Illuminating meningococcal diagnosis with LAMP

Traditional PCR-based assays have enabled reasonably rapid detection of pathogens in clinical specimens with better sensitivity than culture-based microbiology. Unfortunately, actual use of PCR is limited by the requirements for laboratory personnel expertise, sophisticated laboratory equipment, and the high cost of commercial PCR reagents, which make the use of this technique rare outside urban medical centres in high-income countries. Therefore, many PCR-based tests are only available at reference laboratories. The time needed for shipping, processing, and communicating results adds substantial delay to the time when the clinician can act on the findings. Clinicians therefore have to rely on empirical treatment and often pursue a multitude of diagnostics that—had a definitive test result been returned promptly—would have been unnecessary.

In The Lancet Infectious Diseases, Thomas Bourke and colleagues present a well-conducted, prospective clinical cohort study validating the use of loop-mediated isothermal amplification (LAMP) for the detection of meningococcal disease in children. LAMP is a nucleic acid amplification method that is isothermic—ie, the sample and assay reagents are able to rapidly duplicate the DNA of the target at a fairly constant temperature. This approach allows for less laboratory infrastructure requirements—specifically, an expensive thermal cycler for PCR is not needed. LAMP results can be detected by visual turbidity or fluorescence, which makes this method a practical near-patient assay.

The authors showed that meningococcal LAMP had a sensitivity of 89% and negative predictive value of 98% when tested on respiratory and blood specimens, with 100% specificity and 100% positive predictive value, when tested in real-world near-patient settings. Additionally, the test was useful on cerebrospinal fluid samples from patients in whom antibiotic therapy had already been started, which is a common situation in which culture and Gram stain are of limited use. The performance of LAMP PCR was roughly equivalent to that of traditional PCR and was much better than culture.

Perhaps one of the most interesting findings was that the median time to results was around 90 min. Delay in effective treatment of meningitis or sepsis of any cause is highly detrimental and often leads to poor outcomes. A rapid test such as LAMP for meningococcal disease could greatly improve diagnostic capability, especially in cases in which empirical antibiotic treatment has been started.

The use of LAMP has been investigated in several situations, many of which are aimed at assessing the use of the method in resource-limited settings. The technical requirements for LAMP are much less onerous than are those of traditional PCR and, as shown in Bourke and colleagues’ report, LAMP for meningococcal disease is rapid and accurate. The relative simplicity of LAMP makes the test an attractive option. In middle-income and high-income countries, laboratory labour is a substantial component of an assay cost. Therefore, LAMP could be an ideal test for the detection of meningococcal disease in many settings.

However, three challenges exist for commercialisation. First, the implementation of new conjugate meningococcal vaccines in Europe (serotype B) and in Africa (serotype A) could greatly diminish the need for meningococcal diagnostics as the disease prevalence decreases. Second, the meningococcal LAMP is a single-plex test, yet we live in a multiplex world in which the differential diagnosis of sepsis or meningitis is broad. Third, although the path to commercialisation is underway, it might be challenging. Inexpensive, straightforward assays are excellent from public health and global health perspectives, but disruptive new technologies are not always adopted.

Irrespective of how successful the commercialisation process is, the authors have developed a novel diagnostic test for Neisseria meningitidis that is easy to use and provides results within 90 min. In such a timeframe, results can lead to actionable decision-making, most likely to halt further diagnostic testing. The niche for LAMP in meningococcal disease remains to be established, but the fact that the technique allows diagnostic confirmation at the treating hospital rather than a reference laboratory is a good start.

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