



STD/STI TESTING

Molecular assays enable accurate detection, yet sexually transmitted diseases are on the rise.



By Valerie Neff Newitt

Sexually transmitted infections (STIs) and diseases (STDs) pose a unique problem in detection: They often arrive without tell-tale symptoms, or their symptoms may be so non-specific that they are not immediately recognized.

“STDs are important individual, medical, social and economic issues,” declared Seung-Ju Lee, department of urology, The Catholic University of Korea, addressing a 2013 international symposium on new strategies for diagnosis of bacterial infection. “Regular testing is crucial. Some STDs are curable and treatment is affordable, but sensitive diagnostic tests are required for early detection to guide treatment and prevent the development of reproductive sequelae and adverse outcomes of pregnancy, and to interrupt onward transmission.”¹

Yet with this information well entrenched in clinical and diagnostic understanding, in 2015, the CDC reported that “cases of sexually-transmitted diseases are on the rise, some at an alarming rate.”²

The CDC detailed, “Reported cases of three nationally notifiable STDs—chlamydia, gonorrhea and syphilis—have increased for the first time since 2006, according to data published by the CDC in the 2014 STD Surveillance Report. The approximately 1.4 million reported cases of chlamydia, a rate of 456.1 cases per 100,000 population, is up 2.8%

since 2013. Rates of primary and secondary (P&S) syphilis—the most infectious stages of syphilis—and gonorrhea have both increased since 2013 by 15.1% and 5.1%, respectively. In 2014, there were 350,062 reported cases of gonorrhea (a rate of 110.7 per 100,000) and 19,999 reported cases of P&S syphilis (for a rate of 6.3 per 100,000). STDs continue to affect young people—particularly women—most severely, but increasing rates among men contributed to the overall increases in 2014 across all three diseases.

“America’s worsening STD epidemic is a clear call for better diagnosis, treatment and prevention,” said Jonathan Mermin, MD, director of CDC’s National Center for HIV/AIDS, Viral Hepatitis, STD and Tuberculosis Prevention. “STDs affect people in all walks of life, particularly young women and men, but these data suggest an increasing burden among gay and bisexual men.”

Tom West is president of the diagnostic ►►

solutions division at Hologic (maker of the Aptima Combo 2 assay for the detection of chlamydia and gonorrhea). He told *ADVANCE*, “Even though screening has expanded over the past two decades, STIs are on the rise and testing rates remain low because of various barriers. We continue to educate healthcare practitioners and lab professionals about what tests are available and recommended within the guidelines as well as advocate for new approaches to screening, especially among our youth.”

West noted that research in the STI field suggests inherent value in universal screening for chlamydia.³ “Data shows that this approach could decrease infection rates, as well as overall costs, by reducing long term side effects such as pelvic inflammatory disease,” said West. “Hologic recognizes the significant increase in syphilis infections, despite active public health surveillance programs employing syphilis serology tests, and is working with the CDC, infectious disease physicians and clinical diagnostic laboratories to determine the requirements for sensitive molecular tests for these infections.”

STI Testing Goes Molecular

Molecular tests are indeed in demand for STIs, “as they offer unparalleled accuracy, with both high sensitivity and specificity,” according to West.

Rob Jenison, senior vice president of R&D and CTO at Great Basin Scientific, agrees. “Two years ago, hospitals and clinical labs weren’t talking about point-of-care molecular diagnostics for STIs, but we have seen a shift in demand over the past year. Our customers, from rural critical access hospitals to large urban medical centers, are now asking for molecular diagnostic tests for STIs as a result of reporting very high infection rates.”

Knocking culture testing from its throne, nucleic acid amplification tests (NAATs) are now the accepted gold standard due to their very high accuracy (sensitivity and specificity), according to Jenison. He added that sample-to-result systems have also created an easy-to-use approach that can eventually be used in the point-of-care (POC) setting as appropriate. “In the near future, these tests will be broadly inclusive tests for detecting the

causes of STIs. At Great Basin Scientific, our first entry into the STI diagnostics market will be a Chlamydia trachomatis, Neisseria gonorrhoea and Trichomonas vaginalis for men and women, which will provide clinicians results in under 75 minutes.”

West said future-facing trends continue to be greater automation, consolidation of menu and a sample-to-results approach. Fully automated systems (such as Hologic’s Panther integrated platform that automates all aspects of molecular testing), substantially reduce



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hands-on time for laboratories by providing random and continuous access with rapid turnaround time. (In the U.S., Hologic also offers tests for Trichomonas vaginalis and HPV on the Panther system. In Europe and some other countries, the company has tests for Mycoplasma genitalium, HSV, HIV, HCV and HBV on the market and is pursuing similar commercialization in the U.S.)

Noteworthy Changes in Testing

Asked to pinpoint recent movement in the field of STI testing, West pointed to a recent modeling study by CDC researchers that demonstrated the potential benefit to patients of clinicians adopting an opt-out/universal screening strategy for patients. “Current guidelines state that all sexually active women younger than 25 as well as at-risk older individuals be screened for chlamydia

and gonorrhea annually, but we know this doesn’t happen, partly because taking a sexual history is difficult,” West explained. “Some patients may feel uncomfortable talking about sexual health with their healthcare provider or assume that, if they don’t have symptoms, they don’t need to be tested for STIs. These all create barriers to screening.”

With an opt-out or universal screening strategy, healthcare practitioners would automatically screen all patients ages 15-24, according to the CDC guidelines, unless they sign a statement that they prefer to opt-out of these tests. “In the modeling study, adoption of this strategy was calculated to reduce chlamydia incidence by more than 55%,” said West. “This approach also was more cost-effective over time, improving health outcomes at a lower net cost than current testing.”

Jenison pointed to an increase in testing for Trichomonas vaginalis, “a parasite that is now widely acknowledged to be a highly prevalent cause of STIs; its prevalence is greater than chlamydia and gonorrhea combined,” he explained. “It is often not diagnosed in men due to the lack of symptoms. Trichomonas vaginalis is now being added to multiplex NAATs for STIs. This will provide more comprehensive information to direct patient management.

He also noted that tests for STIs currently on the market usually require a urethra swab—a somewhat difficult and painful swab to take from the patient, particularly from men. “Our test for Chlamydia trachomatis, Neisseria gonorrhoea and Trichomonas vaginalis for men and women will only require a urine sample, making it extremely easy and pain-free for patients, both men and women.”

Challenges That Remain

West emphasized that one major challenge that remain within the realm of STI testing is “the fact that we don’t have any FDA-approved molecular tests for Mycoplasma genitalium (MGen), which we believe to be prevalent at levels similar to chlamydia. Like chlamydia, MGen has been linked in a number of studies to similar long-term effects on health, including pelvic inflammatory disease, which can lead to infertility. Antibiotic resistance is also

a growing problem with MGen, and this may be exacerbated if patients are given the antibiotics typically administered for chlamydia.”

Some labs are addressing this situation by developing lab developed tests (LDTs) that utilize NAAT technology, he noted. (Hologic currently has a CE-marked molecular assay for MGen and plans to pursue regulatory clearance in the U.S.)

An additional challenge can be found in the fact that, while screening of women for *Chlamydia trachomatis*, *Neisseria gonorrhoea* is now recommended annually, men are not currently included in this recommendation, said Jenison. “This ignores a significant reservoir of disease, which is proving to be a major contributor in its spread,” he added.

He also commented on what he called “a very prevalent issue in labs: the lack of staffing. Most tests require a microbiologist to run the tests and interpret results. However, most labs don’t staff microbiologists or epidemiologists 24/7, so tests can only be run at certain times of the day. Diagnostics companies can assist in designing tests that are easy-to-use, provide fast, definitive results and can be run on all shifts, which will make diagnostic and detection testing easier for labs to adopt,” Jenison said.

Furthermore, Jenison emphasized an acute need for cost-effective testing in the POC setting so that appropriate therapies can be delivered in a timely manner to both treat the infection and to reduce the risk of spreading it. “The need is well understood both by clinicians and the FDA, which has led to a clear definition of the requirements diagnostic companies must follow in order to get new products approved and available to help fight this growing problem,” he noted.

A Clinician's Perspective

Weighing in from a physician’s point of view, Bruce E. Ruben, MD, founder and medical director of Encompass HealthCare and

Wound Medicine in West Bloomfield, Mich., is not so sure that more advanced tests are the primary answer to rising STI numbers.

“I believe that because new technology is yielding more diagnosed cases, the urgency here isn’t for better tests, but rather for better protection among sexually active people. This comes in many forms: Education and information on how to prevent the spread of STIs and vaccines that are now available for certain types of STD prevention are just two examples,” he said.

Ruben also commented that the turnaround times on STI tests are, in his view, usually within an acceptable 24-48 hours from the time the test is completed. “However, advancements in STI testing are on the rise with smartphone-based testing at the forefront. Last year, a device was in the process of being tested that attaches to a smartphone and performs an ELISA test for HIV and syphilis. In addition, hepatitis C virus (HCV) and syphilis antibodies are now able to be detected with home tests bought at the local drug store. Remarkably, even rapid oral HIV tests are now available at retail stores,” he said. He believes the availability of direct-to-consumer tests will allow patients to find out right away if they are infected and then pass that information on to their partner. “It spurs the ability to protect others by communicating with current and future partners,” he said.

Parting Thoughts

West, Jenison and Ruben were all asked what take-away information they’d hope to impart to readers on the topic of STIs.

West said he wants others to realize that “most STIs are completely treatable, and we have accurate tests to detect them. There is no good reason we can’t turn the tide and reduce their prevalence, thus preventing long-term deleterious health problems. Labs have a valuable role to play by helping to educate their clinical colleagues about the

importance of ordering these tests and by encouraging them to consider the opt-out/universal screening strategy.

Jenison said that a significant portion of the population will be exposed to STIs in their lifetime. Yet, the stigma of STIs continues to be a substantial obstacle in its early detection and treatment. “This has led to STIs emerging as one of the biggest areas of concern to the infectious disease community. STIs are readily treatable if we have testing recommendations that include the entire population as part of an annual health checkup,” he emphasized. “That can only happen through an open and continuous dialogue that’s driven by the healthcare community and one that leads to a change in attitudes about STIs. Insurers, including Medicaid, continue to hinder detection and treatment in that they don’t cover screening and only reimburse for a diagnosis that comes from symptomatic patients. Policies like this ensure the continued spread of infection. If STI screening were a standard, reimbursable practice, we would see a significant decrease in infection rates.”

Ruben added that the public needs to be educated to the facts around STIs, including that STI test results are “very quickly turned around and can be done for free at the patient’s local health department. This information is not widely known and needs to be dispersed.” ■

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