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Brief report

A primer on on-demand polymerase chain reaction technology

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Efforts to reduce health care–associated infections (HAIs) have grown in both scale and sophistication over the past few decades; however, the increasing threat of antimicrobial resistance and the impact of new legislation regarding HAIs on health care economics make the fight against them all the more urgent. On-demand polymerase chain reaction (PCR) technology has proven to be a highly effective weapon in this fight, offering the ability to accurately and efficiently identify disease-causing pathogens such that targeted and directed therapy can be initiated at the point of care. As a result, on-demand PCR technology has far-reaching influences on HAI rates, health care outcomes, hospital length of stay, isolation days, patient satisfaction, antibiotic stewardship, and health care economics. The basics of on-demand PCR technology and its potential to impact health care have not been widely incorporated into health care education and enrichment programs for many of those involved in infection control and prevention, however. This article serves as a primer on on-demand PCR technology and its ramifications.

Health care–associated infections (HAIs) continue to be one of the most critical burdens on the nation's health care system, representing a significant source of patient morbidity and mortality. A multistate point-prevalence study of 183 acute care hospitals in the United States reported an estimated 648,000 inpatients with 721,800 HAIs during 2011.[1] Although efforts to reduce the incidence of HAIs have grown in both scale and sophistication, thanks in part to multidisciplinary collaboration in the medical community, advances in technology, and implementation of and mandates for evidence-based HAI-specific safe practices, the battle against HAIs is far from over.

The ability to rapidly identify the pathogens causing HAIs has been an integral part of this battle. The development of polymerase chain reaction (PCR) testing of blood, sputum, urine, and stool specimens has been a critical step forward in this effort to increase the rapidity, sensitivity, and specificity of pathogen diagnosis. First developed in the 1980s, PCR is a method for amplifying specific sequences of DNA, which can, among other things, aid in the diagnosis of diseases and the identification of bacteria and viruses.[2] Although batch PCR testing has been available for several decades for diagnostic purposes, on-demand PCR testing with results obtainable at the point of care and within 2 hours is a relatively new advancement that, unfortunately, has not yet been widely incorporated into the education and enrichment programs for many involved in infection control and prevention.

A recent survey of more than 200 infection preventionists (IPs) from across the country, of whom 75 responded, identified significant knowledge gaps among IPs with regard to PCR technology[3]:

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- Only 8% reported having PCR testing available at point of care in any department (eg on the inpatient nursing ward or in the intensive care unit [ICU] as opposed to in the microbiology laboratory).
- 69% reported having PCR testing available to all health care departments in their facility.
- 41% reported not understanding how PCR technology works.
- 59% reported using rapid PCR for screening in addition to diagnosis and treatment.
- Only 41% reported being involved in their facility's purchase decision of PCR equipment.
- Only 7% reported having performed studies on PCR and its benefit to their IP program.
- When IPs were asked to name the organisms for which PCR testing does not yet exist but for which testing would be most helpful, carbapenem-resistant Enterobacteriaceae was mentioned most often. Of note, every other response indicated an organism for which rapid PCR testing is already available.
- 57% of the IPs' facilities that did not have access to PCR technology had no plans to obtain it in the near future.
- 30% of the IPs did not know the brand of PCR equipment used in their facility (S. Barnes, personal communication, June 7, 2014).

Given the critical need for accurate and expedient diagnosis of infection in today's health care settings, it is imperative that those professionals at the forefront of the fight against HAIs understand the basics of PCR technology along with its potential impact on HAI rates, antimicrobial stewardship, patient isolation, and health care economics.

ON-DEMAND PCR TESTING

PCR testing of patient specimens involves harnessing the ability of the enzyme DNA polymerase to synthesize new DNA strands complementary to a template strand when exposed to short pieces of single-stranded DNA. These short pieces, called primers, are designed to be compatible with the template strand. In the detection of bacteria and viruses by PCR, specific primers, chosen based on the known gene sequences of particular bacterial and viral DNA, are added to the tested samples and will allow DNA polymerase to amplify numerous copies of the pathogen's DNA if it is present.

In the early days of PCR testing, blood, sputum, urine, or stool samples were collected and run in batches in centralized locations. Although this PCR testing offered more expedient and, in some cases, more sensitive and specific results than other testing modalities, there remained some drawbacks. These included the need for highly skilled laboratory staff to run the tests (some states permit only licensed medical technologists or licensed professionals to run them), high vigilance for contamination given the exquisite sensitivity of PCR, and the time involved in collecting samples, bringing them to a centralized location, and running them at set times of the day or when an optimal number of samples are received. These factors have been made obsolete by the advent of on-demand PCR testing, however.

The on-demand PCR technology does not require specialized training for health care staff and allows for testing of patients at the point of care in numerous settings—emergency departments (EDs), satellite clinics, and ICUs, among others—with turnaround times of approximately 2 hours or less. Health care personnel are able to run the test samples in fully integrated and automated PCR testing units that can be placed in the setting of choice. Currently, on-demand PCR testing is available for methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-sensitive *S aureus*, *Clostridium difficile*, *Mycobacterium tuberculosis* (MTB), *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, vancomycin-resistant *enterococcus*, enteroviral meningitis, norovirus, and group B *Streptococcus*.

The question then becomes how does on-demand PCR testing impact health care delivery? The answer is that the impact is far-reaching: influencing HAI rates, health care outcomes, hospital length of stay (LOS), isolation days, patient satisfaction, antibiotic stewardship, and health care economics.

IMPACT OF ON-DEMAND PCR TESTING

HAI rates

Rapid and reliable identification of pathogens, particularly those that pose the most significant risks to patients, is an integral part of reducing HAI rates. As Sue Barnes, National Leader for Infection Prevention for Kaiser Permanente, says, "the critical first step in preventing transmission of communicable diseases in health care settings, such as CDI [*Clostridium difficile* infection], MRSA, pertussis, and TB [tuberculosis] is prompt diagnosis. This guides expedient isolation of the patient and PPE [personal protective equipment] use as indicated, as well as prompt treatment to minimize and optimize antibiotic use and reduce transmission risk."

In their 2008 *Annals of Internal Medicine* article, Robicsek et al reported implementing on-demand PCR testing followed by isolation and decolonization of patients who tested positive for MRSA. They subsequently saw a "reduction by more than half of health care–associated MRSA disease occurring during admission and in the 30 days after discharge".[4] Similar results have been seen in other institutions that switched to on-demand PCR testing for MRSA. Loyola University Medical Center reported a 68% reduction in MRSA infections,[5] and New England Baptist Hospital reported a 60% reduction.[6] After implementing an active MRSA high-risk patient screening program using on-demand PCR testing, J.T. Mather Hospital reported an 84% reduction in MRSA cases, an 84% cost reduction, and a decrease in average LOS in their ICUs and cardiac care units from 4.4 to 3.3 days between 2008 and 2014.[7] The Albert Einstein Health Care Network reported a 27% reduction in MRSA rates after initiating its Stop MRSA Acquisition and Spread in our Hospital campaign involving on-demand PCR testing and new clinical protocols.[8]

Awad et al reported an overall decrease in health care–associated MRSA infections from 2 to 1 per 1000 bed-days and a statistically significant overall decrease in surgical site infections (SSIs) at the Michael E. Debakey Veterans Affairs Medical Center when universal on-demand PCR screening for MRSA (results obtainable within 70 minutes) was implemented, along with contact precautions for infected or colonized patients, improved hand hygiene, a "cultural transformation campaign with staff and leadership," and "ongoing monitoring of process and outcome measures".[9] This 5-pronged approach, referred to as the "MRSA bundle," was later implemented across the Veterans Affairs health care system, resulting in a 62.2% decrease in health care–associated ICU MRSA infections and a 44.7% decrease in non-ICU health care–associated MRSA infections, as reported by Jain et al in their 2011 study.[10] One study examining CDI incidence noted a decrease in health care onset–, health care facility–associated CDI rates from 52% to 16% in the 6 months after they implemented PCR testing instead of enzyme immunoassay testing (EIA).[11]

Antimicrobial stewardship

Prudent administration of antibiotics has become an issue at the forefront of the fight against HAIs in this era of multidrug-resistant organisms. The State of California has actually mandated that all