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Commentary

Pertussis: Point-of-Care Testing in the Making

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Pertussis or whooping cough is still thought to be a "classical" childhood disease with symptoms so typical that it is easily diagnosed clinically. However, in mostly vaccinated populations, pertussis today occurs in a wide array of clinical presentations from non-typical coughing and apneas in infants to long-lasting non-productive coughs in adults. Although newborns and infants bear the brunt of severe morbidity and mortality, pertussis afflicts every age group as neither infection nor vaccination protect lifelong. Thus the symptoms of an infection with *Bordetella pertussis* can be mimicking those of many other, most viral, pathogens [1]. However, being a vaccine-preventable disease, it is important to diagnose pertussis correctly, which can be done by laboratory tests, with culture of *B. pertussis* being the classical, but least sensitive method [2]. Although serology is important especially for diagnosing the disease in adolescents and adults, the detection of *Bordetella*-DNA by amplification methods such as PCR is now the mainstay in the laboratory diagnosis of whooping cough [2,3].

Amplification methods tended to be time-consuming, laborious, and expensive, and only for a couple of years devices have been developed that allow the detection of *Bordetella*-DNA and other respiratory pathogens also outside of a dedicated laboratory setting [4]. However, these methods still require a rather complicated apparatus for controlling the temperature cycle of PCR, and the reagents are quite expensive. As an isothermal alternative to PCR, LAMP (Loop-mediated isothermal amplification) has been developed in 2000 [5], and it produces various loops of the target sequence, so that the end product can be imagined as something looking like a cauliflower of DNA-loops. This method has been adapted to the detection of *Bordetella*-DNA [6], and it has been used mainly in Japan. In this issue of *EClinicalMedicine*, Dou and colleagues [7] describe a LAMP-method developed as point-of-care (POC) device for detecting *B. pertussis* DNA.

The test system is based on what the authors call a "biochip". It contains a paper–polymer microfluidic chamber, where the reaction is performed; the temperatures needed for the reaction as well as for its termination can be produced by a mobile heater. The signal measured is a spot of fluorescence produced by the fluorophore calcein, which is primarily quenched by manganese ions in the reaction buffer. The visualization is then done using ultraviolet light, something that can be produced even by a mobile phone. An additional problem of conventional amplification methods is that the nucleic acid from the clinical material (i.e., swab or aspirate) must be purified before amplification, which is often done by small columns with ion-exchange resins. As this cannot be done in a clinical setting, the authors simply used a urea solution to extract the DNA to overcome the issue.

The device described here is a "proof-of-principle" for a POC test for pertussis. Before entering the field especially in low-and-middle income countries (LMIC), it must undergo additional refinement and further validation in respect to its sensitivity, and especially its specificity and its robustness. Although — after undergoing sufficient validation — the test may be used in less cost-sensitive industrialized countries to facilitate a prompt diagnosis, the most important thing for LMICs will be the final prize of the device, as this would define its usability worldwide.

Being a vaccine-preventable disease, pertussis is notifiable in most countries of the world. The diagnosis of pertussis by (mostly) PCR is a routine procedure in many industrialized countries, whereas most of the cases and most of pertussis mortality, estimated to be around 160,000 infants per year, occur in LMICs in Africa and Asia [8]. WHO and other organizations rightly lament that surveillance of pertussis is insufficient or non-existing especially in those countries, where it is most urgently needed [9]. The lack of surveillance mainly depends on the lack of adequate laboratory facilities in these countries. Thus, after being thoroughly validated for use in LMIC settings, the POC method for detecting *Bordetella* DNA could offer a first and welcome step for producing data about pertussis incidence in places where the burden of disease is greatest. However, even if POC testing should be possible in the field, some reference laboratory setting is necessary in every country or region to assure that the ongoing circulation of *B. pertussis* can also be continuously monitored by non-POC conventional methods.

Authors Contribution

Carl Heinz Wirsing von Koenig wrote the Comment.

Conflict of Interests

Carl Heinz Wirsing von Koenig has nothing to disclose.

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