Bringing the Diagnostic Lab to Patients

If properly designed and engineered, point-of-care diagnostic tests can have great impacts on health care in resource-limited settings

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Although diagnostic tests affect up to 70% of treatment decisions, such testing accounts for only 2% of the overall cost of U.S. health care. Scientific advances and new technologies are making it possible to develop simple, inexpensive diagnostic tests that can be used at the patient’s bedside. In developed countries, such point-of-care tests (POCTs) offer a convenient, inexpensive alternative to conventional laboratory-based diagnostic tests. In developing countries, where conventional diagnostic testing might not be available, access to POCTs may mean the difference between a treatment decision informed by an accurate diagnosis versus one that is ineffective or even harmful.

New technologies that could contribute to the development of powerful POCTs emerge steadily from the research community, while local health care professionals continue to make treatment decisions with inadequate information. How can these two sets of experts become better connected? What POCTs could make the biggest impact on health? What qualities do POCTs need to be effective in resource limited settings? What are some of the systemic barriers to the development and implementation of POCTs in resource limited settings?

The American Academy of Microbiology (AAM) in September 2011 convened a panel of microbiologists, engineers, epidemiologists, and public health officials—experts involved in every step of the design, development, and implementation of POCTs—to consider these and related questions. Their discussions and recommendations are summarized in the AAM report “Bringing the Lab to the Patient: Developing Point-of-Care Diagnostics for Resource Limited Settings,” available online at http://academy.asm.org/images/stories/documents/pointofcarediagnostics.pdf. To bring their discussions to life, we tell a story about fictitious characters for whom effective diagnostics are anything but imaginary.

Some POCTs Are More Urgently Needed Than Others

Amara wakes up to the sounds of children playing outside her home. She is feverish and weak. For the past few days, she has found it more and more difficult to get out of bed, but she has put off a visit to her regional clinic. With a family to care for, she can ill afford to spend most of her day walking to the clinic a few villages away. Fearing that if she waits longer she will be too weak to make the trip, Amara barely manages to make the 3-hour trek.

The technician on duty listens attentively to Amara’s symptoms: fever and extreme fatigue can be symptomatic of many different illnesses in this area of Africa, anything from a simple bacterial infection to one caused by the more frightening hemorrhagic fever virus. At first, the technician suspects that Amara has a viral infection, but Amara’s symptoms also match those of a serious illness being reported near her village: a bacterial infection attacks the central nervous system and can be fatal if untreated. The only reliable diagnostic test requires drawing spinal fluid by lumbar puncture followed by culturing the sample to de-

SUMMARY

➤ Properly designed point-of-care diagnostic tests can help to overcome health infrastructure deficiencies and lead to improved health care in resource-limited settings.

➤ Scientific and technical advances can speed development of point-of-care tests, but they are only part of a far more complex process of developing tests that work effectively in particular settings.

➤ Key characteristics that contribute to success in resource-limited settings should be included in the earliest design stages.

➤ Developing point-of-care tests requires many stakeholders to communicate and collaborate effectively with one another.
detect the bacteria. A lumbar puncture is a risky and costly procedure, and the technician realizes that, even if the culture is positive, that information will be of little use after waiting a week to complete the test. Amara’s village is distant, and it may not be possible to find Amara when the results are delivered. In practical terms, the technician and her colleagues should treat Amara immediately with the antibiotic that would be effective against the infection she may not have, perhaps wasting a precious course of the drug and fostering drug resistance.

While this story is fiction, similar scenarios play out all the time. Diagnostic POCTs can be powerful. However, there cannot be a POCT to suit every disease and situation. Which POCTs are urgently needed?

In Amara’s case, the cost of misdiagnosis or no diagnosis could be the difference between life and death. Diagnosing CNS infections with lumbar punctures requires highly trained personnel and can be dangerous. Laboratory tests that provide results days after the patient has returned to a distant home are of limited use. The colloquium report discusses many other situations where POCTs could have a big impact, including when the wrong treatment could harm the patient, when there is a high likelihood of overtreatment, or when failure to detect an illness could carry a great public health cost.

Colloquium participants identified a number of medical conditions that meet such criteria—for example, discriminating between bacterial and viral infections is critical because the wrong treatment can be ineffective or even harmful. POCTs capable of determining whether a pathogen is drug resistant or particularly virulent can be helpful in choosing the appropriate treatment. POCTs for sexually transmitted diseases or deadly viral hemorrhagic fevers are urgently needed not only for the individual patient, but because transmission can spark larger public health crises. In addition to POCTs for infectious diseases, a general “state-of-health” test capable of delivering information similar to a physical exam could also make a big impact on health, particularly in settings where resources are limited.

**Qualities that Make POCTs Effective**

*Five years earlier and 2,000 miles away, a scientific breakthrough at a medical college nearly changed Amara’s story.*

The researcher stared at the finished prototype, a machine to detect telltale antigens for seven bacterial pathogens that infect the CNS—pathogens that previously required analysis via culture techniques of samples from lumbar punctures.

The instrument was developed by a diagnostic company in collaboration with the researchers from the medical college. The instrument is sophisticated, but is not yet fully automated, as a technician is needed to pass blood samples over a special grid with antibodies capable of immobilizing each of the seven antigens. The grids are treated with detection reagents and then read by a laser, with the results displayed by LCD on the side of the machine. The technician must also be trained to interpret the results before a confident diagnosis can be made. After testing, the device was approved by the Food and Drug Administration (FDA), and the company received thousands of orders for its new machine from hospitals in developed countries.

The company also sold a handful of machines to hospitals in larger cities of developing nations. But none of those machines made it anywhere near the clinic that Amara visited. That clinic lacked trained technicians and money with which to train them. Moreover, the reagents to run the machine were too costly and the complexity of its operation, the power to run it, and the experience needed to interpret its data output were all impractical or out of reach. It could detect antigens at 1 part per million, but could not be implemented outside city limits. For Amara and others like her, this state-of-the-art diagnostic instrument might as well not exist.

Scientific advances and new technologies are only a few of the first steps needed to deploy an effective POCT. What works in the lab may not be effective in resource-limited settings where trained operators, clean water, or electricity may not be available. The acronym ASSURED has been used to summarize the ideal qualities of a POCT for resource-limited settings—affordable, sensitive, specific, user-friendly, robust and rapid, equipment-free, and deliverable. Additionally, an ideal POCT should be connected to the health care system as a whole; the results of the POCT should be easily captured, stored, and shared. Results of colorimetric assays, for example, can be captured easily with many types of cameras, even those on cell phones.

New technologies can be employed to help
POCTs obtain some of these characteristics, even in settings where resources are limited. For example, advances in battery design could make POCTs less dependent on plug-in electricity. Similarly, test reagents that are less heat sensitive would decrease dependence on refrigeration. Microfabrication, microfluidics, and other nanotechnologies could decrease sample sizes required for tests and decrease reagent costs. Steps to allow multiplexing and automation of POCTs would also decrease costs.

What information should a POCT provide to health care professionals? Diagnostic tests used in resource-limited settings require robust support. Raw data is useless if it cannot be interpreted. POCTs designed for such settings should report information that the end user can readily interpret, and offer other support to help make treatment decisions more manageable. It is also important to incorporate effective training measures into the test to allow users with little experience to conduct and interpret the test properly. A POCT that is too complex will be adopted slowly or not at all, and if the POCT results are not effectively captured, its public health utility will be much reduced.

Moreover, the results from a POCT should be saved in a standardized format and automatically entered into medical records. A good POCT should contain built-in quality control to ensure the test is administered properly and is functioning. Built-in quality control avoids the conflicts that can arise when operators are expected to devote a portion of their reagents to anything but direct patient testing.

**Several Barriers Hinder Development of POCTs**

The new diagnostic test device was not available to help Amara because the deck was already stacked against development of a POCT for her and others living under similar circumstances . . .

The epidemiologist charged with managing health care resources in Amara’s region of Africa is well aware that bacterial meningitis cases are skyrocketing, but he cannot be sure that any of the sample tests that sales representatives regularly send to his office will work if they are made available locally in villages. He has been burned by tests that were cheap knockoffs or fakes. With constrained resources, he has to choose carefully among health services and knows well that money spent on an ineffective POCT cannot be spent for antivirals and antibiotics or to pay technicians—the currency of lives in this part of the world.

Maybe the outbreak will fade on its own, he thinks as he closes the brochure describing the sophisticated machine now used in developed countries—the one that can distinguish seven different pathogens. Such a machine could be a key weapon in the fight against bacterial meningitis, but it would need many modifications to work in this resource-limited setting. Who will make that investment when the payoff is so limited?

Improving communication among scientists, engineers, technologists, and health care workers would help guide more POCTs successfully through design and deployment. In our narrative about Amara’s encounter with the local health care system, such communication channels were lacking, thus preventing an otherwise promising POCT from being adapted for use in a resource-limited setting. Efforts are needed to bridge such gaps. The journal *Lab on a Chip* is an example of one such effort, while the Foundation for Innovative New Diagnostics (FIND) provides another. FIND specializes in linking groups whose members then can work together to develop effective POCTs for resource-limited settings. The ability to engage these parties and put them in touch with local health care workers who will eventually use such tests can help to ensure successful integration into the overall health care system. Without health care workers, nurses, and physicians advocating for specific POCTs, the implementation of tests can stall.

The regulation and licensing of diagnostic tests can constitute another set of hurdles. In the United States and other developed countries, government agencies regulate the commercial accessibility of medical tests by examining evi-
dence and setting standards for their effectiveness. Resource-limited areas may not have agencies with the expertise needed to evaluate such tests, making it easier for criminals to get away with distributing knockoff or counterfeit tests. Having a unified set of standards, or a single approval process recognized around the globe, could help address these issues.

Conclusion

Amara’s fictional story addresses very real problems. Designing and deploying POCTs for use in resource-limited settings is part of a process that requires many players to collaborate effectively to support product development, and efforts to bring a promising POCT into use in such settings can be derailed at any point. Imagine how the story might have ended if the scientists, local health care workers, and diagnostic companies had worked together closely from the start. The AAM report, “Bringing the Lab to the Patient: Developing Point-of-Care Diagnostics for Resource Limited Settings,” highlights the need for such groups to interact in ways that could mean a brighter future for the billions of people like Amara whose health will benefit from access to appropriate POCTs.

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