

Newsletter

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Hot Topics 1

The effectiveness of meningococcal serogroup C conjugate vaccination in England and Wales

A summary of the seminar presented at NCIRS by Caroline Trotter, Modelling and Economics Unit, Communicable Disease Surveillance Centre, Health Protection Agency, UK (Nov 12, 2003).

In November 1999, the UK implemented a meningococcal serogroup C vaccination program (MCV) and was the first country in the world to do so. More recently the Netherlands and, in 2003, Australia also introduced mass vaccination programs. As these public health programs are new and unique they must be evaluated rigorously. Ms Trotter described an evaluation of the effectiveness of the MCV in England and Wales, which provides a valuable insight into what might be the expected impact in Australia.

Epidemiology of meningococcal disease in the UK before vaccination

Prior to the MCV, the UK had the highest rate of endemic meningococcal disease in Europe (6 per 100,000). As in Australia and North America, there was a high case fatality rate (8%), most cases were caused by serogroup B or C, and young children and adolescents had the highest rates.

From the mid 1990s there was an increase in both laboratory confirmed and clinical notifications of meningococcal disease in the UK. Some of this might have been explained by the introduction of more sensitive diagnostic laboratory tests (PCR). However, there was also

an increase in the proportion of serogroup C isolates from 25% in 1994/5 to 40% in 1996/7.

This increase was mostly due to the C2a strain, which is also the most commonly identified strain in Australia.

The UK meningococcal C vaccination program

As a response to the increasing rates of serogroup C meningococcal disease in the UK, a vaccination program was gradually introduced over a one-year period beginning in November 1999. The program included routine vaccination of infants aged 2, 3 and 4 months old as well as a catch-up campaign for all children under 18 years old (about 14 million). Delivery was through schools and GPs, with those most at risk targeted first due to problems with vaccine supply.

The impact of the UK meningococcal C vaccination program

Vaccination coverage

In 2000 vaccination coverage with the infant program was 80%. Coverage ranged from 76% to 89% for 1-14 year olds, but was lower for 15-17 year olds, especially those not in school (43%).

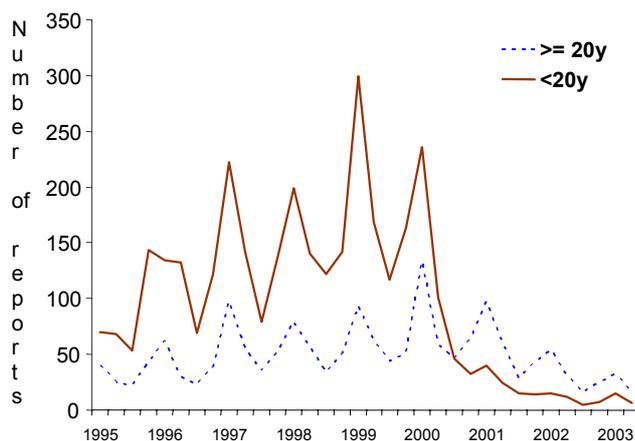
Vaccine effectiveness

The vaccine was licensed on the basis of safety and immunogenicity studies (phase I and II trials) only, as phase III efficacy studies would have taken a long time to perform. Therefore assessment of the effectiveness of the vaccine was an essential part of the evaluation of the campaign. Age-specific vaccine effectiveness was calculated to be above 90% for school-aged children and at least 84% for younger ages.

Disease burden

Following the introduction of the MCV, reports of serogroup C meningococcal disease declined dramatically in the age groups targeted by vaccination (Figure). There was also a targeted reduction in mortality; the number of deaths due to serogroup C in under 20 year olds fell from 80 in 1998/9 to 4 in 2002/3.

Figure-Reports of serogroup C meningococcal disease by month of onset and age group, England and Wales, 1995-2003



In contrast to the success of the MCV in targeted age groups, rates for older ages increased in 2000 (Figure). This led to an extension of the vaccination program to include ages up to 25 years, and by 2001/2 rates in the 20 years and over age group also began to fall.

Evidence of herd immunity

There is evidence that the high vaccination coverage levels have lowered serogroup C carriage in the nasopharynx and that this has led to reduced rates of disease in unvaccinated populations. Carriage studies conducted before

and after the implementation of the MCV, each involving over 14,000 teenagers, found the prevalence of serogroup C carriage was 66% lower one year after the introduction of the MCV.¹ In addition, the attack rate of serogroup C disease in unvaccinated individuals in the age range targeted in the MCV was found to be 67% lower in 2001/02 compared to 1998/99.²

No evidence of increase in other serogroups

Although there has been proportionally more serogroup B isolates since the MCV was implemented, there has been no absolute increase in number. Importantly there is no evidence to suggest that capsular switching has occurred between the predominant C2a strain and B2a.

Conclusion

In summary, the MCV in England and Wales has achieved high coverage and effectively reduced the incidence of serogroup C meningococcal disease in targeted age groups. Rates have also decreased amongst unvaccinated individuals due to lower carriage rates. At this stage, there is no evidence to suggest replacement of serogroup C strains with other serogroups.

References

1. Maiden MC, Stuart JM, The UK Meningococcal Carriage Group. Carriage of serogroup C meningococci 1 year after meningococcal C conjugate polysaccharide vaccination. *Lancet* 2002;359(9320):1829-31.
2. Ramsay ME, Andrews NJ, Trotter CL, Kaczmarski EB, Miller E, Herd immunity from meningococcal serogroup C conjugate vaccination in England: database analysis. *BMJ* 2003; 326(7385):365-6.

Festschrift for Professor Margaret Burgess AO on 5-6 February 2004

A two-day program has been organised in honour of Professor Margaret Burgess' retirement. Guest speakers include Professor Felicity Cutts (UK) and Professor Stanley Plotkin (USA). Topics covered include 'Vaccines for the 21st Century' and 'Congenital and neonatal infections'.

Venue: The Children's Hospital, Westmead, NSW Australia and The Children's Medical Research Institute, Westmead, NSW Australia

Registration Fee: \$55 GST inclusive covers lunch, morning and afternoon tea breaks

Further enquiries: The program and registration forms are available at www.ncirs.usyd.edu.au/publications. Alternatively contact Jan Michniewicz at NCIRS on tel (02) 9845 3075, fax (02) 9845 3082 and email janm4@chw.edu.au

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Hot Topics 2

Surveillance of adverse events following immunisation (AEFI)

The routine, ongoing AEFI provides important information about vaccine safety and program delivery, guides policy decisions and monitors the impact of changes to the immunisation schedule on the incidence of AEFI. Routine AEFI surveillance has been a feature of Australia's immunisation programs for many years, yet its existence is less well known than it should be.

An overview of the system was published recently in a report co-authored by NCIRS staff (*Communicable Diseases Intelligence* 2003;27:307-23). The report also summarised national AEFI surveillance data collated in the Adverse Drug Reactions Advisory Committee (ADRAC) database, which is administered by the

Therapeutic Goods Administration (TGA). This national database holds all reports of AEFIs in Australia received from doctors, other health professionals, hospitals, parents, vaccine companies, and State and Territory Health Departments.

NCIRS has taken on a role in the regular analysis and reporting of national AEFI surveillance data. We plan to publish reports annually for all data and as required for specific vaccines of interest. In the first report, we estimated, for the first time, national AEFI reporting rates per 100,000 doses of the frequently administered vaccines in Australia, using ACIR and influenza coverage data. These estimates allow meaningful comparisons of AEFI reporting rates for different vaccines and age groups and provides important information for immunisation providers and parents.

Hot Topics 3

DTPa immunisation schedule changes

The National Health & Medical Research Council (NHMRC) endorsed Australia's new immunisation schedule in September. The timing of booster doses of diphtheria-tetanus-acellular pertussis (DTPa) vaccine was one of several major changes. With the previous schedule, booster doses were given at 18 months & 4 years of age after the 3-dose primary course at 2, 4 & 6 months of age. The 18-month booster dose has been removed from the new schedule & a booster dose added for adolescents aged 15-17 years.¹ These changes to the DTPa immunisation schedule were evidence-based decisions.

1. National Notifiable Diseases Surveillance System (NNDSS) show that pertussis notification rates among children aged <10 years declined dramatically following the introduction of 4-year (5th) DTPa booster doses.² Pertussis notification rates are now highest among adolescents, compared with other age-groups, due to waning immunity 6-10 years after the 4-year dose.² Targeting this age group with the adult/adolescent DTPa vaccine formulation aims to reduce pertussis incidence and transmission among adolescents and young adults, and their contacts.

2. The removal of the 18-month booster dose from the schedule was related to the relatively high rates of large local reactions and extensive

Picture: Child with extensive swelling of upper arm following a 5th dose of DTPa vaccine (seen at the Immunisation Adverse Events Clinic, The Children's Hospital at Westmead)



limb swelling following the 18-month & 4-year booster doses of DTPa (pictured).³⁻⁸ One study estimated that 2-6% of children receiving booster doses of DTPa vaccines experience these reactions, which are not painful and resolve without sequelae.^{3,5,7,8}

3. Immunity conferred by the primary DTPa course is likely to last up to 6 years of age,⁹ beyond the time when the 4-year booster dose is due. The risk of a severe local reaction appears to outweigh the benefit of the 18-month booster dose. Following the decision to remove this dose from the schedule, it will be important to reassure parents whose children have experienced a local reaction about the importance of the 4-year booster dose prior to school entry.

The impact of the new DTPa immunisation schedule must be monitored via the routine disease, adverse events and immunisation coverage surveillance systems. Specific measures will include changes in the age-specific incidence of pertussis, the age-specific reporting rates of AEFIs (particularly severe local reactions), and coverage rates of the 4-year DTPa booster dose.

A list of references for this article is available on request

Recent NCIRS Publications

- ◆ Lawrence G, Menzies R, Burgess M, McIntyre P, Wood N, Boyd I, Purcell P, Isaacs D. Surveillance of adverse events following immunisation: Australia 2000-2002. *Communicable Diseases Intelligence* 2003;27:307-23.
 - ◆ Leask J, McIntyre P. Public opponents of vaccination: a case study. *Vaccine* 2003;21:4700-3
 - ◆ Hull BP, Lawrence GL, MacIntyre CR, McIntyre PB. Immunisation coverage in Australia corrected for under-reporting to the Australian Childhood Immunisation Register. *Australian and New Zealand Journal of Public Health* 2003;27:533-8.
 - ◆ MacIntyre CR, Leask J. Immunisation myths and realities. *Journal of Paediatrics and Child Health* 2003;39:487-91.
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Recent journal club topic

Varicella vaccine failure - why?

Verstraeten T, *et al. Pediatrics* 2003;112:e98

Varicella breakthrough disease occurring more than 42 days post-vaccination indicates vaccine failure. This study investigated the association between vaccine failure and asthma, use of inhaled or oral steroids, the age at vaccination, and the timing of varicella vaccination following measles-mumps-rubella (MMR) vaccination. The investigators conducted a retrospective cohort study, using linkage of vaccination, medical and pharmacy records, among children enrolled in two health maintenance organisations (HMO) who were at least 12 months old when they received a varicella vaccination.

In HMO A, 80 584 children were studied (median follow-up of 21.3 months) and 268 cases of vaccine failure were identified. For HMO B, 8 181 children were studied (median follow-up of 14.7 months) with 97 cases of vaccine failure. The study team found that vaccine failure was not associated with asthma, inhaled steroids at any time, or oral steroids prescribed before vaccination. However, there was an increased risk at HMO A when varicella vaccination occurred less than 28 days following MMR vaccination (adjusted relative risk (aRR) 3.1, 95% CI 1.5-6.4), and when varicella vaccine was given before 15 months of age (aRR 1.4, 95% CI 1.1-1.9). In both HMOs, there was an increased risk of vaccine failure in the three months following a prescription for oral steroids for any condition (HMO A: aRR 2.4, 95% CI 1.3-4.4; HMO B: aRR 2.8, 95% CI 1.0-7.8).

These data illustrate for the first time the importance of the recommendation that varicella vaccination should not occur less than 28 days following MMR vaccination, and the slightly increased risk of vaccine failure if varicella vaccination occurs before 15 months of age. The finding in relation to oral steroids requires further study to determine whether the drug itself or conditions treated with the drug are associated with vaccine failure. That neither asthma nor inhaled steroids was associated with vaccine failure is reassuring in view of the large number of children in developed countries such as Australia who are diagnosed with asthma and managed with inhaled steroids.

NCIRS -AIP Australian Immunisation Professionals

The NCIRS-AIP electronic email discussion list is now available. To subscribe to this group please log on at <http://mailman.ucc.usyd.edu.au/mailman/listinfo/ncirs-aip> and follow the instructions.

This group will facilitate communication between Australian immunisation practitioners, policy makers and researchers and has been modelled on a similar group in the UK. Items proposed for inclusion are in three main categories:

1. News items/publications and meetings of interest,
2. A forum for questions and feedback, and
3. An avenue for rapid information about media controversies.