

Newsletter

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**Merry Christmas and best wishes for a safe and happy New Year
From everyone at NCIRS**



Hot Topic 1

Varicella - update

Each month in Australia a median of 133 people are hospitalised with varicella (chickenpox) infection, and each year there are an average of 8 deaths due to varicella. A vaccine against varicella has been available in Australia for over 4 years. In 2003 varicella vaccination was added to the Australian Standard Vaccination Schedule for all children aged 18 months and at 10-13 years for those who do not have a history of varicella disease. However, the availability of varicella vaccine has been limited to the private market and vaccine uptake has been low. It has been estimated that, nationally, less than 10% of 1-4 year old children have received varicella vaccine.

In the United States, a universal varicella vaccination program has existed for 9 years. The vaccine is available for all children aged 12 months and older, and is required for day care and/or school entry in most states. By 2003 varicella vaccine coverage among children in the U.S. aged 19-35 months had reached 85%. A substantial decline in varicella disease incidence, morbidity, hospitalisations and deaths has occurred. The burden of disease from varicella has declined by 90%. Varicella-related deaths have fallen from an average of 105 per year to 26 deaths in 2001, and even fewer in recent years. Morbidity and mortality from varicella have also

declined markedly in adolescents and adults as a result of herd immunity.

Vaccine effectiveness in community-based studies in the U.S. remains high at around 85% although breakthrough disease (natural infection of vaccinees) does occur. Cases of breakthrough chickenpox in vaccinees are usually mild but can be contagious (although much less so than natural infection). This highlights the need for health care providers and parents to be aware of breakthrough infection and its clinical appearance. Preliminary information from surveillance areas regarding the impact of varicella vaccination on the incidence of herpes zoster (HZ) in the U.S. suggests a decline in the rate of HZ among children, and no change in the rate of HZ among adults. Ongoing surveillance of HZ is important in light of the suggestion from mathematical modelling in the United Kingdom that the incidence of HZ, and therefore the overall burden from varicella-zoster virus, could increase following the introduction of widespread varicella vaccination.

Some jurisdictions in Canada and Italy fund routine varicella vaccination programs. Several other countries, including 10 in Europe, have targeted varicella vaccination programs.

References for this article are available on request.

Hot Topic 2

Vaccine Storage- 'Keep it cool'

A summary document of proceedings from the National Vaccine Storage Workshop held in Brisbane in June 2004 is now available. The workshop was attended by representatives of health agencies from most Australian jurisdictions as well as NCIRS, WHO, New Zealand, the Therapeutic Goods Administration and the Pharmacy Guild of Australia. The objectives of the workshop were (1) to produce a set of structured proceedings to provide key material and background to inform the updating of 'Keep it Cool' and to assist policy development and (2) to identify and share useful information related to vaccine storage.

The proceedings document contains lots of really useful background information and papers on vaccine storage, including chapters on: effects of heat and cold on vaccines; technical issues with refrigerators; issues with temperature monitoring, measuring and recording; buying a purpose- built vaccine refrigerator; storage and transport of vaccines; principles of managing a breach; and vaccine cold chain management training.

The summary document is available on the Commonwealth Immunisation website at

<http://immunise.health.gov.au/vaccinestorage.htm>



The 'Camel Fridge' is one of the world's leading solar electricity vaccine refrigerators for use in remote parts of the world.

A revised version of the current 'Keep it Cool' guidelines document will be released in 2005.

Recent NCIRS Publications

- ◆ McIntyre P. Festschrift for Margaret Burgess - Foreword. *Expert Review of Vaccines* 2004;3:337.
- ◆ McIntyre P. Vaccine strategies for prevention of neonatal pertussis. *Expert Review of Vaccines* 2004;3:375-8.
- ◆ Andrews RM, Counahan ML, Hogg GG, McIntyre PB. Effectiveness of a publicly funded pneumococcal vaccination program against invasive pneumococcal disease among the elderly in Victoria, Australia. *Vaccine* 2004;23:132-8.
- ◆ Lawrence GL, Boyd I, McIntyre P, Isaacs D. Surveillance of adverse events following immunisation: Australia 2002 to 2003. *Communicable Diseases Intelligence* 2004;28:324-38.
- ◆ Brotherton JML. Festschrift for Margaret Burgess. *Communicable Diseases Intelligence* 2004;28:349-55.
- ◆ Leask J, Williams A, McIntyre P, O'Dea D. Are General Practice Registrars prepared for immunisation? A cross sectional survey. *Australian Family Physician* 2004;33:665-7.
- ◆ McIntyre PB, Turnbull FM, Egan A, Burgess MA, Wolter JM, Schuerman LM. High levels of antibody in adults three years after vaccination with a reduced antigen content diphtheria-tetanus-acellular pertussis vaccine. *Vaccine* 2004;23:380-5.
- ◆ Ackermann D, Chapman S, Leask J. Media coverage of anthrax vaccination refusal by Australian Defence Force personnel. *Vaccine* 2004;23:411-7.

Report: Festschrift for Prof Margaret Burgess AO, 5-6 February 2004

NCIRS is pleased to offer you the opportunity to purchase a fully bound copy of a selection of papers presented at the Festschrift for Professor Margaret Burgess AO in February 2004.

The papers include: Clinical principles. S Prescott; Developmental immunology & vaccines in premature infants. D Robertson; Vaccines against Neonatal Herpes. C Jones; Hepatitis B virus. F Cutts; Developing a live respiratory syncytial virus vaccine. F Malinoski; Rotavirus. G Barnes; Neonatal immunisation for pneumococcal disease. P Richmond; Is neonatal group B streptococcal disease vaccine preventable? L Gilbert; Neonatal pertussis. P McIntyre; Tuberculosis. W Britton.

It is available for only A\$16.50ea (incl. GST). To order please contact NCIRS on 02 9845 0520, or Email **Jan Michniewicz** (janm4@chw.edu.au) or **Kirsty Whybrow** (kirstyw@chw.edu.au)

Recent Journal Club topics

Efficacy of RIX4414 live attenuated human rotavirus vaccine in Finnish infants, Vesikari et al. *Pediatr Inf Dis Journal* 2004;23:937-943.

Rotavirus gastroenteritis (RV GE) causes considerable morbidity & mortality worldwide. Previously a tetravalent rhesus-human rotavirus vaccine, was licensed in the USA but was withdrawn in 1999 due to a small but real increase in the rate of intussusception. A human serotype G1, P1A rotavirus isolate 89-12 has been developed as a vaccine candidate by passage in tissue culture. Bernstein et al (*Lancet* 1999;354:287-290) showed that the vaccine had 89% efficacy against any RV GE and 100% efficacy against severe infection in 1st year post vaccination but was 'mildly reactogenic' in 3-5mo infants. To reduce the reactogenicity of the vaccine, strain 89-12 was further passaged and cloned in vero cells in Rixensart, to produce the RIX4414 vaccine. Earlier this year Vesikari et al (*Vaccine* 2004) demonstrated that the vaccine was immunogenic and well tolerated in 2-4mo Finnish infants. The present study evaluated the efficacy and immunogenicity of the vaccine following the cohort for two epidemic seasons.

This study was a randomised, double blind, placebo controlled trial. 40% of parents of newborns approached by phone enrolled (n=405) in Aug-Nov 2000 at 6 sites in Finland. The 1st dose was given at mean 8.3 weeks (6-12) & 2nd dose at mean 16.2 weeks (10-27). Doses were given orally by syringe (1mL). Parents recorded daily rectal temperatures, diarrhoea, vomiting, irritability, and loss of appetite for 15 days after each vaccination. All other symptoms or signs were recorded for 43 days post vaccination. IgA serology was measured before the 1st dose, 1 month after the 2nd dose and at the end of each rotavirus season. Active fortnightly phone surveillance for acute GE occurred during each rotavirus season (Dec 1- June 1). Parents contacted the study team outside these times if infant developed GE. Two stools samples were collected on consecutive days. Samples were classified positive for rotavirus if ELISA & PCR were positive.

The vaccine was well tolerated, with no significant differences in rates of fever, gastroenteritis, irritability or loss of appetite between vaccine and placebo groups. Five infants dropped out for perceived vaccine related side effects including four vaccine recipients who developed mild GE a few days after vaccination. There were no cases of intussusception.

In the both years there was a 73% reduction in any RV GE for the vaccine group compared with placebo and in year 1 a 90% reduction for severe RV GE, falling to 83% in year 2. Overall there was a 72% (42-87) efficacy for any RV GE ($p<0.001$) and 85% (42-97) efficacy for severe RV GE ($p=0.001$). GE from any aetiology (RV or other) occurred at similar rates in both groups (66% v 65%).

The vaccine produced lower seroconversion rates than the parent vaccine but had comparable efficacy to other rotavirus vaccines. It was less reactogenic (fever and diarrhoea) than the parent vaccine or Rotashield. The vaccine induced protection against subclinical infection, but not protection against other RV serotypes.

Epidemiology of invasive *Streptococcus pneumoniae* among Navajo children in the era before use of conjugate pneumococcal vaccines, 1989-1996. O'Brien et al. *Am J Epidemiol* 2004;160:270-278.

This paper provides the results of enhanced surveillance carried out in health services in and around the Navajo lands in the U.S. The highest rates of invasive pneumococcal disease (IPD) recorded in the world are in Aborigines in Central Australia, followed by several Native American tribes, including the Navajo. The reasons for the high rates in the Navajo were regarded as most likely to be due to living conditions, exposure to environmental smoke from home heating and exposure to large numbers of children.

The study found that the rate of IPD in Navajo children aged 0-23 months decreased by around two thirds between 1989 and 1996, before the introduction of vaccination in 2000. This trend was not seen in the general population. The reasons for the decrease were not clear, but could include improvements in living conditions, changes in referrals for culture after the introduction of Hib vaccine, and herd immunity from limited use of pneumococcal vaccine in adults. The age group with the highest rate was 6-11 months, younger than the general US population, where the highest rate is in the 12-23 months group. In those with IPD, meningitis was more commonly found in younger children (<2 years) and pneumonia in older children (3-18 years). 61% of cases were 7-valent vaccine serotypes, although this decreased over time to only 51% between 1994-1996. The percent of cases covered by the 9-, 11-, and 23-valent vaccines were 72%, 75% and 87% respectively.

Commonly asked immunisation questions (and answers!)

In this newsletter feature, we share some of the commonly asked questions we receive. If you have any "common questions" that you'd like to see addressed in this format, please e-mail us (karynp@chw.edu.au) & we'll publish the answer in an upcoming newsletter.

1. What is the minimum time period between doses for the primary course of 7-valent conjugate pneumococcal vaccine (*Prevenar*), starting at 2 months of age?

The Australian Standard Vaccination Schedule (ASVS) recommends that the primary course of conjugate pneumococcal vaccine (7vPCV) is given at the ages of 2, 4 and 6 months of age. For healthy older infants catching up, 2 doses, with a recommended spacing of at least 2 months apart, are recommended for children aged 7 to 17 months, and a single dose is recommended for children aged 18-23 months.

Should a more rapid catch up be desired, to bring a child's 7vPCV visits in line with other scheduled immunisations for instance, the minimum spacing of vaccine doses, as per the Product Information, is one month apart. However this is NOT routinely recommended practice and where possible providers should adhere to the recommended schedule. Providers should note that the absolute minimum spacing for any vaccine dose including 7vPCV, in order for it to be recorded as valid on the Australian Childhood Immunisation Register, is at least 27 days.

Ref: *The Australian Immunisation Handbook 8th Edition*, pages 229-232.

2. Is there any problem with giving Varicella-Zoster vaccination before the recommended age of 18 months?

The NHMRC recommends that children aged between 12 months and 13 years receive one dose of vaccine and this is routinely scheduled for administration at 18 months of age, or as a catch up for those without previous history of the disease at 10-13 years. The recommended age for administration is 18 months both for convenience, with 3 other vaccines due at 12 months of age, and because there is some evidence from investigations of varicella outbreaks that younger age at vaccination (ie below 15 months) may be associated with an increased risk of developing break-through varicella infection.

One of the available brands of vaccine, Varilrix, is approved by the TGA for use in Australia from the age of 9 months. However, this is not recommended as routine practice. In an outbreak setting such use may be appropriate and may provide some protection.

Adolescents 14 years and over and adults require 2 doses of varicella-zoster vaccine one to two months apart.

Ref: *The Australian Immunisation Handbook 8th Edition*, pages 280-281

Galil K, Fair E, Mountcastle N, Britz P, Seward J. Younger age at vaccination may increase risk of varicella vaccine failure. *Journal of Infectious Diseases*. 2002;186:102-5.

3. What is the recommended spacing between Varicella-Zoster vaccine and any other live attenuated vaccine, including MMR?

Varicella-Zoster vaccine can be administered at the same time as other vaccines, including MMR, Hepatitis B, DTPa and Meningococcal conjugate C vaccine, using separate syringes and injection sites.

If Varicella-Zoster vaccine is not given simultaneously with other live attenuated virus vaccines, they should be given at least 4 weeks apart because there is an increased chance of a poor response to the vaccine and subsequent break-through varicella disease if given within 4 weeks.

Ref: *The Australian Immunisation Handbook 8th Edition*, pages 53 and 281

CDC. Simultaneous administration of varicella vaccine and other recommended childhood vaccines - United States, 1995-1999. *MMWR Morb Mortal Wkly Rep* 2001;50:1058-1061.

4. What catch up is required for children who previously resided overseas and instead of MMR have previously received monovalent measles vaccine only (eg some Asia-Pacific countries, some children from the UK?)

To be fully protected against measles, mumps and rubella children should receive 2 doses of MMR vaccine at least 4 weeks apart. In Australia MMR dose one is routinely scheduled at 12 months and dose two at 4 years of age. Having previously received a dose of monovalent measles, rubella or mumps vaccine is NOT a contraindication to MMR vaccine and is not associated with any increased risk of adverse events. Only monovalent rubella vaccine is available in Australia, thus full protection against measles, mumps and rubella can only be achieved through the use of MMR vaccine.

Ref: *The Australian Immunisation Handbook 8th Edition* page 53

Please note that answers provided here are consistent with current recommended practice but are not a substitute for individual medical advice.