

# PhD defence Sien Ombelet

## Implementing clinical bacteriology in low-resource settings. A new perspective on old methods.

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Dit is de omschrijving

### Supervisors

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### Abstract

Resistance of bacteria to antibiotics is a global public health challenge. Low-income or lower-middle-income countries, so-called "low-resource settings", are disproportionately burdened by antibiotic resistance. However, reliable figures on the occurrence of antibiotic resistance in these settings are scarce, mainly because of limited availability of clinical bacteriology laboratories. As a result, bacterial infections often cannot be diagnosed, and the correct treatment cannot be instituted in time. The gap between high- and low-resource settings is widening; while richer countries use increasingly sophisticated technology, laboratories in low-resource settings often rely on traditional techniques, developed in the early half of the last century. However, the latest techniques are often too expensive for use in low-resource settings or not adapted to the environmental conditions in, for example, tropical countries.

The aim of this PhD was to identify the optimal methods and techniques for laboratory diagnosis of bacterial infections, with a focus on blood cultures. Blood cultures are important in the diagnosis of bloodstream infections, which require rapid initiation of the correct therapy (usually antibiotics). In high-resource settings, blood culture automates are used. These devices perform continuous detection of bacterial growth, enabling a fast result, but are rarely used in low-resource settings due to their cost. Therefore, we have concentrated on so-called "manual" blood culture techniques, which use visual detection of growth in the blood culture bottle.

In the first chapter of this PhD, we compared such manual blood culture bottles with automated systems, in terms of yield (percentage of grown bottles) and speed of growth. In this study, manual had the same yield as the automated system, with a comparable percentage of grown bottles, but the detection of the growth was slower. In the second chapter, a bacterial identification system for use in low-resource settings was evaluated. Overall, we found good performance of the system for identification of the most common pathogens in low-resource settings. However, the user-friendliness, robustness and storage conditions were inadequate for labs in low-resource settings. The concepts of traditional bacteriology were subsequently applied in two different settings: a hospital laboratory in the capital city of Cambodia and a hospital laboratory in a small village in Benin. In Cambodia, we found that earlier blind subculture (subculture of the blood culture bottle in the absence of visual signs of growth) led to faster growth detection and faster appearance of colonies on solid media. However, if the subculture was performed too early, growth of important pathogens could be missed.

In Benin, we implemented blood cultures in a small hospital in a semi-rural village. We collected 3353 blood culture bottles in patients presenting with fever and signs of severe infection. Most patients in this study were children < 15 years of age. We observed that bloodstream infections were frequent, and that most infections were caused by *Klebsiella pneumoniae*, *Salmonella* Typhi and *Staphylococcus aureus*. Among these bacteria, antibiotic resistance was common; we found considerable resistance against commonly used broad-spectrum antibiotics (third-generation cephalosporins) (12.8-77.6%, depending on the type of pathogen).

In summary, this PhD shows that traditional, manual techniques can still play a role in low-resource settings, and that, with good supervision, satisfactory results can be achieved even in difficult conditions. However, it is also clear that there is still room for improvement for these techniques, and diagnostic companies should focus more on this. Moreover, we were able to demonstrate that antibiotic resistance is higher than expected even in rural areas in West Africa. Further strengthening and support of bacteriology laboratories in low-resource settings is therefore a necessary and urgent strategy to put a stop to rising antibiotic resistance.

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