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'Bacterial meningitis in Nouna Health District: Burkina Faso: From the understanding of the dynamics of colonization and disease patterns to improved control'

Promotionsfach: Infektiologie  
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### Background

Bacterial meningitis remains one of the major public health problems in the so-called 'meningitis belt' of Sub-Saharan Africa threatening the life of millions of people, mainly children. The 'meningitis belt' is defined by the environmental conditions prevailing in the zone south of the Sahara desert. Large epidemics occur every 5–12 years causing death, disability, disruption of societal life and poverty. Notable features are that the outbreaks of meningococcal meningitis and the meningococcal serogroup distribution are highly regional and seasonal with the highest burden of the disease during the dry season. The dynamics of these epidemic cycles is incompletely understood but it appears that seasonal and geographic clustering of meningococcal serotypes in patients with meningitis is related to nasopharyngeal colonisation and carriage. While the large epidemics could be attributed to *Neisseria meningitidis* serogroup A, meanwhile other serogroups, in particular C, X and W135 have been isolated during outbreaks demonstrating the potential of these serogroups to cause epidemics. The situation is worsened by recently emerging that *Streptococcus pneumoniae* plays also an important role in seasonal waves of bacterial meningitis in the same 'belt'. Surveillance of bacterial meningitis cases and laboratory confirmation of the infectious agent are essential for an early alert and response system. However, even with rapid diagnosis and treatment, 5–10% of patients die, typically within twenty-four to forty-eight hours. The lack of functional infrastructure and skilled health workers particularly in the remote area of the region aggravates the problem.

As part of the VolkswagenFoundation funded research program "Knowledge for Tomorrow – Cooperative Research Projects in Sub-Saharan Africa", the Nouna Health Research Centre, the Section Clinical Tropical Medicine, Department of Infectious Diseases, Heidelberg University Hospital and the Swiss Tropical and Public Health Institute initiated in 2006 a colonisation and disease study in the Nouna Health District (NHD) with a long term follow-up over five years.

### Objective

The study aimed to enhance the understanding of the dynamics of meningococcal meningitis epidemics in the African Meningitis Belt for early outbreak detection and improved intervention.

This thesis as part of the long-term study on meningococcal colonization and disease, concentrates on the clinical features of bacterial meningitis and the distribution of the bacterial pathogens in the community of Nouna Health District (NHD) in Burkina Faso between 2006 and 2010. The nasopharyngeal meningococcal colonization and the epidemiological profile of the causative agents are described and the performances of the laboratory tests employed for the diagnosis of bacterial meningitis were investigated.

### Study area

The study was conducted in NHD located in northwest Burkina Faso. The Nouna area is a dry orchard savannah with a mean annual rainfall of 796 mm, populated almost exclusively by subsistence farmers with approximately 304,000 served by 44 primary care health facilities and one district hospital. The average distance to the closest primary care facility is 8.48 km. The Nouna Health Research Centre located in NHD runs a health and demographic surveillance system (HDSS) in the South of the district covering 85,000 individuals of the district population with regular update of vital demographic events.

### Patients and methods

The study comprises two independent arms: the colonization and the case study to capture nasopharyngeal colonization of the pathogen in the community and the occurrence of disease respectively. The main colonization study consisted of a sub-sample of the Nouna HDSS population selected by proportional cluster randomization sampling. This sub-population was followed-up prospectively with two surveys per year. Additionally, a site in the North of the district was surveyed alongside with the main study after an outbreak had occurred.

The case study is a prospective observational study of all suspected bacterial meningitis patients attending the health facilities of Nouna Health District over the study period.

### Results

During the five years study period completed so far, the systematically collected nasopharyngeal swabs revealed colonization with fluctuating rates of pathogenic and apathogenic meningococcal serogroups between surveys. Waves of high colonisation were associated with an outbreak of serogroup A (in the North of the district) while a serogroup Y (in the South of the district) led only to very few cases. In CSF samples collected at health posts and the district hospital from patients with the clinical suspicion of bacterial meningitis the three most frequently isolated pathogens were *Neisseria meningitidis* (Nm), *Streptococcus pneumoniae* (SP), and *Haemophilus influenzae* (Hib) with varying age distributions and health outcomes. The worst outcome was observed with *Streptococcus pneumoniae* which was associated with a ~8-fold higher risk of death compared to the other two (OR 7.98, 95%; CI: 3.35-19.00). The seasonality of bacterial meningitis was demonstrated in the laboratory confirmed cases with a peak in the dry season while most of the negative CSFs were reported in the rainy season.

Fever, CSF cell count > 100 leucocytes/  $\mu$ l, CSF glucose < 40 mg/ dl and CSF turbidity were found to be the most sensitive predictors for the diagnosis of bacterial meningitis. However, a substantial proportion of non-turbid CSF was not associated with negative bacteriological findings.

### Conclusion

Our study contributes to the knowledge of bacterial meningitis epidemiology in the meningitis belt with implications for the clinical management and vaccination strategies.

The nasopharynx colonization with *Neisseria meningitidis* A meningococci were associated with an epidemic while the concomittent Y colonization was not. Differences in virulence could be an explanation. Uncertainties remain, however, about the dynamics and relationship between colonization and disease.

Clinical diagnosis of bacterial meningitis remains a problem in Sub Saharan Africa (SSA) due to a wide range of differential diagnoses. Furthermore, the visual aspect of CSF turbidity, one of the corner stones of clinical judgement, is not reliable and likely to miss around 11% of bacterial meningitis cases.

On the basis of the WHO case definition largely utilized in SSA for disease surveillance we detected 92% of the confirmed cases supporting its good performance and usefulness. To further improve surveillance PCR-based diagnosis needs to be made more widely available, however.

We recommend the development of a new and affordable conjugate vaccine targeting *N. meningitidis* serogroups A, X, Y and W135 simultaneously plus *S. pneumoniae* including serotype 1 for effective control of bacterial meningitis to control bacterial meningitis disease in the SSA meningitis belt.