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Meningococcal strain evolution, dusty dry air and respiratory tract infections: An explosive relationship

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In this article of *EBioMedicine*, Topaz and colleagues [1] present a phylogenetic overview with more than 700 meningococcal strains isolated since the introduction of a serogroup A-specific conjugate vaccine (MenAfriVac®) in the meningitis belt. This vaccination has led to quasi-elimination of serogroup A disease, which used to be the predominant burden, but the emergence of a new serogroup C strain during the vaccination roll-out substantially reduced the net benefit for the region.

Since their importation into this area on the Southern border of the Sahara in the early 20th century [2], meningococci have engaged into an explosive relationship with regional climate, causing thousands if not millions of deaths from meningitis. This phenomenon of the African meningitis belt, characterized by regular epidemic waves, frequent small localized epidemics and a steadily ongoing pronounced seasonal pattern [3] is a human tragedy and at the same time a most fascinating example of the complex interactions between environment, bacterial and viral pathogens, human biology and behavior.

Do we understand these interactions? Only partially, but progress in epidemiological and climatological surveillance, microbiological methods and data analysis capacity have allowed a substantial leap over the last 20 years. According to the current understanding, genetic evolution of meningococcal strains are responsible for the epidemic waves that occur every 7–10 years, can span over several countries and include several consecutive dry seasons. Multilocus sequence typing, used since late 1990s, suggested that new epidemic waves were usually associated with emergence of a new sequence type. However, it was only with the arrival of whole genome sequencing (WGS) that the reasons for such emergences could be understood and questions about the importation of strains or the role of vaccination be answered. For example, Topaz et al. refer to the evidence that the ST-11 strain causing the first serogroup W epidemic in 2001 in Burkina Faso was not imported from the 2000 Hajj outbreak, but had emerged from a common ancestor that was present in West Africa already during the 1990s. Similarly, Brynildsrud et al. had suggested that the ST-10217 serogroup C strain that had caused an epidemic wave over several years in Nigeria and Niger was not a result of vaccine pressure, but had emerged from an unencapsulated carriage ancestor already before the introduction of MenAfriVac® [4]. Topaz et al. now show the quick ongoing evolution of this new ST-10217 in genetic lineages in neighboring populations, even during the epidemic wave and possibly towards less virulent strains. As suggested from analysis of genomic hot spots of recombination observed in case and carrier strains in Ghana [5], such rapid evolution likely occurs in response to preexisting immunity of human populations, in particular natural immunity against non-capsular antigens. These elements pose the question how such evolution could be impacted by human behavior or technology. An urgent question is whether the evolution of new or hyperinvasive lineages can be predicted or at least be detected early during emergence.

With their comprehensive synopsis, Topaz et al. thus prepare the ground for future advances in disease control. In addition, by analyzing in their strain collection the presence of peptide types that are included as antigens in current protein-based vaccines (developed against serogroup B meningococcal disease which is so far absent from the belt) they suggest that serogroup-unspecific immunization using shared proteins could be a relevant approach for the meningitis belt.

This synopsis has been made possible through the collaboration of three Collaborating Centers of the World Health Organization and long-term investment of national Public Health institutions and technical partners. Each isolate in the phylogenetic tree represents a clinical consultation, lumbar puncture and culture isolation, all of which require ongoing training and investment in the resource-poor and in part insecure settings of the meningitis belt. In addition, meningococcal evolution occurs during nasopharyngeal carriage, the natural condition of the bacterium, and regular carriage studies are therefore needed to thoroughly interpret WGS information.

This brings the focus back to the complexity of the meningitis belt phenomenon. The new serogroup C ST-10217 appeared in Niger during 2014–15 and caused epidemics; however, epidemics did not occur in all districts where the new strain was found [6]. This raises the question whether there are necessary co-factors for meningococcal epidemics. Viral upper respiratory tract infections are strongly associated with localized epidemics at the ecological level [7] and through acquisition of meningococcal carriage [8]. This supports the hypothesis that viral microepidemics cause the observed surge in meningococcal carriage during meningitis epidemics [3]. A minor correlation between viral and meningococcal disease has been described outside the belt, but the question occurs whether

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there are specific meningococcal strain characteristics that allow this interaction with viruses at such strength?

Finally, epidemics occur exclusively during the dry season and our understanding is that the 10- to 100-fold seasonal increase in bacterial meningitis incidence – typically including cases due to low-virulence strains – is less related to meningococcal biology than to the specific environmental conditions, characterized by a single 6-months long dry season with high natural mineral aerosol load [9]. However, there is no confirmed mechanism and no research to evaluate hypotheses around the noxious effect of low air humidity and high aerosol load on the nasopharyngeal mucosa. Besides describing evolutions of meningococci, we must understand why climate increases so strongly the risk of invasion for a bacterium that actually engages in asymptomatic nasopharyngeal infection. Given the ongoing climate change, these aspects should be studied to prepare for future disease emergence.

While I am impatient to learn more about all these questions, my hope is that the use of a pentavalent conjugate vaccine against all current serogroups in the belt [10] or possibly the use of protein-based vaccines will make the meningitis belt phenomenon vanish before we fully understand it.

Authors contribution

JM wrote the commentary.

Conflicts of interests

JM has no conflicts of interests to declare.

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