

## Mobile laboratory to improve response to meningitis epidemics, Burkina Faso epidemic season 2004

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**Abstract.** A Mobile Laboratory was developed for use primarily during the epidemic meningitis season in Burkina Faso. This report describes the Mobile Laboratory characteristics, its use to date, problems encountered and their resolution, and future directions. During 2004, the mobile laboratory intervention in three remote Burkina Faso districts experiencing meningitis epidemics led to more specific case management and led directly to vaccination of one district. However, in a second district, the intervention occurred too late to allow vaccination. During 2006, the Mobile Laboratory was used to conduct an emergency carriage study that for the first time occurred during the peak of a meningococcal serogroup A epidemic. This information is critical for the design of meningococcal conjugate vaccine schedules and vaccine approaches. During 2004–6, technicians in 11 district laboratories received training by Mobile Laboratory staff. Numerous problems with the initial prototype laboratory were identified, namely that the solar power cells could not provide enough energy to the refrigerator and incubator to maintain appropriate temperatures and having a single integrated unit required use of a separate vehicle for specimen transport. A second laboratory was developed during 2005–6 that used a generator or local energy source for power and that had a laboratory that could be detached from the vehicle. Currently the main limitation of the Mobile Laboratory is that it has not been integrated into routine Ministry of Health activities, limiting its use both during and between meningitis seasons.

**Keywords.** diagnosis, epidemics, laboratory, meningitis, mobile laboratory, treatment, vaccine response

### 1 Introduction

Until recently, acute bacterial meningitis epidemics in Sub-Saharan Africa were assumed to be due to *Neisseria meningitidis* (Nm) of serogroup A and epidemic response consisted of vaccination with bivalent A/C vaccine. The recent occurrence of epidemics due to Nm W135 and the availability of a limited supply of trivalent A/C/W135 polysaccharide (PS) vaccine have created a need for timely Nm serogroup information to tailor vaccine response to the needs of specific districts or regions (1–3). In Burkina Faso, the identification of agents of acute bacterial meningitis usually relies on reference hospital laboratories. These laboratories, however, cover only 30–40% of reported cases and meningitis epi-

demiology might differ considerably in more rural or remote areas. In addition to low surveillance coverage, countries like Burkina Faso often encounter shortages of reagents and consumable laboratory supplies. Lastly, developing countries have training needs for laboratory technicians as most technicians working in peripheral laboratories receive little formal training. To address these issues, AMP and the Burkina Faso Ministry of Health implemented a mobile laboratory designed to strengthen Ministry of Health capabilities to confirm bacterial meningitis etiology during epidemics, particularly in remote areas.





**Figure 1.** Mobile Laboratory Prototype 1. Note that the unit is one piece and contains solar panels.



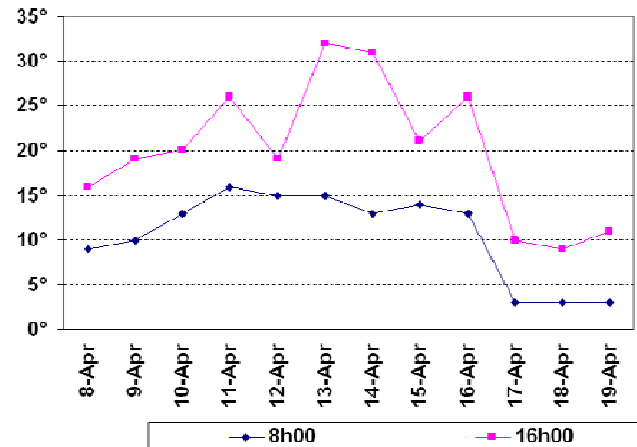
**Figure 2.** Interior of Mobile Laboratory 1.

## 2 Mobile Laboratory design

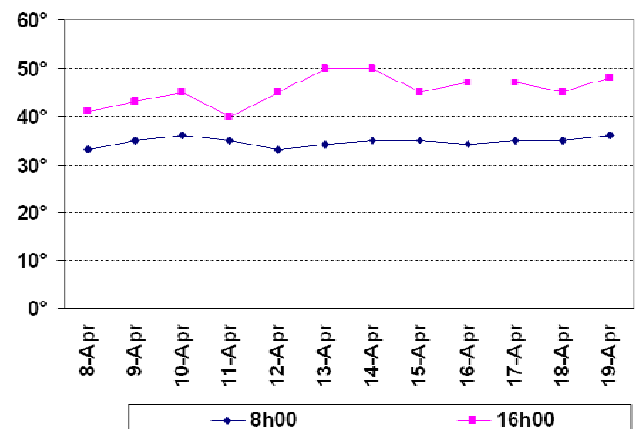
### 2.1 Mobile Laboratory 1

During 2003, AMP conceived, designed, and tested in the field a vehicle with microbiological laboratory facilities (Fig. 1). The laboratory unit was developed as a modified, commercial four-wheel drive van (Renault “Kangoo” 4x4 diesel). Outfitting was performed by the University of Münster, Germany. The Mobile Laboratory was outfitted for performance of routine microbiology to allow provision of immediate feedback to local medical staff and District and National Ministry of Health decision-makers. It also had the capacity to transport specimens back to a reference laboratory in Bobo-Dioulasso or Ouagadougou for further analysis.

To allow these functions, the Mobile Laboratory was air-conditioned and outfitted with a refrigerator, hot plate, incubator, sink, microscope, and centrifuge (Fig. 2). Electricity was provided by solar panels on the vehicle’s roof (Fig. 2). The refrigerator was installed for storage of reagents. The sink was installed to allow performance of Gram staining.



**Figure 3.** Refrigerator temperature of the Mobile Laboratory 1 during field conditions in Burkina Faso, 2004.



**Figure 4.** Incubator temperature of the Mobile Laboratory 1 during field conditions in Burkina Faso, 2004.

The microscope allowed evaluation of Gram stain slides and determination of cerebrospinal fluid white blood cell count. The incubator was set at 37°C and with an appropriate CO<sub>2</sub> concentration for bacterial culture.

During actual implementation, several issues arose. The solar panels on the unit did not provide sufficient electricity to maintain the temperature of the refrigerator (Fig. 3) and the incubator (Fig. 4) during the evening and night. The air conditioner of the selected vehicle did not perform well under field conditions. Having the laboratory integrated into the vehicle meant that a separate vehicle was required to transport specimens and culture back to the reference laboratory. Lastly, the space available for laboratory technicians was not sufficient for optimal work.



**Figure 5.** Mobile Laboratory 2. Note the lack of fixed solar panels and the detachable laboratory unit.

## 2.2 Mobile Laboratory 2

The Mobile Laboratory 2 was based on a Toyota Hilux 4x4, air-conditioned diesel vehicle (Figs. 5 and 6). We employed a detachable body that could remain on site, leaving the vehicle free to continue activities requiring mobility. The detachable body also fully isolates the driver's cabin from the laboratory facilities, possibly decreasing the risk of contamination of specimens and increasing the safety of the driver and passengers. We employed fixed electricity rather than solar panels, using a 2500 watt Honda diesel generator. Wiring allows for both 230V and 12V electricity. The incubator is a Binder GmbH CO<sub>2</sub> incubator (Tuttlingen, Germany), which has a capacity of approximately 56–90 mm plates. Water is supplied via a 20l canister with a similar 20l canister for wastewater.

## 3 Methods

### 3.1 Mobile Laboratory 1 and outbreak response

The Mobile Laboratory was sent to three remote districts during 2004 that were experiencing epidemics. Once on site, Mobile Laboratory staff received cerebrospinal fluid (CSF) specimens collected by local health facility personnel from suspected bacterial meningitis cases based on the WHO case definition (4). The Mobile Laboratory staff then performed Gram staining, cytology, culture on chocolate agar and latex agglutination tests (Pastorex<sup>®</sup>). In addition to the Mobile Laboratory staff, two MOH technicians under the supervision of an MOH biologist accompanied the laboratory to the field. A microbiologist from the Marseille-Pharo (France) WHO collaborating reference laboratory provided training for the technicians.

Antibiotic resistance was determined in a reference laboratory using the disk-diffusion technique and measurement of



**Figure 6.** Interior of Mobile Laboratory 2.

minimal inhibitory concentrations by E-test (Solna, Sweden) (5). One aliquot of CSF for each case was shipped to Centre Muraz (Bobo-Dioulasso) for polymerase chain reaction (PCR) testing as previously described (3). Available results were provided immediately to the patient's physician. A case was confirmed if latex agglutination, culture, or PCR yielded a positive result. External quality control was performed at the National Reference Laboratory in Ouagadougou.

### 3.2 Mobile Laboratory 2 and technical assistance

Based on the use of the first prototype, a second Mobile Laboratory was built and placed in the field during 2005 and 2006. The Mobile Laboratory was not used for epidemic evaluation during this period. However, we describe here its use during a carriage study conducted in a rural area experiencing an epidemic and its use for the training of technicians in five district laboratories.

### 3.3 Ethical issues

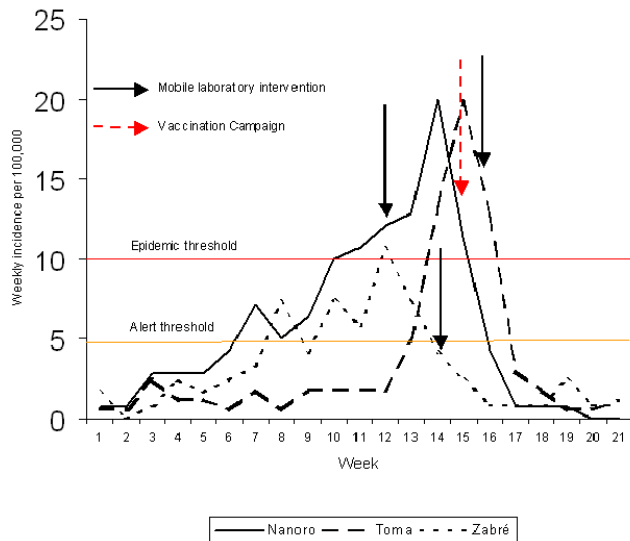
The Mobile Laboratory was used as part of the routine MOH emergency epidemic response. All tests performed were clinically indicated or were part of the MOH epidemic surveillance system. Under these circumstances of routine clinical management and public health surveillance, informed consent and institutional review board approval were neither sought nor obtained.

## 4 Results

### 4.1 Mobile Laboratory 1 and outbreak response

#### 4.1.1 Mobile Laboratory activities

The Mobile Laboratory 1 was provided to the Burkina Faso Ministry of Health to intervene in districts in alert or



**Figure 7.** Weekly number of suspected cases of acute bacterial meningitis in Nanoro, Zabré and Toma, 2004.

epidemic for suspected acute bacterial meningitis. During 2004, three remote districts with poor access to laboratory facilities reported acute bacterial meningitis epidemics and were considered appropriate sites for the Mobile Laboratory. Nanoro passed the alert threshold during week 7 of the epidemic season and the epidemic threshold during week 12, and the Mobile Laboratory 1 intervened during week 14 (Fig. 7). In Zabré, these events occurred during weeks 10, 12, and 14 and in Toma weeks 13, 14, and 16. The weekly reported incidences of suspected cases of acute bacterial meningitis in Nanoro, Zabré, and Toma the week before the intervention were 11, 7.4 and 20 per 100 000 inhabitants. No collection and evaluation of CSF specimens was performed and reported before the Mobile Laboratory interventions. In general, clinical staff reported cases based on standard clinical criteria for suspected acute bacterial meningitis, but we did not have a mechanism for determining if this always occurred.

Cerebrospinal fluid specimens from 58 suspected cases were evaluated including from Nanoro ( $n=19$ ), Zabré ( $n=26$ ), and Toma ( $n=13$ ) (median age, 2.5 years; 58% <5 years). Of these cases, 23 (40%) had a confirmed bacterial etiology (median age, 9.0 years; 43% <5 years). Etiology differed by location with eight NmW135 and five *Streptococcus pneumoniae* (Sp) in Nanoro, three NmA and one Sp in Zabré, and five NmW135 and one Y/W135 (identified by latex agglutination) in Toma. Meningococcal meningitis with coma and all pneumococcal meningitis were treated with multi-day courses of intravenous ampicillin; the remaining Nm cases were treated with a single intramuscular dose of oily chloramphenicol. Of 10 Nm and three Sp tested, all were sensitive to chloramphenicol, oxacillin and ceftriaxone.

#### 4.1.2 Vaccine interventions related to the Mobile Laboratory 1 intervention

Before the Mobile Laboratory intervention, no specimens had been collected and analyzed from Nanoro and vaccination was delayed. Following the Mobile Laboratory confirmation of a meningococcal epidemic, and documentation of NmW135 as the primary agent, Nanoro residents aged 2–29 years received mass vaccination with trivalent Nm A/C/W135 polysaccharide vaccine during week 15 (post-epidemic, the Burkina Faso Ministry of Health at two international meetings affirmed that the vaccine response was prompted by results from the Mobile Laboratory intervention). A total of 112 421 doses were administered during 3 to 8 April for an administrative vaccine coverage of 113% in the target population (Source: Burkina Faso Ministry of Health). No vaccine responses were organised in Zabré or Toma. In both districts, results were obtained after case counts had begun decreasing and in Zabré an A/C vaccination campaign had been conducted the previous year.

#### 4.1.3 Cost of the Mobile Laboratory 1 intervention

We performed an assessment of the cost of the Mobile Laboratory for the intervention period. The Mobile Laboratory unit itself cost \$44 200, including the cost of the vehicle (\$23 300) and fixed equipment (\$20 900). The total intervention period was 2 months with 25 actual days in the field. Operational costs for this period were estimated at \$44,200 including \$13 800 for staff and fuel, \$6800 for use of a separate car by accompanying Ministry of Health staff, \$8900 for consumable reagents and other laboratory supplies, \$6400 for reference laboratory costs (supplies and wages), and \$8300 for miscellaneous costs. The total cost associated with intervening in the three districts was \$88 400, of which half were fixed costs that would not be repeated until the unit or equipment required repair or replacement.

#### 4.2 Mobile Laboratory use during an emergency carriage study

Meningococcal conjugate vaccines will be available during the next few years for preventive vaccination of the population of the meningitis belt. However, optimal immunization schedules and approaches (such as infant immunization, mass vaccination, catch-up campaigns, and booster doses) have not been defined. One of the primary missing pieces of data has been the degree of meningococcal carriage during an epidemic. These data are difficult to collect because of the unpredictable location and timing and frequent short duration of meningococcal epidemics in combination with the logistical difficulties of implementing a carriage study rapidly in impoverished and poorly accessible areas and before the implementation of an emergency vaccine campaign (which may alter results).



In February 2006, AMP and Centre Muraz (with funding from Sanofi-Pasteur) were notified of a meningococcal serogroup A epidemic in the Hauts-Bassins region of Burkina Faso. The study team was able to organize and implement, within two weeks of notification, an evaluation of Nm and Sp carriage and seroprevalence in three villages located 60 km from Bobo-Dioulasso. The two Mobile Laboratories performed initial processing of blood samples for serological analysis, including centrifugation and serum aliquoting. The Mobile Laboratories also performed initial microbiological processing of nasal swabs, including plate streaking and incubation and preparation of swab suspensions. The Mobile Laboratories allowed processing of up to 110 specimens per day and eventual collection of the entire planned sample size of 624. Quality control of all equipment, including monitoring of the refrigerator and incubator temperatures, was performed during the study and no deficiencies were found. In addition, cerebrospinal fluid samples from meningitis cases during the carriage study period could be prepared for culture analyses in the Mobile Laboratories.

#### 4.3 Mobile Laboratory use for technician training

A secondary goal of the Mobile Laboratory is to provide ongoing and onsite training to laboratory technicians in district hospitals. During the 2004 evaluation of epidemics, technicians in the three intervention districts received training on bacteriological techniques. During May 2005, technicians in five district laboratories (Boussé, Gourcy, Manga, Pô, and Zabré) received training while during April 2006, technicians from three district laboratories (Boussé, Sapouy, and Léo) received training.

Training goals included review of storage and transport conditions of cerebrospinal fluid specimens from health posts to district laboratories, evaluation of the use of trans-isolate media, performance of quality control of Gram staining, and identification of critical issues such as reagent shortage. The Mobile Laboratory team identified three broken microscopes, lack of incubators in all laboratories, lack of latex agglutination kits (necessary for serogroup determination and thus determination of the appropriate vaccine intervention), and poor cytology technique. During 2004, five technicians received training in the Mobile Laboratory facilities followed by another five during 2005 and nine during 2006.

## 5 Discussion

### 5.1 Epidemic intervention to guide vaccination

We found that the epidemiology of acute bacterial meningitis epidemics differed substantially at the district level with one of the districts experiencing an outbreak of primarily Nm A, another primarily Nm W135 and the third a mix of NmW135 and Sp. As a direct result of these findings, the Ministry of Health implemented trivalent A/C/W135 vaccine

in Nanoro. In the absence of results from the Mobile Laboratory, a greater delay would have existed between notification of the epidemic, confirmation of etiology, and vaccine response. In addition, some districts do not have adequate supplies or personnel to determine etiologic agents of disease during epidemics, potentially leading to use of an inappropriate vaccine or no vaccine response at all.

The primary goal of the Mobile Laboratory is to provide information to allow appropriate epidemic response, including the need for and type of vaccine. During the first year of implementation, this goal met with partial success. Nanoro received trivalent A/C/W135 vaccine when they otherwise would have received bivalent A/C vaccine; nevertheless, the intervention occurred after the epidemic was subsiding. In Zabré and Toma results were obtained after the epidemic had begun to subside and thus no vaccination response was implemented. These circumstances resulted partly from delays associated with implementing a new technology, such as staffing, training, and equipping the vehicle, and partly from having only one vehicle available. In addition, the Mobile Laboratory did not have the level of political support and integration into routine Ministry of Health activities that would allow for optimal use. In the future, the Mobile Laboratory should be prepared well in advance of the epidemic season and sent to the field when the alert rather than the epidemic threshold is passed, activities that are more likely with political support from the Ministry of Health.

### 5.2 Additional Mobile Laboratory benefits

In addition to directing epidemic vaccine response, the Mobile Laboratory provides additional benefits. First, standard clinically-based case management strategies during the epidemic season call for treatment with one or two doses of oily chloramphenicol (6). Because this treatment is potentially inadequate for pneumococcal and *Haemophilus influenzae* type b meningitis, immediate provision of results to clinicians coupled with the availability of systemic ampicillin or ceftriaxone may improve clinical outcome (7). Second, the Mobile Laboratory provides data on disease epidemiology in relatively remote districts. Our data, collected over a relatively short period in each District, suggest that the importance of various etiologic agents of disease changes over relatively short geographic areas and that Sp plays a substantial role in some areas. Third, Mobile Laboratory staff trained 19 local technicians, who then provided ongoing data during the course of the epidemic. This is of particular importance in countries where rural and other MOH laboratory staff often receive little formal training. In theory, training does not need to rely on the existence of a Mobile Laboratory. However, the Mobile Laboratory creates efficiencies by conducting training at the same time as it assists with outbreak evaluation, allows technicians to receive training during an actual epidemic, and ensures that necessary equipment for training is available. Fourth, the Mobile Laboratory can be

used to assess reagent stocks during an epidemic and to assist with replenishing them. Finally, the Mobile Laboratory was a critical tool in the successful implementation of a carriage study during the peak of a meningococcal serogroup A epidemic. This information will allow the development of models of how to use conjugate meningococcal vaccines and could not have been collected without the Mobile Laboratory. In general, Mobile Laboratory technology may be useful for research by allowing studies during epidemics and in rural areas that otherwise do not have adequate laboratory facilities to process biological specimens.

### 5.3 Mobile Laboratory cost

The Mobile Laboratory allows the MOH to direct resources specifically to areas in epidemic without requiring that the entire country have adequate local diagnostic capability. Thus, the \$88 400 cost of the Mobile Laboratory must be balanced against the costs of strengthening and maintaining all district level laboratories in the country. For example, just the costs of purchasing 100 latex agglutination test kits per year for each of the approximately 55 districts in Burkina Faso will cost \$82 500 based on a test price of \$15. Because of the short shelf life of latex agglutination kits, this cost would be repeated each year. Also, this cost does not include staff, training, quality control, antibiotic resistance testing, and other costs included in the Mobile Laboratory cost estimate. Other cost issues need to be taken into account. Each Mobile Laboratory can only intervene in one district per week, a clear limitation when multiple districts simultaneously pass the alert or epidemic threshold. Ideally, any particular country would maintain a fleet of Mobile Laboratories sufficient for most epidemic seasons. Also, once a Mobile Laboratory is purchased, and assuming it is well adapted to field conditions in Africa, costs will be limited to the operational costs of the intervention (approximately \$44 200 for three interventions) and system maintenance.

### 5.4 Fixed vs. Mobile Laboratories

In theory, the Mobile Laboratory should not be needed because district laboratories could perform all needed functions. In practice, though, this is unlikely to occur in the near future. Laboratories in some areas are not considered part of the Ministry of Health structure and thus may have no fixed budget. There are an inadequate number of trained microbiologists and technicians to staff all district laboratories and lack of money for bringing staff to a central location for ongoing training. Finally, there is no manufacturing capacity in Africa for low-cost reagents adapted to conditions in the meningitis belt. Consequently, tests such as latex agglutination are expensive (in excess of US \$10 per test) and frequently in short supply, past their expiration date, or poorly implemented. Because of these limitations, the epidemic response system used in much of the meningitis belt relies on

shipment of cerebrospinal fluid specimens from district to central laboratories. This process, however, is limited by the lack of transport media and vehicles for transportation. In Burkina Faso, for example, during 2003 only an estimated 40% of districts in alert or epidemic sent the minimum required 15 CSF specimens. When specimens did arrive, 32% were contaminated (Burkina Faso MOH, unpublished data, 2003).

## 6 Conclusions and future directions

This report demonstrates that in meningitis belt countries lacking adequate resources for nationwide laboratory improvement, the Mobile Laboratory can be successfully implemented to guide vaccine intervention and clinical management, expand knowledge of meningitis epidemiology and conduct studies in rural areas, and provide training to local technicians. Nevertheless, the impact of the Mobile Laboratory was not ideal. Future improvements should include costing, budgeting and programming the integration of the Mobile Laboratory into the national surveillance system to facilitate intervention when the alert rather than the epidemic threshold is passed. This integration may require a critical number of vehicles rather than just the two vehicles currently existing. This also would allow intervention in multiple districts simultaneously. The efficiency and benefit of the Mobile Laboratories could be improved as well by using them outside of the epidemic meningitis season for other activities such as use during the rainy season for evaluation of diarrheal disease outbreaks and epidemiology.

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