

# GLOBAL HEALTH

## Innovation Insight Series



Dr. Helen Lee at work in the lab

Photo: Wellcome Trust

## DIAGNOSTICS FOR THE REAL WORLD I: Addressing Stakeholder Resistance

CAMBRIDGE, ENGLAND AND  
SUNNYVALE, CALIFORNIA

ESTABLISHED 2002

HELEN LEE, FOUNDER

### THE PROBLEM/SOLUTION SPACE

Globally, *chlamydia trachomatis* infections are the most prevalent sexually transmitted bacterial disease.<sup>1</sup> The World Health Organization estimated that 92 million new cases of chlamydia were diagnosed worldwide in 1999, with the highest prevalence among sexually active adolescents and young adults.<sup>2,3</sup> If identified promptly, chlamydia is easily cured with a single dose of antibiotics.<sup>4</sup> However, because up to 75 percent of women and 50 percent of men with chlamydia are asymptomatic, millions of cases go undetected, and the chance of unknowingly transmitting the bacteria to sexual partners is high.<sup>5</sup>

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Untreated, chlamydia can lead to devastating complications for women. According to the Centers for Disease Control and Prevention, up to 40 percent of women with untreated chlamydia will develop pelvic inflammatory disease (PID), as the infection-causing bacteria move in to the upper reproductive organs and cause the formation of scar tissue. Long-term consequences of PID include infertility, life-threatening ectopic pregnancy, and chronic pelvic pain, as well as a significantly increased risk of contracting HIV. Pregnant women can pass chlamydia to their babies, resulting in neonatal ophthalmia (eye disease) and pneumonia.<sup>6</sup> Chlamydia also causes trachoma, one of the most common infectious causes of blindness in the developing world.<sup>7</sup>



Photo courtesy of DRW

*Health workers testing the CRT at Brook Birmingham*

Because the infection often has no symptoms, most individuals are unlikely to seek treatment until they develop complications linked to the condition.<sup>8</sup> Accordingly, efforts to control the disease rely on opportunistic testing and screening. In developed countries, the gold standard of testing for genital chlamydia infections is the nucleic acid amplification test (NAAT). While extremely sensitive, NAATs are expensive and technically complex, requiring specialized equipment and reagents, as well as highly trained laboratory personnel.<sup>9</sup> Accordingly, NAATs are rarely available in resource-poor settings.

Another drawback of NAATs is that, in many settings, the samples must be sent to a centralized lab for testing, causing a delay in diagnosis.<sup>10</sup>

Across all socioeconomic segments, informing patients of test outcomes and getting them to return for treatment is difficult and resource-intensive. This challenge is especially pronounced in developing countries where communication infrastructures can be under-developed and patients may live hours from the nearest clinic. For these reasons, point-of-care testing with diagnosis and treatment provided while the patient is still in the clinic represents a unique opportunity for cost-effective chlamydia intervention.

### ABOUT DIAGNOSTICS FOR THE REAL WORLD

After a successful career developing diagnostics in a corporate setting, Dr. Helen Lee moved to the University of Cambridge to co-found the Diagnostics Development Unit with seed funding from the World Health Organization, the U.S. National Institutes of Health, and the Wellcome Trust. As director of research for the new organization, she hoped to address the unmet diagnostic needs of patients in developing countries. To commercialize the technologies developed at the university, Lee also created a commercial spinout, called Diagnostics for the Real World (DRW), headquartered in Sunnyvale, California.

DRW's first product was a rapid diagnostic test for chlamydia. Describing the project, Lee explained, "Chlamydia has all the emotional tags to make testing an important need. It has a high prevalence and devastating consequences for women and babies born from infected mothers. Yet the drugs are totally effective—one pill, one time and you're

cured. So the problem has been how to screen the apparently healthy individuals. The asymptomatic nature of the disease is such that infected individuals will not come to the clinic. Rather, you need to go to the sexually active group, find innovative ways to screen them, and then treat them.”<sup>11</sup>

In response to that need, Lee and her team developed a Chlamydia Rapid Test (CRT) that was designed for simplicity. It was easy to use, did not require skilled technicians or laboratory processing, and provided stable and robust results even in high heat and humidity. In women, it relied on a self-collected vaginal swab, while men self-collected their urine using a container called FirstBurst. By capturing only the first voided urine, in which the bacteria load was the highest, FirstBurst increased the test’s accuracy.<sup>12</sup> FirstBurst received the Medical Futures “Best Diagnostic Innovation” award in 2003. The CRT was granted regulatory approval in Europe (CE mark) and Canada.

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*The person responsible for overseeing the nurses on the island ... simply refused to have young women tested. The country is very religious, and her response was basically, ‘We have no promiscuity.’*

Delivering results in half an hour, the CRT allowed providers to utilize a “test and treat” strategy. “For many patients, you either test them and treat them, or you’ve

lost them,” noted Lee. The ability to perform diagnosis and treatment in a single visit minimized patient anxiety, reduced the risk of complications, and helped prevent onward transmission of the disease. It also eliminates the logistics and expense of transporting samples to a lab, obtaining results, and re-contacting patients. Additionally, the simplicity and speed of the test facilitated the screening and treatment of more people and provided an effective option for testing certain high-risk groups and hard-to-reach populations. Finally, the low cost and stability of the CRT made it feasible to conduct chlamydia screening in remote, resource-poor settings.

### ONE CHALLENGE: ADDRESSING STAKEHOLDER RESISTANCE

From the outset, Lee and her team believed that a more effective rapid test for chlamydia represented such a compelling need that commercial success was bound to follow once the technology was developed. “But it turns out that it was very difficult to launch this product,” she said. “I learned that it’s really not about the need. It’s about the demand.”

DRW discovered that demand was directly affected by other factors at play within the markets it was targeting. For example, in many settings, the company underestimated the obstacles created by religious or cultural resistance. Lee recalled how DRW sought to make its CRT available in one country in the South Pacific. In the absence of routine screening for sexually transmitted disease, chlamydia had become endemic. For example, at one antenatal clinic, more than 25 percent of female patients were infected with the disease.<sup>13</sup> Stunned by the magnitude of the problem, Lee met with local health officials and offered to provide two year’s-worth of the CRT, free of charge, provided that infected individuals would be treated with azithromycin. “However, the program had to be approved by the person responsible for overseeing the nurses on the island, and she simply refused to have young women tested,” Lee said. “The country is very religious, and her response was basically, ‘We have no promiscuity.’” Despite DRW’s offer, social and cultural values proved stronger drivers of stakeholder behavior than disease prevalence.



*DRW's FirstBurst urine collector, winner of the Medical Futures "Best Diagnostic Innovation" award*

In other settings, DRW faced a different set of obstacles from stakeholders in the chlamydia ecosystem. Even though point-of-care testing offered numerous benefits and could complement centralized testing, DRW met with resistance from large, established companies that manufactured the equipment used to process traditional chlamydia tests, as well as from the centralized labs that bought this machinery and performed the testing services. Interestingly, Lee had been forewarned of this possibility by one of her advisors: "He said, 'You know, Helen, just because the need is obvious doesn't mean that the CRT will be adopted. Everybody will fight to protect their territory.' And he was exactly right. This is the commercial reality we've faced."

### THE SOLUTION: TAKING ON DAVID INSTEAD OF GOLIATH

Reflecting on these experiences, Lee acknowledged that developing a technology and bringing a new innovation to market is difficult in the best of times, even for large companies. "The bottom line is that if you want to launch anything, you will face resistance," she said. Overcoming these obstacles requires persistence, solid technology, and most of all, funding. "The ability to get enough funding to sustain your efforts is one of the most critical factors," she said.

To confirm the effectiveness and advantages of the CRT, DRW published studies in major medical journals. Many of these studies were subsequently picked up by the general media.<sup>15</sup> "Still," Lee noted, "translating this publicity into sales has been very difficult." Accordingly, DRW refocused its efforts and sought to gain a foothold in markets such as France and Italy, where there was a prevalence of small, private clinical labs. These smaller, decentralized facilities had fewer resources and did not perform as many tests, making the adoption of the CRT much easier.

Drawing on the resources and connections of a board member with extensive commercial experience, DRW also signed a distribution agreement with Oxoid, a fully-owned subsidiary of Thermo-Fisher. The agreement resulted in strong sales in France. Oxoid also distributed the test in Italy, Portugal, Spain, and North Africa. Separately, DRW received orders from India, Seychelles, Vanuatu, St. Helena, and the Falklands, as well as inquiries from Cuba, Colombia, Mexico, and Kenya.<sup>15</sup> Although these countries did not represent the largest available markets or patient populations in need of the CRT, Lee hoped that they would serve as a beachhead from which DRW could expand its reach over time. Sales from these areas also provided a source of funding to help sustain the organization's efforts. They also contributed to a growing base of evidence regarding the benefits of the test. Commenting on this outcome, Lee remarked, "I'm glad that the test we killed ourselves to develop is being used, because if it wasn't, that would be the ultimate disappointment."

Looking back, Lee acknowledged that despite the overwhelming need to diagnose and treat chlamydia, it may have been the wrong test to start with given the lack of commercial demand and the presence of significant resistance in the field. Lee pointed out that for nongovernmental organizations and other potential customers, the product needed to align with their priorities. Otherwise, it would not have the same staying power (and consistent sources of funding) as technologies to diagnose and treat other, more prominent conditions such as HIV.

Accordingly, the Cambridge Diagnostics Development Unit was applying its rapid, point-of-care diagnostic technology to other targets, including HIV and Hepatitis B infection. “We should have developed the HIV tests first,” said Lee. “But it doesn’t matter, because it was a very interesting experience and we had to start somewhere. Maybe it’s not a commercial success, but it’s a technical success in that we developed the platform. We are, I believe, at the cusp of a much greater success for our HIV point-of-care tests for the developing world. The need is there, but so is the demand. So I think next year or two will finally tell whether we’ll be able to reach our goal.” ♦

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## NOTES

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- 3 “Tracking the Hidden Epidemics 2000,” Centers for Disease Control and Prevention, 2000, <http://wonder.cdc.gov/wonder/help/STD/Trends-Chlamydia.html> (June 27, 2012).
- 4 J. Paavonen, W. Eggert-Kruse, “Chlamydia Trachomatis: Impact on Human Reproduction,” *Human Reproduction Update*, 1999, Vol. 5, No.5 pp. 433-447, <http://humupd.oxfordjournals.org/content/5/5/433.full.pdf> (June 28, 2012).
- 5 “Tracking the Hidden Epidemics 2000,” op. cit.
- 6 “Pelvic Inflammatory Disease (PID) – CDC Fact Sheet,” Centers for Disease Control and Prevention, September 28, 2011, <http://www.cdc.gov/std/pid/stdfact-pid.htm> (July 5, 2012).
- 7 “Initiative for Vaccine Research (IVR) Sexually Transmitted Diseases,” op. cit.
- 8 J. Paavonen, et al., op. cit.
- 9 “Screening Tests To Detect Chlamydia Trachomatis and Neisseria Gonorrhoeae Infections---2002,” Centers for Disease Control and Prevention, October 18, 2002, <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5115a1.htm> (June 30, 2012).
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- 12 C.A. Wisniewski, J.A. White, C.-E.C. Michel, L. Mahilum-Tapay, et al., “Collection of First Void Urine Samples Using the FirstBurst Collection Device Improved the Performance of a C. Trachomatis Rapid Test,” *Journal of Clinical Microbiology*, 2008;46:1466-69, [http://stidiagnostics.org/literature\\_reviews/display\\_article.php?ANUM=512&NTUF=1bd62acf3c6fdbeb8ef21d50d59a143a](http://stidiagnostics.org/literature_reviews/display_article.php?ANUM=512&NTUF=1bd62acf3c6fdbeb8ef21d50d59a143a) (June 28, 2012).
- 13 S. Cliffe, S. Tabrizi, E. Sullivan, “Chlamydia in the Pacific Region, the Silent Epidemic,” *Sexually Transmitted Diseases*, September 2008, Vol. 35, no.9, pp. 801-806, [http://journals.lww.com/stdjournal/Fulltext/2008/09000/Chlamydia\\_in\\_the\\_Pacific\\_Region,\\_the\\_Silent.6.aspx#](http://journals.lww.com/stdjournal/Fulltext/2008/09000/Chlamydia_in_the_Pacific_Region,_the_Silent.6.aspx#) (June 28, 2012).
- 14 The studies described the benefits of CRT, from immediate treatment and contact tracing, to its viability as an affordable, simple, and reliable alternative to NAAT in resource-poor settings.
- 15 “Get Real: Developing Diagnostic Tests for Infectious Diseases,” Wellcome Trust, <http://www.wellcome.ac.uk/Funding/Technology-transfer/Technology-transfer-showcase/WTX052911.htm> (July 3, 2012).