

## DYNAMICS AND ALTERNATION OF *NEISSERIA MENINGITIDIS* SEROGROUPS IN NIGER 2005—2024, FROM THE ERA OF POLYSACCHARIDE VACCINES TO THE ERA OF CONJUGATE VACCINES

OUSMANE Sani<sup>\*1</sup>, HAMADOU Idrissa<sup>1</sup>, OUBAYYOU-YAROUKOY AMB<sup>1</sup>, ALKASSOUM NB<sup>1</sup>, BOUBACAR IB<sup>1</sup>, INOUSSA Abdoulaye<sup>1</sup>, MOUSSA SM<sup>1</sup>, TAHIROU Zar<sup>1</sup>, MAMANE KH<sup>1</sup>, ABDOULKARIM BZ<sup>1</sup>, SABO HS<sup>1,2</sup>

<sup>1</sup>Centre de Recherche Médicale et Sanitaire (CERMES), 634 Bd de la Nation YN034 BP10887, Niamey, Niger.

<sup>2</sup>Abdou Moumouni University, Faculty of Science and Technology, Department of Chemistry and Nutrition, Niamey, Niger.

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\*Corresponding Author: OUSMANE Sani

Centre de Recherche Médicale et Sanitaire (CERMES), 634 Bd de la Nation YN034 BP10887, Niamey, Niger.

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### ABSTRACT

**Background:** Niger, located in the heart of the African meningitis belt, is regularly hit by meningitis epidemics. **Objective:** To describe the spatiotemporal dynamics and alternation of *Neisseria meningitidis* serogroups over a 20-year period of surveillance. **Method:** national epidemiological and laboratory surveillance data recorded from 2005 to 2024 were collected and analyzed. **Results:** Prior to the introduction of MenAfriVac®, epidemic waves were mainly caused by *Neisseria meningitidis* serogroup A (NmA), which co-circulated with serogroups X and W. Reactive vaccination, done with polysaccharide vaccines (monovalent A, bivalent AC or tetravalent ACWY), only allowed to break the chain of transmission but did not offer lasting immunity. After the introduction of MenAfriVac® in 2010, a dramatic drop in NmA cases was observed. As of 2013, no case due NmA was detected in Niger. However, outbreaks due to serogroup W have been observed and the proportion of cases due to serogroups X and C, as well as *Streptococcus pneumoniae*, has increased. In 2015, serogroup C caused an unprecedented outbreak and was since continuing to dominate outbreaks in Niger. The country began using the new MEN5C vaccine for epidemic response and planned mass campaigns in December 2025. Like MenAfriVac, MEN5C is expected to eliminate outbreaks due to the 5 serogroups included. Nevertheless, vigilance must be the order of the day as nature has a horror of a vacuum. **Conclusion:** Niger's experience illustrates the success of targeted conjugate vaccination and the resulting capsular replacement phenomenon. Continuous surveillance is essential to monitor the evolution of serogroups and other bacterial etiologies with a view to eliminating meningitis by 2030.

**KEYWORDS:** Niger, Meningitis, Alternation, Serogroups, MenAfriVac®, ME.

### INTRODUCTION

Bacterial (or purulent) meningitis is a serious, often fatal infection that affects the entire world but particularly sub-Saharan Africa, a region nicknamed the "meningitis belt" due to the disproportionate impact of epidemics, especially during the dry season.<sup>[1,2]</sup> The three main bacterial causes are *Neisseria meningitidis* (Nm), *Streptococcus pneumoniae* (Spn) and *Haemophilus influenzae* type b (Hib).<sup>[3,4,5]</sup> Nm is the main cause of

acute forms and epidemics, often on a large scale, mainly through its six serogroups A, B, C, X, Y and W.<sup>[6]</sup>

For more than a century, sub-Saharan Africa has recorded explosive and repeated cases, with major epidemic cycles every 5 to 12 years.<sup>[7,8]</sup> In 1995-1996, an epidemic wave of NmA caused 250,000 suspected cases and 25,000 deaths.<sup>[9]</sup> Prior to 2010, serogroup A dominated outbreaks, although serogroups W and X

occasionally caused major outbreaks, such as in Burkina Faso in 2002 (NmW)<sup>[10]</sup> and Niger in 2006 (NmX). The response was based on polysaccharide vaccines (A, AC, ACWY) used in reactive campaigns.<sup>[12]</sup>

From 2010, a new conjugate vaccine against serogroup A, MenAfriVac®, was introduced massively in the countries of the belt, including Niger in 2010-2011.<sup>[13,14]</sup> While this vaccine has led to the virtual elimination of NmA, as nature abhors a vacuum, an emergence of serogroup C (NmC) has been observed, causing a major epidemic in Niger in 2015. Since then, the NmC has dominated the epidemiological landscape. To create hope in sub-Saharan Africa, a pentavalent meningococcal vaccine, MEN5C, protecting against serogroups A, C, W, X, and Y, was first approved and rolled out in Nigeria in March 2024, a world-first introduction for this broad-spectrum vaccine, aiming to combat severe meningitis in the African meningitis belt, funded by Gavi and developed by PATH and Serum Institute of India.<sup>[14,15]</sup> Niger planned mass campaigns with MEN5C in December 2025 after its use in response to NmC outbreaks in few health districts in 2024. The objective of this study is to describe the spatiotemporal dynamics of the main etiologies of bacterial meningitis in Niger from 2005 to 2024, in order to document the epidemiological paradigm shifts induced by successive vaccine strategies.

## MATERIALS AND METHODS

For this descriptive retrospective study, we analyzed data on meningitis cases reported to the Directorate of Surveillance and Epidemic Response (DSRE) via the Notifiable Diseases (MDO) registry for the period 2005-2024. Biological confirmation data from cerebrospinal

fluid (CSF) samples were extracted from the database of the National Reference Laboratory for Meningitis (NRL) of the Medical and Health Research Center (CERMES) over the same period.

## Description of the monitoring system

Niger adopted enhanced surveillance for meningitis in 2015. A suspected case of meningitis is defined as any person with a sudden onset of fever (>38.5°C rectal or 38.0°C axillary) and one of the following signs: stiff neck, altered consciousness, or other meningeal signs. Health districts are divided into surveillance zones of 100,000 inhabitants. The alert threshold is reached at 3 suspected cases per 100,000 inhabitants in one week, and the epidemic threshold at 10 cases per 100,000 inhabitants.<sup>[16,17]</sup> The system is supported by a network of laboratories for case confirmation, including Polymerase Chain Reaction (PCR) for the three major bacterial etiologies.

## Data analysis

The data were captured and analyzed using statistical software. Annual and regional incidences, case fatality rates, and proportions of different etiologies were calculated. The analysis of the spatial distribution was carried out to identify regional particularities, based on the biological confirmation data.

## RESULTS AND DISCUSSION

The profound transformation of the epidemiological landscape of bacterial meningitis in Niger, an evolution largely dictated by successive vaccination strategies. Our results confirm the resounding success of MenAfriVac® and vividly illustrate the resulting capsular replacement phenomenon.

**Table 1: Annual distribution of number and percentage of noticed, sampled and analyzed cases of meningitis in 2005- 2024.**

Year	Reported cases	Cases taken	Percentage	Positive case	Percentage
2005	1296	1249	96%	388	31%
2006	5069	3137	62%	1258	40%
2007	1097	1203	110%	367	31%
2008	3851	2714	70%	1231	45%
2009	13943	3915	28%	1783	46%
2010	3025	2405	80%	1041	43%
2011	1307	1041	80%	483	46%
2012	314	303	96%	61	20%
2013	341	281	82%	46	16%
2014	337	399	118%	81	20%
2015	8991	4653	52%	1578	34%
2016	1969	2093	106%	519	25%
2017	3506	3668	105%	1274	35%
2018	1539	1291	84%	571	44%
2019	1188	1107	93%	319	29%
2020	600	594	99%	110	19%
2021	1577	1535	97%	662	43%
2022	1884	1607	85%	591	37%
2023	2820	2097	74%	831	40%
2024	4243	3776	89%	1400	37%
<b>Total</b>	<b>58897</b>	<b>39068</b>	<b>66,3%</b>	<b>12363</b>	<b>32%</b>

### Surveillance challenges and prospects

Over the period 2005-2024, 58,897 suspected cases of meningitis were reported in Niger. Of these, 39,068 (66.3%) CSF samples were collected and analyzed at CERMES, of which 12,363 (32%) were confirmed positive by PCR for one of the three major bacterial etiologies (Table I). The study also reveals persistent challenges in the surveillance system (Table I). The CSF collection rate, although improved since 2015, remains variable and falls during major epidemics (e.g. 28% in 2009). A low rate of biological confirmation can mask the true etiology and delay an adequate vaccine response. Continued strengthening of case-based surveillance, including sample collection and analysis, is fundamental.<sup>[17]</sup> In this context, the introduction of the pentavalent conjugate vaccine MEN5C in 2024 is a logical and promising step.<sup>[15]</sup> By targeting the five main epidemic serogroups (A, C, W, Y, X), this vaccine has the potential to control almost all the strains of meningococci currently circulating in Niger. It can be expected to prevent the devastating epidemic waves seen since 2015. Nevertheless, vigilance is still required to detect any new replacement phenomenon, by serogroup B or other pathogens.<sup>[22]</sup>

The distribution of cumulative cases between 2005 and 2024 shows that the regions of Zinder (10,342 cases) and Niamey (10,385 cases) were the most affected, with Niamey having the highest cumulative case fatality rate (14.2%). Analysis of the spatial distribution of confirmed etiologies (Figure1) reveals significant heterogeneities across the country. While *N. meningitidis* serogroups A, C and W circulated more intensively in the central and western parts of Niger, a distinct epidemiology was observed in the Diffa region in the far east of the country. Over the study period, *S. pneumoniae* (Spn) and *H. influenzae* (Hi) prevailed over *N. meningitidis* as the causative agents of confirmed bacterial meningitis. This is in stark contrast to other regions in Niger, where Nm remains the predominant cause of outbreaks, even after NmA has been replaced by NmC. This epidemiological particularity of the Diffa region underlines the importance of decentralized surveillance and a diagnostic approach that does not focus solely on meningococcus, even in an epidemic context.

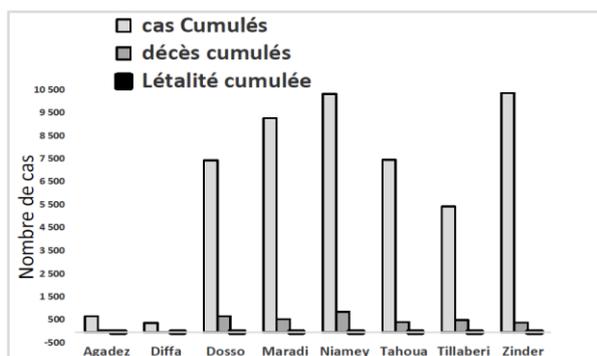


Figure 1: Regional distribution of reported, death and lethality cumulative of meningitis 2005-2024 in Niger cases.

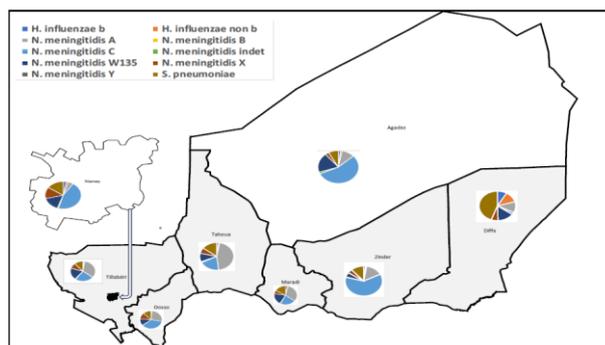


Figure 2: Spatial distribution of meningitis etiologies 2005-2024 in Niger.

The discovery that *S. pneumoniae* and *H. influenzae* prevail over *N. meningitidis* in the Diffa region is a major result. Several hypotheses can explain this particularity. Environmental, demographic (population movements), or host-related factors (immune profile of the local population) could play a role. This distinct epidemiological situation has important implications for public health in this region. This observation indicates that the response strategy to meningitis alerts cannot be uniform across the country. In Diffa, a broader diagnostic approach and the use of antibiotic treatments covering Spn and Hib are crucial from the outset of an alert. In addition, it reinforces the importance of pneumococcal (PCV) and Hib vaccination under the Expanded Programme on Immunization (EPI) to reduce the overall burden of meningitis in this specific region.

### Temporal dynamics of bacterial etiologies

Analysis of the annual proportion of confirmed etiologies reveals a marked epidemiological transition (Figure 1). From 2005 to 2010, epidemics were dominated by NmA, with a co-circulation of NmX (especially in 2006) and NmW. After the introduction of MenAfriVac®, the share of NmA dropped drastically, disappearing from confirmed cases from 2012 onwards. A period of low incidence followed (2012- 2014), during which *S. pneumoniae* (Spn) became the predominant agent among confirmed cases. In 2015, an explosive outbreak of NmC occurred, and this serogroup remained the main cause of outbreaks in the following years, with resurgences of NmW and NmX.

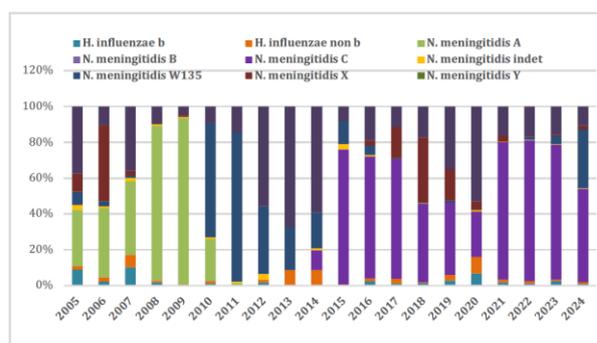


Figure 3: Temporal distribution and trends of bacterial etiologies of meningitis in Niger 2005-2024.

### The impact of vaccine strategies

The pre-MenAfriVac® period (2005-2010) was characterized by the overwhelming dominance of NmA, responsible for devastating cyclical epidemics.<sup>[18]</sup> The response with polysaccharide vaccines, although useful in the short term, did not confer lasting immunity and had a limited impact on carriage, explaining the recurrence of epidemics.<sup>[12]</sup> The introduction of the MenAfriVac® conjugate vaccine in 2010-2011 was a historic turning point. Our data show a near-total elimination of NmA as early as 2012, a success attributable to the superior properties of conjugate vaccines that induce long-lasting immunity and herd immunity by reducing nasopharyngeal carriage.<sup>[19,20]</sup> However, this victory opened up an ecological niche that was quickly occupied by other serogroups. The explosive emergence of NmC in 2015, responsible for an epidemic of nearly 9,000 cases, is the most striking example of this capsular replacement. NmC has since adopted the cyclical epidemic behavior once characteristic of NmA, probably favored by the horizontal transfer of genes between strains under the selective pressure of the monovalent vaccine.<sup>[21]</sup> At the same time, the persistence and resurgence of NmW and NmX have created a complex epidemiological landscape, making response strategies based on limited-valence vaccines increasingly obsolete.

### Limitations of the study

This study, although covering a long period, has certain limitations. First, it relies on surveillance data that may be subject to under-reporting, especially in remote areas. The number of "notified" cases is probably only a fraction of the actual number of cases. Second, variations in sampling and analysis rates (Table I) over time may introduce bias in the distribution of confirmed etiologies. Years with a low confirmation rate may not accurately reflect the diversity of circulating pathogens. Finally, the study focuses on the three main pathogens (Nm, Sp, Hib) and does not provide information on other possible causes of purulent meningitis.

### CONCLUSION AND PERSPECTIVE: Towards the MEN5C Era

Despite its limitations, our study paints a clear picture of the evolution of meningitis in Niger over the past two decades. It vividly demonstrates both the resounding success of a targeted vaccination strategy (MenAfriVac® against NmA) and the inevitable consequence of capsular replacement that has resulted from it. The post-MenAfriVac® era has become the era of serogroups C, W, and X, creating a new challenge for public health. The arrival of the MEN5C<sup>[2,34]</sup> vaccine ushers in a new era of hope. By targeting the five main serogroups responsible for outbreaks (A, C, W, Y, and X), this vaccine has the potential to drastically reduce the incidence of meningitis due to serogroups C, W and X, thus preventing the devastating epidemic waves observed since 2015 in Niger and the region. However, vigilance is still required. History has taught us that

meningococcus is an adaptable adversary. Enhanced epidemiological and genomic surveillance will be essential to rapidly detect any phenomenon of replacement by non-vaccine serogroups (such as serogroup B, although rare in Africa, and other emerging strains) or the emergence of other pathogens. The fight to defeat meningitis by 2030, a WHO goal, will require an integrated approach combining broad-spectrum vaccination, robust surveillance and rapid response capacity.<sup>[5-7]</sup> Niger's experience will serve as a valuable guide for the years to come.

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