The biggest public health intervention of the decade: meningitis C immunisation

In this article on landmark drugs, Jenny Bryan looks at how the meningitis C vaccine has reduced the annual number of cases of this infection

In the 10 years since a conjugate vaccine against meningitis C was introduced to the UK, the annual number of cases of this life-threatening infection has fallen by 99 per cent — a record that must surely make the prodigious efforts of medical research to be proud of.

Meningitis C immunisation has been the biggest public health intervention of the decade, and you can’t get better than that. Last year, there were only 10 cases of meningitis C in England and Wales, which was fantastic,” says Ray Borrow, who heads the vaccine evaluation unit at the Health Protection Agency’s regional laboratory in Manchester.

By contrast, there were 955 cases of meningitis C in the year before the vaccine was introduced in 1999, and the emergence of a hyper-virulent strain of meningococcal C in Canada, Spain and the Czech Republic in the early 1990s had given extra urgency to the need for an effective vaccine.

The assumption proved correct, with early post-licensing efficacy estimated at 88 per cent for toddlers and 96 per cent for adolescents in the first 16 months after immunisation. Immunisation of school-age children started in November 1999, with priority given to the highest risk 15- to 17-year-old age group, followed shortly afterwards by immunisation of infants and younger children. Immunisation of other groups was phased in so that, from June 2002, the conjugate vaccine was available to everyone up to the age of 25.

The meningitis C vaccine was formulated using mutated diphtheria toxoid to boost the immunogenicity of the meningococcal C polysaccharide and turn it from a T-cell independent antigen to a T-cell dependent antigen was already under way during the mid 1990s. But, as Professor Borrow points out, it takes time and effort to determine the exact amount of conjugate protein to polysaccharide that is required and the need for other adjuvants. A research programme of the National Vaccine Evaluation Consortium, which is largely funded by the Department of Health, was set up to obtain the safety and immunogenicity data needed to license a vaccine and prepare for a national immunisation programme.

Three MCC vaccines went on trial. A vaccine using tetanus toxoid as conjugate was developed and subsequently marketed as NeisVac-C by Baxter Biosciences, while vaccines using mutated diphtheria toxoid were tested and marketed as Meningitec by Novartis. Phase III studies demonstrated that the vaccines were immunogenic and triggered immunological memory, and were well tolerated in infants and young children. But, as Professor Borrow explains, formal efficacy studies were not done at that time.

Levels of meningococcal disease were still relatively low, so it would have taken some time to get results from controlled trials of efficacy. Instead, we had good surrogate immunological endpoints which, we knew from previous vaccines such as Haemophilus influenzae b (Hib), correlated well with efficacy,” he says.

Immunisation with the meningitis C vaccine of school-age children started in November 1999, with priority given to the highest risk 15- to 17-year-old age group

Impressive responses

The assumption proved correct, with early post-licensing efficacy estimated at 88 per cent for toddlers and 96 per cent for adolescents in the first 16 months after immunisation. Immunisation of school-age children started in November 1999, with priority given to the highest risk 15- to 17-year-old age group, followed shortly afterwards by immunisation of infants and younger children. Immunisation of other groups was phased in so that, from June 2002, the conjugate vaccine was available to everyone up to the age of 25.

Immunogenicity data showed that it was possible to reduce the original three-dose immunisation schedule for infants to two doses at three and four months, followed by a booster with a combined meningococcal C and Hib conjugate vaccine at around 12 months of age. A catch-up campaign ensured that infants and young children aged five to 12 months were offered two doses of the MCC vaccine, and those over 12 months a single dose.

Uptake has consistently been excellent, with 93 per cent of children immunised by the age of two. This compares with an immunisation rate for measles, mumps and rubella in England, which fell as low as 80 per cent in 2003-04 and now hovers around 88 per cent.

“Over the years, many surveys have shown that parents fear meningitis for their children more than any other disease, and media reports about the ‘killer brain bug’ and students dying of the infection have also helped to drive meningitis C immunisation levels,” Professor Borrow points out.
Benefits of herd immunity
What has come as a surprise has been the impressive degree of herd immunity achieved with the MCC vaccines. Studies have shown that fewer people now carry the meningococcal serogroup C organism than before MCC immunisation was introduced, and the number of cases of meningitis C in those aged 25 and over has dropped by 90 per cent compared with pre-immunisation days. Cases have also fallen among babies too young to have completed their course of immunisation, also supporting an indirect protective effect of reduced exposure.

Professor Borrow explains that, without immunisation, carriage of meningococci rises at around the age of 12 and peaks at 15–19 years, when it is linked to kissing and increased social interaction, for example, when teenagers go to college. Adolescents probably pass on the organism to their peers who are not generally affected by it, but who can pass it on to younger children and babies with more serious consequences.

“If we can prevent adolescents from acquiring the organism and passing it to their peers, we can break the cycle so that it stops passing on to younger children. But we still don’t know how long the conjugate vaccines we have been using for the past 10 years will confer protection. Our latest estimates suggest immunisation, also supporting an indirect protective effect of reduced exposure.

In mid-March, Novartis received European licensing approval to market its new quadrivalent conjugate vaccine against meningococcal A, C, Y and W-135 — and the company also expects to release results of pivotal phase III studies of a meningococcal B vaccine this year, with the product launched as early as 2011/2012.

Professor Borrow concludes: “The ideal solution will be a single vaccine against all types of meningitis, but that’s still some way in the distance. A great deal has already been gained by the Department of Health, the Health Protection Agency and pharmaceutical companies working together to get the new vaccines tested and licensed, and then incorporated into immunisation programmes. This co-operation has played a major role in enabling us to achieve the high levels of coverage and outstanding reduction in infection rates that have occurred in the past decade with the conjugate meningitis C vaccine.”

References

Parkinson's Disease in Focus
Charles Tugwell
Part of the ‘In Focus’ series, this text is an overview of the pharmaceutical care of patients with Parkinson's disease, providing practical information on the care, medication and management of patients.

Parkinson’s Disease in Focus provides a framework for good practice, with a particular focus on drug therapy management. Chapter contents include:

- The condition and its symptoms
- Pharmacotherapy
- Non-drug treatments
- Complementary therapies
- Surgical options
- Management of symptoms not specific to Parkinson’s disease
- Development and future treatments
- Specific drug interactions and adverse effects

Parkinson's Disease in Focus is an invaluable resource for pharmacists and other healthcare practitioners who are involved with patients suffering from the condition. It will also be helpful to students of pharmacy and medicine, and to patients and those who care for them.

To Order
Online: www.pharmpress.com
Pharmaceutical Press, c/o Macmillan Distribution (MDI), Burrell Road, Houndmills, Basingstoke, Hampshire, RG21 6XS, UK
Tel: +44 (0) 1256 302692 • Fax: +44 (0) 1256 812558/812521
Email: direct@macmillan.co.uk

The Americas
Pharmaceutical Press, 1573 S Paul Avenue, Glenview, Illinois, 60031 USA
Tel: +1 847 623 4747 • Fax: +1 847 244 6689
Email: orders_americas@pharmpress.com

For personal use only. Not to be reproduced without permission of the editor (permissions@pharm.org.uk)