

### Fighting Meningitis in Africa: A Call for a Multi Sectorial Action

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## Introduction

This opinion letter focuses on fighting meningitis in the African meningitis belt. Another meningitis season has ended in the region stretching from Senegal to Ethiopia [1]. The 2016-2017 meningitis season had left behind 28,000 suspected cases and 2,500 deaths. Bacterial meningitis is mainly due to 3 types of bacteria that are independently targeted by specific vaccines [2]. Since the introduction of the low-cost monovalent conjugate MenAfriVac® vaccine starting in December 2010 to everyone aged 1-29 in 27 countries, over 277 million people were immunized against serogroup A meningococcal meningitis (NmA). Despite the major success in controlling the NmA in that specific region, meningitis at large still circulates and other variants of the disease cause local outbreaks [3]. *Streptococcus pneumoniae* (Sp) causes recurrent epidemics in the region [2] and *Neisseria meningitidis* (Nm) serogroups C, W and X currently cause the majority of cases [4,5].

## The Current Situation and its Challenges (What is the problem?)

The WHO Weekly Meningitis Bulletins and the WHO-AFRO Weekly Bulletin on outbreaks and other emergencies during the last 2016-2017 season [6] report NmC as the major pathogen responsible

for local epidemics (72% of positive samples). The second most prevalent pathogen identified during this season was Sp, which was detected in 11 countries, followed by NmX in 7 countries. Finally, NmW was detected in 11 countries, mainly in Togo, Ghana and Burkina Faso. Outside the belt, in the Democratic Republic of Congo (DRC) and Central African Republic (CAR) for example, Sp now represents a major pathogenic threat for meningitis epidemics [7]. Additionally, the recent devastating outbreaks caused by NmC [5] and W [4] remain an important public health concern. Efforts to rapidly respond when the epidemic onset do arrive are frustrated by vaccine shortages and logistics issues [8] and lives continue to be lost. *Haemophilus influenzae*, another pathogen that can cause meningitis, is nowadays under control thanks to routine vaccination through the Expanded Program of Immunization (EPI). To date, no global vaccination response strategy has been implemented for Sp meningitis epidemics, and the impact of Sp meningitis of PCV vaccines which was recently introduced in to EPI to control respiratory infections, remains unknown. While the European experience shows that serotype conversion occurs rapidly after vaccine implementation [9], the circulation of Sp serotypes for meningitis is poorly understood in the African belt [10].

The mass implementation of a vaccine singularly targeting *NmA* has modified its natural ecological niche, the nasopharyngeal tract, that is competitively shared with other *Nm* serogroups and *Sp*. Any intervention against one pathogen involves (and co-evolves with) the other, and the independent delivery of the PCV vaccines in the same population is expected to have jointly impacted the bacterial meningitis pathogens community. For this reason, we suggest that all bacterial meningitis cases be analyzed collectively so as to better understand the joint dynamic of the different pathogens. The recent preventive vaccine approach targeting a single serogroup through the MenAfriVac® campaigns has thus brought two challenges in controlling meningitis to the front: i) access to the appropriate vaccines; and ii) strengthening surveillance and response in communities to answer the fundamental questions underlying the epidemiological evolution of meningitis. At this decisive juncture, targeting one serogroup alone (*NmA*) with neither adequate vaccine availability for other serogroups (*NmC*, *NmW*) nor intervention for other pathogens (*Sp*), ignores fundamental scientific knowledge about the dynamics of infectious disease transmission.

## What are the Solutions? The Urgent Needs

With outbreaks of meningitis still occurring seven years after the roll-out of MenAfriVac®, public health and research communities must work together towards an innovative global approach to meningitis control that goes beyond the vertical targeting of one single subtype or pathogen at a time. The unpredictability of outbreaks “in time”, “in place” and “in pathogen” continues to challenge existing surveillance, diagnostic and response capabilities. Strengthening active community surveillance along with seamless, coordinated data sharing across district, national, and international levels are necessary for a rapid and effective response. Promises of case by case lab confirmation have not yet been met and should remain high priority. Across all reporting countries, only 29.8% of suspected cases were tested, revealing 65.5% negative [6]. Overall, only 10.2% of suspected cases were lab confirmed, reflecting a crucial need for improvement of laboratory capacity and diagnostics training.

Priority should therefore be given to support an effective surveillance and response network that will inform a multi-sectorial operational network. Strong collaboration and active engagement between sectors (Public Health, NGOs, Research, Industry) are critical to better understand the evolution of this infectious disease and to improve vaccination strategies. While informative for research, the current WHO surveillance network remains inadequate for timely response. The global community must act to address the urgent need to strengthen local human resource capacities and improve coordinated response.

To control meningitis demands a strategy focusing on the pathogens community, meaning integrating the two pathogens predominantly responsible for epidemics, i.e. *Nm* (all serogroups) and

*Sp*. It is unrealistic to expect meningitis to be under control in the belt without addressing the following key operational research questions:

- What are the pathogens’ community dynamics? Controlling meningitis demands a strategy focusing on the pathogens community that integrates the two pathogens predominantly responsible for epidemics, i.e. *Nm* (all serogroups) and *Sp*, given that they competitively share the same ecological niche, the nasopharyngeal tract. We need to better understand their joint dynamics. In order to better understand the epidemiology of the disease, and because keeping herd immunity high is critical for epidemic prevention, population immunity must be tracked. One limitation for this is due to the use of combined *NmA/C* vaccine in the last decade of reactive campaigns which has complicated baseline measures of immunity against *NmA* in the population receiving only MenAfriVac® (i.e., and no other meningitis vaccine) since 2010.
- What is the potential impact of PCV vaccines [10], in preventing *Sp*-meningitis in Africa? (Are these types responsible for Meningitis included in the vaccine?)
- How might the meningitis belt definition be extended to better adapt to the evolution of meningitis epidemiology under vaccine pressure over recent years?

## What Needs to Happen Next?

Ideas of projects to be developed

- Build capacity to improve surveillance, diagnostic training and lab confirmation of community health workers. To better understand the epidemics and *Nm* serogroups/*Sp* serotypes dynamics, comprehensive community data with methodologically robust reporting, including information on the full range of interventions and interactions taking place, are urgently needed.
- Reinforce multi-sectorial and global action through the organization of an annual international African workshop to create a network that includes all stakeholders, i.e. national and international public health experts, academic researchers, NGOs, civil society, funders, and international agencies. This workshop would aim to (1) advocate for multivalent vaccines for meningococcal meningitis, based on the current epidemiological situation; (2) identify the causes of the current vaccine shortages and push manufacturers to produce vaccines for the meningitis belt, paid by ICG, UNICEF; and 3) advocate for prevention at the centre of meningitis control and vaccine strategy.
- Develop a common platform for timely information sharing for local suspected and confirmed meningitis cases, facilitating analysis of meningitis dynamics, along with serogroups/pathogens dynamics. Support community-based research

projects to address specific questions, e.g., serotyping the *Sp* responsible for meningitis during outbreaks and comparing results to the vaccine-included serotypes; serological studies to determine the immunity against *NmA* in populations that received only MenAfriVac®. Document the social history of epidemics and analyze the socio-cultural and political economic factors affecting the emergence of disease.

## Opportunities and Action to Achieve these Goals

Meningitis remains a public health threat in Africa that continues to mobilize stakeholders. A well-recognized panel of meningitis vaccine experts is ready to work together for better research and operational action. A multi-disciplinary researcher network, the Multi-disciplinary Approach for Meningitis Epidemiology and Modeling in Africa (MAMEMA) already exists [11] with its 4<sup>th</sup> international workshop is scheduled in 2018 in Dakar gathering academics researchers, NGOs, international organizations, funders: "MAMEMA4: Meningitis control in Africa: Time for a Global action".

A major objective of this workshop is to identify innovative

strategies for meningitis control and to co-build operational projects to address the key issues listed above. We encourage interested people to contact us to join the working groups or set up collaborations.

Successful experiences of sharing data for other diseases can be transferred to the meningitis community. The World Wide Anti-malarial Resistance Network (WWARN), for example, is a collaborative platform generating innovative resources and reliable evidence to inform the malaria community on the factors affecting the efficacy of anti-malarial medicines. Epidemiological and vaccination data that are currently stored in various agencies and organizations should be systematically collected and merged into a new unique collaborative platform to be used for quick and relevant analyses.

## Conclusion

Following the success of MenAfriVac® in controlling *NmA*, persistent epidemics of meningitis due to other subgroups and subtypes of meningitis highlight the need for the international community and national authorities to propose a global and multi-sectorial strategic approach to meningitis control in Africa.

### ABOUT MAMEMA ...

**What:** MAMEMA "Multi-disciplinary Approach for Modelling and Epidemiology of Meningitis in Africa." is a multi-disciplinary group of around 15 researchers that gather annually to share results and develop projects to improve the understanding of meningitis dynamics in Africa and its control, in order to inform public health stakeholders.

**When:** MAMEMA was established following a work group on "meningitis modelling in Africa" at the MERIT meeting in Addis Abeba, Ethiopia. MERIT (Meningitis Environmental Risk Initiative Tool) was created in 2007 by WHO to gather climate and health researchers along with public health authorities to share information and ideas in order to improve the meningitis control strategy.

**Where:** MAMEMA members gathered annually from 2012 to 2014 in Montpellier and in Paris (France) for research exchange and discussions. The next meeting is in 2018 in Dakar, Senegal with other health sectors

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