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Elimination of meningitis—are we there yet?

Helen Marshall

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Meningitis remains a killer disease, mostly of young children and adolescents but can occur at any age. In his book *Brain fever—how vaccines prevent meningitis and other killer diseases*, Richard Moxon provides both a historical and contemporary account of progress in the treatment and prevention of bacterial causes of meningitis.

Viruses and bacteria will be an ever present risk to mankind, no matter how sophisticated our health systems become. From the earliest recording of the illness “meningitis” on the banks of Lake Geneva in 1805 to present day cases, it is the rapidity and severity of bacterial meningitis that sets it apart from other infections and raises angst not only in parents but also in treating physicians.

Children still risk death from bacterial meningitis in 5% of those afflicted and a further 20–40% suffer long term consequences, the worst of which may occur with coexistent septicaemia. The long-term disability from complications requiring surgical limb amputation (sometimes all four limbs), deafness, blindness and brain injury cannot be underestimated. Moxon takes us through the sadness, devastation, and learnings from the children who don't survive, even despite early treatment.



book, Moxon pays tribute to those who originally identified the bacterial causes of meningitis, and the early research into the mechanisms of disease. He takes us through a transatlantic rollercoaster of the early days of *Haemophilus influenzae* type B (Hib) and meningococcal vaccine development. Through a description of his first years as a clinician developing an interest in research, we have clear insight into the challenges and rewards of combining bedside medicine with rigorous scientific investigation in the 1970s and 1980s.

Evident throughout the book is the serendipitous nature of science and the excitement of research discovery. Moxon describes several of his contributions to understanding the clinical pathogenesis of meningitis and determining the safety and immunogenicity of the first meningitis vaccines. He provided the pivotal clinical trial data for introduction of Hib vaccine in the UK, but is consistently reflective of the team approach. Also outlined are the challenges and barriers to researchers, so dependent on the whims of funding from governments and research funding agencies and the complexities of the research funding relationship between industry and academia.

The main focus of the second half of the book is on the bacterial causes of meningitis and how vaccines have been developed to prevent these scourges. Moxon takes us through the discovery of the microbes that cause disease in humans with the focus being on two of the three most common causes of meningitis, Hib and *Neisseria meningitidis*.

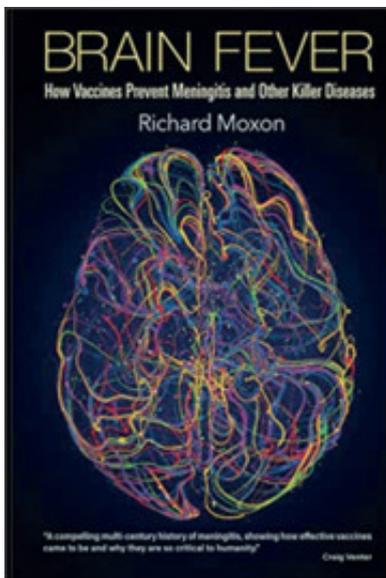
From the development of the polysaccharide vaccines to discovery of the conjugation process resulting in improved vaccine effectiveness in young infants, the excitement of success is clear, with unprecedented reductions in Hib and meningococcal C (MenC) meningitis cases evident in the UK. Part of this success was due to the unexpected “herd immunity” impact whereby Hib and MenC population programmes also resulted in reduced transmission of the bacteria between individuals.

Despite these impressive reductions in meningitis, meningococcal B (MenB) infection remained the commonest cause of meningitis in children. Through difficulties associated with development of a conjugate MenB vaccine, a different approach was required. Previous outer membrane vesicle MenB vaccines had been developed for epidemics caused by specific MenB strains but a vaccine that could provide broader protection was needed. Advances in microbiology at this time with genomic sequencing of bacteria, allowed further understanding of the bacterial components associated with virulence of the organism and potential for development of vaccine targets. During the remaining

narrative, we learn about the development of a multi-component MenB vaccine, 4CMenB.

A final few chapters are devoted to a description of the rigors, challenges, and barriers researchers face and the complexity of vaccine development and implementation. Political agendas and government funding provide a further layer of complexity in availability of population immunisation programmes, even when a vaccine becomes available. This is particularly challenging for meningococcal vaccines as they are introduced in population programmes to prevent an uncommon infection, which is always challenging for cost-effectiveness estimates.

The book leaves us with the current challenges in vaccine development, including the herd immunity impact that is the “value add” to individual protection that makes vaccines such effective public health tools. Although there is evidence of high protection for the individual, the 4CMenB vaccine does not show evidence of herd immunity. As Moxon concludes, “the 4CMenB vaccine had achieved notable success, but improving the breadth of coverage and above all, the imperative of inducing community protection remain major challenges for future research”.



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