theranos). These companies share the philosophy that people have a right to know their health status and therefore have a right to order their own tests. Because patients are unlikely to understand the nuances of test ordering and result interpretation, I consider these services to be "recreational" testing. Overtesting of asymptomatic subjects is likely to cause more harm than benefit.

Harvey W. Kaufman: Quest Diagnostics also has a DTC offering, based on an employee wellness service we provide to large companies, and we were an early and energetic supporter of the Department of Health and Human Services' efforts to expand direct patient access to laboratory results in all 50 states. Some tests, particularly genomic tests, involve complex interpretations for which the involvement of a physician and even genetic counselor may be appropriate.

Norman Moore: Healthcare reform is putting more focus on best patient outcomes. Therefore, hospitals have to put increased effort into preventing healthcare-associated and secondary infections as they will have to bear the costs. That means running the right diagnostics in a timely fashion and acting on the results. If a patient needs to be isolated due to the infectious agent, timing is important, so the laboratory may need to do the test rather than a reference laboratory. With something as highly infectious as influenza, there will be an increased push to do that as close to the patient as possible to minimize time that other patients—and hospital staff—might be exposed and potentially affected.

With healthcare reform, there will be a push to give a specific sum per illness. That means that having better patient outcomes like reduced length of hospital stay and elimination of unnecessary testing needs to happen for a hospital to be profitable—and a central portion of that is having the right tests in a timely manner.

Is the traditional IVD industry reacting to these changes or not? If yes, how?

Susan Evans: Traditional IVD companies continue to invest in systems, automation, and informatics solutions that will improve laboratory operations, thus improving turnaround time and lowering overall costs. The goal is to support hospital and commercial laboratory customers as the number of patients entering the system increases but cost containment and challenges to reimbursement increase financial pressures. Additional advances in the central laboratory are essential as healthcare reform impacts volumes and economics. With the advancements in MDx platforms, this testing is now moving from the specialty laboratory to the central laboratory. More instrumentation and automation is being added to other specialties, including clinical microbiology. In addition, partnerships, targeted acquisitions, and collaborations enable the large companies to explore new areas of testing and technology. Companies with a focus on POC continue to add menu and investments to advance decentralized testing.

Harvey W. Kaufman: In a vibrant free market, entrepreneurs and inventors will develop improved testing solutions that meet the needs of the market. The established IVD companies will continue to invest in new technologies and acquire companies that offer novel solutions.

Charles S. Eby: New advances in nanotechnology and microfluidics, which lead to using less blood and reagents, are being rapidly pursued by startup companies; it does not seem that the major vendors are taking the lead in this area. These newer technologies have the potential to be "game changers" in laboratory testing and will certainly come to fruition in the next 10 years or so.

Norman Moore: Absolutely! Many thought leaders are extolling that we are reaching a new "Golden Age" of

diagnostics as companies are making assays better, faster, and more portable. It wasn't too long ago that hospitals had to ask whether it was better to have the result faster or more accurate. With newer technologies, physicians are getting both.

Having said that, the thought leaders getting behind new paradigms is one thing. Having hospital staff get behind them is another. Laboratories are concerned that they may lose too much control of testing. Furthermore, if more testing is done at the patient bedside, nurses may not want these added responsibilities and may prefer leaving testing to central laboratories. Newer technologies are going to be disruptive and challenges will have to be met and overcome. However, we can't conquer medical challenges like antibiotic resistance without changing how we operate.

What are the main challenges for expanding the role of POC?

Susan Evans: Broader adoption of POC testing has been slowed by the economics and the performance of many systems. In a hospital setting there is the added question of quality control and quality assurance programs. It has been difficult for traditional POC technologies to deliver analytical and clinical performance equivalent to those of tests performed in the clinical laboratory. There are exceptions and times when the need for a rapid result will win but these applications have been limited. If the laboratory can deliver a lab-quality result with the required turnaround time, the additional cost of a POC is difficult to justify. Today, utilization of new approaches in detection, multiplexing, microfluidics, and miniaturization has the potential to address the question of analytical and clinical performance. With the heightened interest in decentralized testing, investments in startups with exciting new approaches have increased. In the near horizon we should see the launch of a variety of new POC platforms. The challenges remain the same, cost, relevant menu, quality, and ease of use. With that in mind, companies are targeting lower cost per result and user and sample interfaces compatible with a variety of testing environments.

Harvey W. Kaufman: The main challenges for expanding POC have remained the same for the past two decades: technical performance, connectivity, and costs.

Charles S. Eby: Cost per test and test performance by nonlaboratory staff who struggle to appreciate the importance of preanalytical variables, quality control, and competency. In addition to increased costs per test, substitution of POC for test performance in a central laboratory is typically accompanied by an increased usage. While this could be due to pre-POC testing underutilization, for example glucose monitoring in diabetic and critically ill patients, I believe it is more often evidence of excessive utilization of laboratory resources.

Edward R. Ashwood: Test mix is a formidable challenge for POC testing. For example, the University of Utah Hospitals and Clinics has approximately 525 staffed beds, 24 000 admissions, and 1 600 000 outpatient visits (American Hospital Association data report, 2015). In the past 12 months, this health system ordered 3014 different laboratory tests. Only 449 were ordered more than once per day, 1040 more than once per week, and 1659 more than once per month. Twenty tests comprised 50% of the entire annual testing volume. Companies that manufacture POC devices will be well served to concentrate on the high-volume tests. Successful implementation will allow them to amortize the high development and regulatory costs over a large number of units. POC testing will grow to about a hundred of the most common tests.

Norman Moore: One of the main issues is that the laboratory is responsible for testing throughout the hospital. That means that they are responsible for verifying and reviewing the quality controls and every other issue that impacts testing. There will definitely be role shifting between nurses and medical technologists as to who will be performing testing outside the laboratory. Simply put, we need to keep the laboratory involved. More education is needed so medical professionals know what is now at their fingertips and how to best utilize it.

Communicating data back to a patient is not always useful; a patient needs information, an interpretation of the data that is a time-consuming process. Is there an efficient and effective way of doing it? Is there a role for the industry in this postanalytical step?

Susan Evans: The laboratory as consultant is an important topic and an opportunity for the clinical laboratory. Hospital networks and healthcare providers have adopted simple tools to provide data to patients. I typically get an e-mail with my laboratory results often before I get a call or e-mail from my doctor. Today, my physician provides the interpretation and discusses the impact on therapy. It would be so helpful if that initial email with "my data" were more informative, enabling a more productive dialogue with my doctor. If you believe in consumer-driven decentralized testing, the need for information vs data is even more critical, and where there is a need, someone will develop the product or service to fulfill that need. I cannot recommend a single efficient and effective way to approach this important issue, but there are many digital communication and information sharing tools to build on. Not necessarily a role for the

traditional diagnostic industry. More likely an integrated component of platforms and services targeted for nontraditional settings. The further removed the physician is from the process, the greater is the need to deliver high-quality and useful information to the patient.

Harvey W. Kaufman: Patients have varying levels of health literacy, interest in their own health, and ability to manage their own health. Sometimes another family member or caregiver is more able and responsible for the patient's health. Genetic counselors, health educators, nurses, pharmacists, and other professional healthcare providers may also be well suited to support and advocate on behalf of patients.

The laboratory community can improve the readability and comprehension about laboratory tests, their value, and result interpretation. With consent, we can work with other family members, caregivers, and other healthcare providers to ensure that patients receive appropriate tests and that the right follow-up is provided.

Charles S. Eby: Hospitals and insurance companies are increasingly giving patients access to their test results in real time or after a short delay. However, very few laboratory results are accompanied by either a generic or customized interpretation. The more tests performed, the more likely an abnormal quantitative or qualitative result will occur due to chance, or because the reference range is not specific for the age, sex, or stage of life of the patient. For example, if the reference interval is based on the central 95% of values of healthy population and a panel of 30 tests is performed the probability of all results being normal in a healthy subject is only 21% (assuming independent tests and the probability of a normal result for any test = 0.95). Healthcare providers are expected to interpret results within the context of an individual patient's condition and inform the patient of their significance, which a patient cannot usually do. However, post-analytical errors due to poor communication between clinician and patient or incorrect interpretations by a clinician are justifiable concerns. Reference laboratories, IVD manufacturers, and laboratory medicine organizations, either independently or together, can help patients cope with their own interpretation of test results or correct misinformation from healthcare providers by providing generic information that is suitable for a lay person and accessible through smart phones and social media applications.

Edward R. Ashwood: As a clinical pathologist, I've always found that discussing test results with the patient's primary physician most efficient and effective. Patients often don't know their diagnoses and cannot relate their medical history in an efficient manner.

Norman Moore: Communication is key, and it is often something we do very poorly now. Let's take the simple example of parents bringing their kids in for sore throats. The odds of it being Strep A is around 30%. However, many physicians are under time constraints and find communicating with the parents and explaining to them why antibiotics are not needed to be time consuming. So they take the easy route and give an antibiotic. We need better communication to prevent such situations. Antibiotic overuse in now linked not only to resistant microorganisms, but to childhood obesity and autoimmune diseases. Communication is key. We can also take complex examples like sexually transmitted infections. In these cases, patients may give false information just out of embarrassment. Rapid test results are the only way physicians can give the right treatment since they may never see that patient for follow-up again.

How will newer technologies such as mass spectrometry (MS) and NGS be adopted in the near term? Will they be centralized in major medical centers and reference laboratories or will there be major adoption in moderate and smaller hospital settings?

Susan Evans: New technologies are important. Application of an analytical tool such as MS has already been shown to enhance laboratory operations, enable rapid assay development, and improve turnaround times. In major medical centers and commercial laboratories the technology is well established in toxicology and other areas of the laboratory. MS is disrupting traditional approaches to infectious disease and antibiotic susceptibility testing. Adoption in microbiology laboratories is growing with the availability of US Food and Drug Administration (FDA)-approved applications. Manufacturers are working to develop simplified clinical laboratory systems, and provide methods for clinically relevant targets. The ultimate goal is to increase adoption and bring MS to more hospitals and laboratories, especially for analytes where turnaround times are important. NGS is one of the hottest new technologies and a powerful research tool. The potential to provide valuable diagnostic information is enormous but the field is young and rapidly evolving. There are daily articles on advances in the technology itself, such as read lengths, costs, capabilities, and quality. Clinical bioinformatics is an essential element of the total system. Manufacturers are focused on the development and introduction of clinical platforms and studies to demonstrate the clinical value of NGS-based assays. Although interest and early adoption is moving faster than many predicted, there are still many issues to be worked through. Near term, NGS-based testing will be focused in commercial laboratories, major medical centers, and clinical service businesses.

Charles S. Eby: Owing to the sensitivity and specificity of the technology, MS will continue to grow for small-molecule analysis as costs come down and instruments become easier to operate. Reagent costs for MS testing are generally far less than those for immunoassays. One caveat here is what will happen with FDA oversight of laboratory-developed tests (LDTs) since most MS testing is LDT. Probably the most remarkable and rapid advance in the use of MS has been in microbiology, where MALDI-TOF is rapidly becoming standard practice. MS proteomic testing has been slower to demonstrate clinical utility or advance personalized medicine but there are certainly huge funding efforts in this area. I think we just need to see what becomes of this field in the next 5–10 years before we see it in routine clinical use.

Reference laboratory–based whole genome, gene panel, and targeted exome sequencing volumes will grow when supported by clinical validation and insurance reimbursement. Larger specialty hospitals will internalize NGS over the next decade as costs decline and volumes increase in areas such as HLA, oncology, and possibly infectious disease. I do not expect NGS to become routine in moderate-to-small hospitals in the next 10 years.

Edward R. Ashwood: These technologies will be centralized for the next decade. The financial barrier to entry is too high for moderate and small hospitals. Commercial laboratories have embraced these technologies. ARUP has over 150 mass spectrometers and several NGS instruments. Both types of instruments are expensive ($250 000 to $800 000) and require advanced laboratory personnel for operation. The laboratory professionals that direct the laboratory sections housing these instruments are highly specialized.

Norman Moore: NGS may not need a quick turnaround so it may remain centralized. Things like MALDI-TOF are inexpensive to operate and fast per assay, but the initial investment is huge so that has been somewhat of a deterrent for hospitals. Many are enthusiastic that these technologies, along with rapid molecular, will improve medical decision-making, but I don't yet see that they will be brought closer to the patient like rapid molecular is poised to do.

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