Clinical trials for bacterial meningitis treatments are not keeping pace with the rise of resistance

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New vaccines and drug treatments are urgently needed for bacterial meningitis, a devastating disease which kills or maims around a fifth of people who contract it, according to medical experts writing in a new Series on bacterial meningitis, published in *The Lancet*.

Meningitis occurs when the protective membranes that surround the brain and spinal cord become inflamed, and can be caused by a number of different agents, most commonly viruses. Although bacterial meningitis is less common than the viral form of the disease, it is much more serious, and was estimated to have killed 180 000 children under five years old in 2010.

In a comment accompanying the Series, Professor Diederik van de Beek, of the University of Amsterdam in the Netherlands, highlights the fact that although bacterial meningitis causes high rates of death and disability across the world, the burden of disease is especially high in lower-income countries, with the fatality rate as high as 50% in some resource-poor countries. The global emergence of antibiotic-resistant strains of the bacteria that cause meningitis is further cause for concern, since many inexpensive and widely available antibiotics are starting to show reduced effectiveness as resistant strains become more prevalent. Although various new antibiotics for the treatment of meningitis are in development, according to Professor van de Beek, "Clinical data for these new drugs have not kept pace with the rise of resistance."

Professor van de Beek states that large, controlled trials of new bacterial meningitis treatments are urgently needed, as are those for vaccines, but that governments and charities will need to step up their involvement in such research, adding that "because drug-development companies are generally not interested in a disease that affects mainly patients in resource-poor countries, preclinical and clinical studies will need to be funded by governments or charitable foundations."

In the first Series paper, a group of authors from the Netherlands, United States, and the United Kingdom outline the dilemmas and difficulties in accurately diagnosing bacterial meningitis, which can be caused by a number of different bacteria, and results in symptoms that vary widely between patients. The so-called "classic" symptoms of meningitis – rash, neck stiffness, and impaired consciousness – often do not develop until the patient is already in hospital, or do not develop at all. The authors highlight the latest findings on how bacterial meningitis should be diagnosed, as well as common pitfalls and uncertainties. However, they stress that gaining an accurate diagnosis as early as possible is paramount, as early treatment with appropriate antibiotics is the best way to improve prognosis.

The second Series paper examines the management of bacterial meningitis more closely, although the authors point out that bacterial meningitis is "an evolving therapeutic challenge." Exploring the best treatment options for different types of bacterial meningitis, as well as new therapies that are emerging, the authors also discuss the increasing problem of antibiotic-resistant strains of the bacteria that cause meningitis, and how this threat may be best contained. However, the authors warn that "Determination of which antibiotic agent will be most effective is becoming ever more difficult in the face of increasingly drug-resistant bacteria," and they conclude that in the future, widespread adoption of vaccination is likely to have the greatest effect on the burden of illness due to bacterial meningitis.

The final Series paper, which describes the effect of vaccines on bacterial meningitis, highlights the fact that three main species of bacteria – *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Neisseria meningitidis* – are responsible for most cases of bacterial meningitis worldwide. All three infections can be prevented by vaccines that are highly effective against specific types of each bacterium, known as conjugate vaccines. The impact of conjugate vaccines on meningitis has been most striking for *Haemophilus influenzae* meningitis, with reductions in cases of over 95%. The authors, from Australia, the United States, the United Kingdom and the Netherlands, highlight the lack of pre- and post-vaccine data from low- and middle-income countries, where the disease burden from bacterial meningitis is greatest, and where vaccine introduction has been most recent or is yet to occur.

Researchers predict that widespread deployment of currently available vaccines in optimum schedules can be predicted to have a major effect on the burden of bacterial meningitis in future years. However, according to the authors, "Important challenges remain. These include delivery of potent vaccines to difficult-to-access populations at risk, and appropriately designed and conducted studies of effectiveness, which require adequate surveillance to be in place before vaccine introduction. Development and testing of vaccines able to provide protection against the greatest range of bacterial types is an important future goal, even more so because of the striking reductions in disease in unimmunised older age groups which can be achieved through vaccination of young children."

More information: www.thelancet.com/series/bacterial-meningitis

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