Researching meningitis: the latest progress

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Every day, scientists are working to expand our knowledge and understanding of how to diagnose, treat and support those affected by meningitis, alongside finding new ways to prevent this devastating disease.

Here we summarise some of the very latest research, which could take us closer to defeating meningitis by 2030.

Since Meningitis Research Foundation was founded in 1989, we've invested over **£19.5 million into vital scientific research** on all aspects of meningitis.

MenB vaccine could unlock protection against gonorrhoea

Gonorrhoea is caused by *Neisseria gonorrhoea*, a bacterium which shares up to 90% of its genetic material with meningococcal bacteria. The idea that MenB vaccines could offer protection against gonorrhoea first emerged in New Zealand with the rollout of the 'MenZB' vaccine in the 2000s. Since then, evidence has been mounting that those vaccinated against MenB have a reduced chance of getting gonorrhoea.

In November 2023, the UK's Joint Scientific Committee on Vaccination and Immunisation recommended use of a MenB vaccine to prevent gonorrhoea in individuals at high risk. A review by Ladhani and colleagues explains the significant implications of this decision. Their paper highlights that this could provide 33 - 47% protection against gonorrhoea, with its use reducing cases in people at higher risk of infection who are attending sexual health services in the UK.

With no licensed vaccine currently available, the JCVI's recommendations mean the UK could become the first country to vaccinate against gonorrhoea. This would be a landmark step in preventing the two infections (MenB and gonorrhoea), using one vaccine.

Expanding protection against pneumococcal meningitis

Pneumococcal conjugate vaccines (PCVs) have made huge strides towards a world free from meningitis. They work by providing direct protection to the person vaccinated, and by stopping the bacteria from being carried in the back of the nose and throat. This reduces circulation of the bacteria, creating 'population protection', so that even those who are unvaccinated are protected from pneumococcal meningitis.

Currently, vaccines are available that protect against up to 21 different strains. Yet PCVs are costly and, with over 100 different strains of pneumococcal bacteria, it isn't possible to vaccinate against them all.

Instead, vaccines are designed to protect against the strains most likely to cause disease. This does, however, mean that serotype replacement can arise (this is a rise in pneumococcal disease caused by strains not covered in the vaccine). To tackle some of the drawbacks of currently available PCVs, scientists are working on new approaches.

Research published in March 2024 showed the potential of whole cell pneumococcal vaccines, designed to provide broad protection independent of different strain types. Early evidence suggests that, in the future, whole cell vaccines could hold promise for use in children in low- and middle-income countries, where the rates of carrying bacteria are known to be high.

We also saw results from the first-in-human clinical trial of a pneumococcal vaccine made through cell-free protein synthesis. Developed without the use of living cells, this approach aims to enable more strain coverage, without compromising the overall immune response. 'Proof of concept' data has shown the vaccine produces a robust immune response against 24 strains, with this vaccine now poised to move into Phase III clinical trials.

Another technology that hopes to overcome the limitations of current pneumococcal vaccines is MAPS (multi-antigen presenting system). This vaccine platform has developed a unique way of attaching bacteria-specific proteins to the sugar capsule of the pneumococcal bacteria.

The vaccine, which aims to protect against 24 strains, is currently being tested in Phase II trials. Another vaccine, offering protection against 30+ strains, is also in the early stages of development. MAPS holds promise for future prevention of other infections too, including *Klebsiella pneumoniae* – an important cause of meningitis in newborns. Prevention of *Klebsiella* infections is becoming ever more important, as it becomes increasingly harder to treat due to antimicrobial resistance.

Treatment of bacterial meningitis in the face of antimicrobial resistance

Antibiotics have played a key part in allowing us to treat many life-threatening bacterial infections. Over the decades, however, the misuse and over-exposure to antibiotics has allowed bacteria to develop resistance. Today, antimicrobial resistance (AMR) is a recognised global health threat by the WHO.

Recent research reviewed evidence of resistance to antibiotic treatment for childhood infections in Southeast Asia and the Pacific. The findings show that commonly prescribed antibiotics are now less than 50% effective in treating meningitis and sepsis in newborns. Antibiotics (like ceftriaxone) were found to be effective in only one in three cases of sepsis or meningitis, while gentamicin was effective in treating fewer than half of all cases in children. This research calls into question current WHO antibiotic guidelines for serious infections in vulnerable babies and children. As a result, we support this research's call for new antibiotic regimes that can more effectively treat meningitis and sepsis in babies and children globally.

The research identified *Klebsiella* and *Escherichia coli*, as important causes of infection in newborns and children that are frequently resistant to antibiotics. The news that an E. coli vaccine candidate has shown promise in pre-clinical research is therefore a welcome development. This vaccine is planned to target women at risk of, or with a history of, preterm delivery so newborns are protected against *E. coli* infections. While at a very early stage, if successful, this would be an important step in limiting the use of antibiotics, preventing the spread of resistant *E. coli*.

Enabling rapid diagnosis of meningitis

Rapid diagnosis of meningitis is key to enabling prompt and effective treatment and better outcomes for people affected by meningitis. A study published in March, part-funded by Meningitis Research Foundation, is the first of its kind to describe childhood meningitis in the UK, following the introduction of conjugate vaccines. Researchers recruited just over 3,000 children, aged up to 16 years old, who had suspected meningitis.

They found that while 180 children had bacterial meningitis, 423 had viral meningitis. This emphasises the importance of clinicians being able to distinguish between the two forms so that patients receive the most effective treatment, preventing unnecessary use of antibiotics. This study also aimed to develop new rules to assist with identifying children with bacterial meningitis, for faster clinical assessments. If implemented, these rules could not only lead to quicker diagnosis but improved outcomes in children.

Improving healthcare pathways and symptom recognition

In 2012, Meningitis Research Foundation funded the ASPIRE Project which aimed to tackle the devastating discovery that children in Malawi were dying during travel to, or in queues for, health centres. To address clinics not prioritising the urgency of a child's condition, mobile health (mHealth) technologies and training manuals were implemented. These interventions enabled quick and accurate triage, prioritising the sickest of children first. A later study confirmed that the mHealth training packages developed during ASPIRE were well received amongst health workers, with a consistency in use between health care workers and clinician assessment.

Despite these interventions improving the quality of care, further analysis has revealed that, of over 155,000 children triaged at primary health care centres, less than 2% (3,004 children) were referred to other sites (with only half of these patients reaching the referral facility). Of particular concern was the finding that over 370 children sent home from primary health care centres were later self-referred, revealing that some seriously ill children are still being missed. A referral system is a crucial component of health care systems and these findings highlight a critical need to keep strengthening referral training, and overcome constraints, to reduce child morbidity and mortality.

Understanding the long-term after effects of bacterial meningitis

Studies investigating the risks of long-term disabilities after childhood bacterial meningitis are limited. We were therefore delighted to see that Sweden's Karolinska Institutet have documented the long-term outcomes following bacterial meningitis. Their results show significantly higher probabilities for cognitive disabilities, seizures, hearing loss and motor function disorders after pneumococcal infections, with 29% of cases being linked with at least one disability. These results are crucial, emphasising the need for preventive measures against the disease and efforts to detect disabilities among surviving children. This is particularly important when considering the inequality in the burden of pneumococcal meningitis between high- and low-income countries. Data from Mbakwe and colleagues shows that the risk of death from pneumococcal meningitis was five times higher in Latin America than in Finland. Angolan children had a 17-fold increased risk for poor outcome when compared with Finnish children. Their research echoes the Karolinska Institutet, pointing to poor outcomes and drawing attention to the need to better detect disabilities in children surviving meningitis.

This summary has been produced by the Research team at Meningitis Research Foundation to support greater knowledge and understanding of the advances being made in defeating meningitis.

*To find out more about our work, and to support it, visit **meningitis.org**.*