Global burden of meningitis and implications for strategy

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Meningitis is the inflammation of the membranes surrounding the brain and spinal cord which can be caused by bacterial, viral, fungal, or protozoan infections. From disease onset, meningitis can progress rapidly to kill within hours and survivors can be left with lifelong disabilities[1]. The roll-out of conjugate vaccines that protect against *Haemophilus influenzae* type B, *Neisseria meningitidis*, and *Streptococcus pneumoniae* have contributed to the reduction of meningitis mortality globally[2,3]. The Global Burden of Disease (GBD) 2016 study reported an estimated 21% decrease in meningitis deaths between 2000 and 2016, whereas incident cases increased from 2.50 million in 2000 to 2.82 million during this period[4]. Since these data were published, the WHO Defeating Meningitis 2030 Roadmap has set visionary goals to eliminate meningitis epidemics, reduce cases of and deaths from vaccine-preventable meningitis, reduce disability, and improve quality of life among survivors[5].

The GBD 2019 study[6] published in *The Lancet Neurology* is timely and addresses crucial gaps in our knowledge of the global, regional, and national burden of meningitis. Setting priorities for meningitis pathogens and the development of effective meningitis control strategies depends on accurate regional disease burden estimates, including data on infectious aetiologies. Using a broad range of data sources and standardised analytic approaches, the 2019 GBD study provides updated estimates of meningitis cases and deaths, including data for at least ten aetiologies some of which were not available in previous meningitis GBD reports. The authors estimate that in 2019 there were 236 000 deaths attributable to meningitis and 2.51 million incident cases of meningitis, which are modest declines from 2016[4]. Consistent with previous reports, the largest burdens of meningitis morbidity and mortality in 2019 were among children less than five years old and populations in sub-Saharan Africa.

It is concerning that, despite being vaccine-preventable, *N meningitidis* remains the leading cause of meningitis, accounting for 17.3% of cases globally. The burden of *N meningitidis* meningitis was largest in the African meningitis belt, where hypervirulent serogroup C, W, and X strains with the propensity to cause epidemics have emerged following the roll-out of the serogroup A conjugate vaccine[3]. Life-saving polyvalent meningococcal vaccines have remained out of reach for populations across sub-Saharan Africa, in part due to their high costs, and the limited vaccine availability and stockpiles. The imminent roll-out of an effective and affordable pentavalent ACWXY conjugate vaccine has the potential to substantially reduce the burden of meningococcal disease and might herald the end of meningococcal epidemics[6].

Despite the widespread implementation of pneumococcal conjugate vaccines, *S pneumoniae* was the deadliest meningitis pathogen in 2019, accounting for 18% of all-age meningitis deaths globally. The emergence of non-vaccine serotypes, the persistence of some vaccine serotypes (eg, serotypes 1 and 3) and suboptimal vaccine coverage might all be contributing to the persisting burden of pneumococcal meningitis[7]. The benefits of pneumococcal conjugate vaccine infant immunisation schedules with booster doses and/or catch-up campaigns to enhance control of vaccine serotypes are under investigation to improve control of vaccine serotypes. Modelling studies are needed to determine whether higher valency pneumococcal conjugate vaccine formulations are likely to improve control of meningitis caused by serotypes not included in the 10-valent and 13-valent pneumococcal conjugate vaccine formulations currently in use.

The GBD 2019 meningitis report[7] also highlights the importance of non-vaccine preventable causes of meningitis, including *Klebsiella pneumoniae*, Group B *Streptococcus*, *Staphylococcus aureus*, and *Listeria monocytogenes*. *K pneumoniae* has high rates of antimicrobial resistance and Group B *Streptococcus* is the leading cause of meningitis among neonates. *K pneumoniae* and Group B *Streptococcus* vaccines are at various stages of development;[8] however, effective control of meningitis might require multimodal interventions such as infection prevention control in healthcare settings, improved antimicrobial stewardship, promotion of safe water, sanitation, and hygiene, and maternal screening for Group B *Streptococcus*.

Viruses accounted for nearly 30% of all meningitis cases in 2019 but virus-specific aetiologies were not available in the GBD 2019 study. A wide range of viruses that affect people with varying age, geographic, and seasonal distributions cause meningitis, and data on the virus-specific burdens of meningitis are needed to inform public health control

measures and prioritisation. For example, it will be important to determine the burden of vaccine-preventable viral meningitis (eg, measles and mumps viruses)[9]. The 2019 GBD study highlights the need for strengthening laboratory capacity to diagnose bacterial, viral, fungal and protozoan meningitis, which might be achieved through leveraging the molecular and sequencing infrastructures that are being developed rapidly and globally.

Overall, the GBD 2019 meningitis data provide new and crucial insights into the epidemiology of meningitis globally, including different aetiologies and their fatality rates across different populations. This study will be invaluable for reviewing priorities and developing strategies as we strive towards a world free of meningitis.

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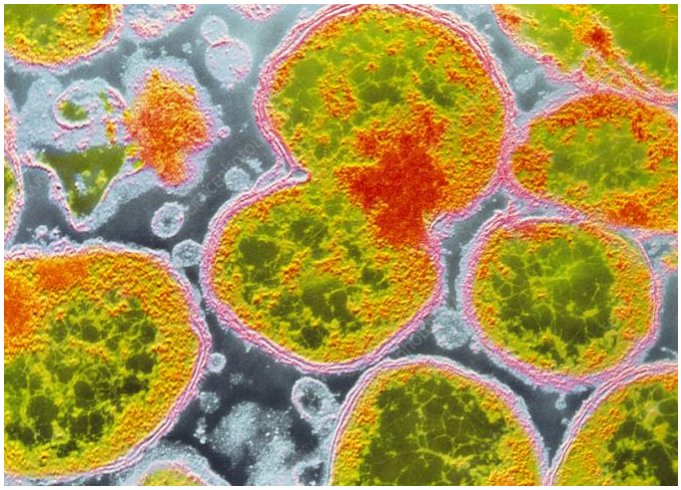

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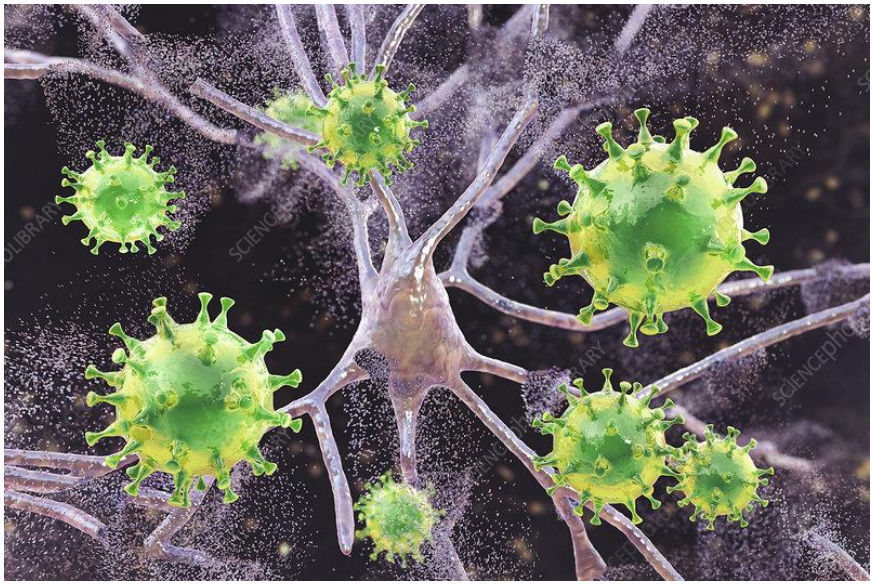

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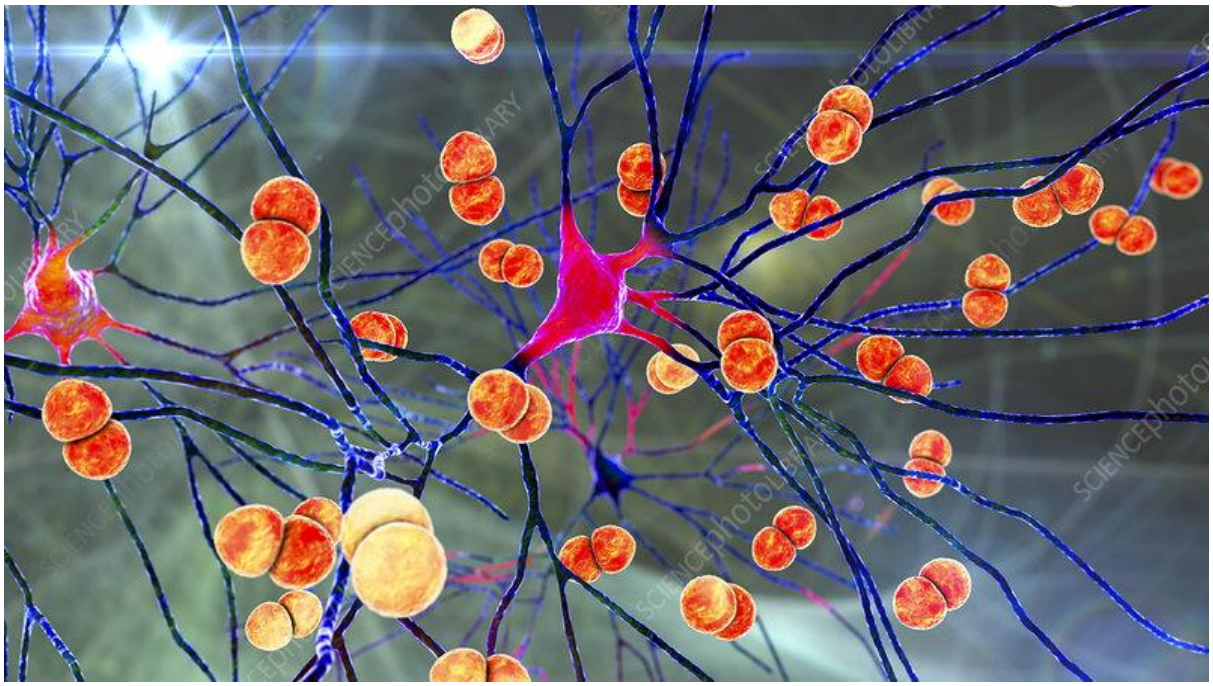

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Declarations

The authors have no conflicts of interest to declare.

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