Hot Topic 1
Future Vaccines for Australia

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A range of promising vaccines is likely to become available in Australia in the near future. The following is a brief overview of six such vaccines which may be of particular relevance to the Australian context.

Human papillomavirus (HPV)
HPV, the cause of genital warts, is oncogenic and persistent genital infection has been shown to be the cause of cervical cancer, the second-most common malignancy in women worldwide. A proof-of-principle HPV-16 vaccine (Merck) conferred up to 100% protection from HPV-16 infection. A bivalent HPV-16/18 vaccine (GSK) conferred 91.6% protection against incident infection, and 100% protection against persistent infection. A tetravalent HPV-16/18/6/11 vaccine (CSL Vaccines/Aventis Pasteur MSD) is currently undergoing Phase III clinical trials.

Herpes simplex virus (HSV)
Herpes simplex virus disease affects up to 80% of the Australian population, and is caused by the HSV type 1 (HSV-1) or type 2 (HSV-2). Biocine™ (Chiron) was found to be ineffective, with an overall efficacy of 9%. Simplirix™ (GSK) had a 74% efficacy against HSV-2 genital herpes disease in HSV-seronegative women, but only 40% efficacy overall - being ineffective in men, and HSV-seropositive women.

Varicella-zoster virus (zoster prophylaxis)
VZV is the causative agent of varicella (chickenpox), a ubiquitous childhood infection in Australia, with reactivation of the virus in later life resulting in herpes zoster (shingles). The risk of zoster is inversely correlated with the status of VZV-specific cell-mediated immunity. The existing live attenuated VZV Oka strain vaccine has been shown to stimulate VZV-specific cell-mediated immunity, and forms the basis of a version being developed as a zoster vaccine for persons aged 60 and over.

Neisseria meningitidis serogroup B
Neisseria meningitidis (meningococcus) infection results in acute bacterial meningitis or severe sepsis (meningococcaemia), with a high risk of death or permanent sequelae. Successful outer membrane vesicle (OMV) vaccines have been developed against specific epidemic strains in Cuba (VA-MENGOC-BC™; Instituto Finlay) and New Zealand (MeNZB™; Chiron). To date, efforts to produce a conjugated capsule polysaccharide vaccine against serogroup B disease have been unsuccessful, but efforts to develop a broadly efficacious vaccine continue.

Rotavirus
Rotavirus is the leading cause of acute gastroenteritis (AGE) in infants, especially in developing countries, resulting in considerable morbidity and mortality worldwide. An efficacious vaccine, RRV-TV (Rotashield™; Wyeth) was introduced in the USA in 1998, but withdrawn due to association with intussusception. More recently, Rotarix™ (GSK) has been licensed in Mexico, and was found in studies to be 72% efficacious against any rotavirus AGE, and 85% efficacious against severe rotavirus AGE. Rotatet™ (Merck) is currently undergoing Phase III evaluation. A developmental version of the vaccine showed 74.6% efficacy in preventing rotavirus AGE, and 100% efficacy in preventing severe rotavirus AGE.

Influenza virus (intranasal live attenuated vaccine)
Influenza virus is a common infection with the potential to cause serious complications in high risk groups. Existing influenza vaccines are trivalent inactivated influenza vaccines (IIV) administered by the subcutaneous or intramuscular route. FluMist® (MedImmune) is an intranasal, trivalent, cold-adapted, live, attenuated influenza virus vaccine (LAIV), introduced in the USA in 2003 for use in healthy persons aged 5 to 49 years. LAIV was found to have an efficacy of up to 93% in children and confer cross-protection against poorly-matched influenza strains. It was also found to be safe and efficacious in adults. Further studies are underway to obtain data for use in children under 5 and adults over 50 years of age.

A list of references for this article is available on request.
Recent Journal Club topic

The epidemiology of N. meningitidis (NM) infection varies globally. The CDC in Taiwan conducts active surveillance of various infectious diseases. Between 1996-2000, 10-20 cases of NM were reported per year (population 22 million). There is a low incidence of NM in Taiwan, as shown in previous studies, but an increase in incidence of NM was reported in 2001.

The authors identified 659 cases between 1950-2001. The annual incidence peaked in 1953 (78 cases, 0.94/105) and decreased in the next 30 years to a very low incidence in 1975-1979, and no cases during 1980-87. There were 42 cases in 2001, the "epidemic" year. The mean age of cases was 19 years, 33% were serogroup B (compared to 85% in 1999) and 42% serogroup W-135. In 2001, the case fatality rate was 26% (43% for group B). Four major clones (2 B, Y, W-135) were found at different times and regions in 2001, none genetically related to overseas outbreaks. The cause of the emergence of meningococcal disease in Taiwan is unclear. Increased recognition and diagnosis may be a factor, but there is no apparent reason for increased diagnosis in 2001 compared to other years. The Taiwan experience shows how variable the epidemiology of NM can be, with significant, unexplained changes in both incidence and serogroup. The lesson for Australia is that good surveillance of NM is essential in view of our recent vaccination programs.

Hot Topic 2
New NCIRS Co-Director,
Professor Robert Booy

Professor Robert Booy joined NCIRS in early March. Professor Booy has taken up the role of Co-Director with a particular remit for research.

Professor Booy is a medical graduate of the University of Queensland (1984) and trained in Paediatrics at the Royal Children’s Hospital, Brisbane.

In 1990, he joined Professor Richard Moxon’s Department of Paediatrics, University of Oxford, as a Research Fellow in charge of co-ordinating phase II and III studies of the Hib conjugate vaccine. Subsequently, he designed and implemented a national phase IV post-marketing study, which addressed long-term effectiveness of the Hib conjugate vaccine. This was done with the British Paediatric Surveillance Unit. His MD thesis was entitled Haemophilus influenzae type b: epidemiology and evaluation of vaccination.

In 1994, Professor Booy moved to Professor Mike Levin’s Department of Paediatrics, St Mary’s Hospital, London, to work as a Lecturer in Paediatric Infectious Diseases. In 1996, he was awarded a Wellcome training fellowship in epidemiology focusing on genetic factors important in meningococcal disease.

In 1999, he was appointed Professor of Child Health at St Bartholomew’s and the Royal London School of Medicine & Dentistry, Queen Mary & Westfield College, University of London.

He has interests in influenza, varicella, HPV, Hib, pneumococcal and meningococcal disease; in particular, documenting the morbidity resulting from disease, understanding genetic factors important in susceptibility to, or severity of, disease, testing the effectiveness of vaccines and assessing risk factors for disease and efforts in the community, primary care and hospital settings to improve outcomes.

Recent Journal Club topic

NCIRS is pleased to announce that there are now over 200 Australian immunisation professionals subscribed to the NCIRS-AIP email discussion list...and the number is still rising!

NCIRS-AIP is an electronic email discussion group that has been set up for Australian immunisation professionals. This group facilitates communication between Australian immunisation practitioners, policy makers and researchers. If you are interested in subscribing to this group, please log on at http://mailman.ucc.usyd.edu.au/mailman/listinfo/ncirs-aip and follow the instructions located there.
Recent NCIRS Publications


Hot Topic 3
Travel vaccination

The Australian Government Department of Health and Ageing has recently published the document “Health precautions for humanitarian workers travelling to tsunami-affected areas”. The purpose of this document is to provide information about personal health protection to people who are planning to travel to tsunami-affected areas in Asia as a member of a health or humanitarian relief team (Link: http://www.health.gov.au/internet/wcms/publishing.nsf/Content/phd- tsunami_relief.htm/$FILE/relief_teams.pdf).


Hot Topic 4
Clinical Trials

Newborn pertussis vaccine trial
Pertussis deaths are now almost exclusively in infants less than 3 months of age and possibly preventable by early vaccination. This trial compares the immunogenicity and adverse reactions of two schedules of acellular pertussis vaccine commencing at birth versus controls commencing at 2 months of age. It is being conducted by NCIRS in collaboration with Women’s and Children’s Hospital in Adelaide.

Influenza vaccine trial
NCIRS is one of the centres involved in an immunogenicity trial of a reduced formulation 2005 southern hemisphere Sanofi Pasteur influenza vaccine. Fifty patients were recruited into this trial, the aim of which is to measure the immune response following vaccination with an influenza vaccine that has a reduced amount of the A/Wellington antigen than is recommmended and results will be available very shortly.

Long term immunity following hepatitis B vaccination in infancy
NCIRS is involved in a study examining long term immunity following hepatitis B vaccination in infancy, in children who were vaccinated as part of a targeted program. This study is being conducted in South Western Sydney in partnership with Dr Leon Heron at Sydney South West Public Health Unit.

Pneumococcal conjugate vaccine in hospitalised elderly
NCIRS is about to commence a pneumococcal conjugate vaccine trial in the elderly hospitalised at Westmead Hospital. This study is being conducted with Professor Richard Lindley of Westmead Hospital.
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. If I use the DTPa - Hexavalent combination vaccine for the primary immunisation schedule, is a further dose of Hib vaccine required at 12 months old?

Yes. The current DTPa -HepB-Hib-IPV vaccine contains purified Hib capsular polysaccharide 10 µg conjugated to 20-40µg of tetanus toxoid (PRP-T). Children require a fourth dose of any Hib containing vaccine at 12 months old to ensure immunity. Vaccines containing PRP-T do not achieve protective PRP antibody levels until at least after a second dose has been given and require 3 doses to complete primary immunisation. A 4th booster dose at 12 months old aims to provide long term immunity.

Ref: The Australian Immunisation handbook 8th Edition, p 130-1

2. Who should receive the pneumococcal polysaccharide vaccine?

The pneumococcal polysaccharide vaccine (23vPPV) contains polysaccharides derived from the 23 most frequent or virulent capsular types of *S. pneumoniae*. At least 90% of healthy adults respond to the vaccine with a 4-fold rise in type-specific antibody within 2 to 3 weeks. 23vPPV, like other polysaccharide vaccines, is not considered to be immunogenic in children aged under 2 years. 23vPPV is recommended for all adults aged 65 years and over, Aboriginal and Torres Strait Islander people aged 50 years and over and those aged 15-49 years with high-risk underlying conditions. 23vPPV is also recommended for all adults aged 65 years and over and those aged 15-49 years with high-risk underlying conditions. 23vPPV is also recommended for children over 5 years with underlying chronic illnesses, predisposing to invasive pneumococcal disease, asplenia or immunodeficiency (See Australian chronic illnesses, predisposing to invasive pneumococcal disease).


3. A 2-month-old was mistakenly given pneumococcal polysaccharide vaccine (23vPPV) instead of pneumococcal conjugate vaccine (7vPCV). What should be done?

23vPPV is not considered to be effective in children under 2 years old. However, there are no known significant side effects from its inadvertent administration. In this case 7vPCV should be administered shortly after the error was discovered, and the schedule for 7vPCV completed as usual. For children aged 2-5 years who have previously received 23vPPV vaccination because of a predisposing condition, The Australian Immunisation Handbook recommends that 1 dose of 7vPCV be administered at least 2 months after 23vPPV.


4. Do vaccines contain human cell lines?

Live attenuated viral vaccines, such as MMR and varicella vaccine, contain modified viruses that have been grown in cells (cell lines) in the laboratory. Viruses will only grow in cells, and usually only in certain cell types. For example, the rubella component of the MMR vaccine (Wistar RA 27/3 strain) requires propagation in the human WT-38 human diploid cell line. These cells were originally obtained from fetal tissue obtained following an abortion in 1966. However, since that time no new fetal tissue has been used for growth of the virus (the original cells change to adapt to growth in the laboratory - a cell line - and are stored in certified cell banks). Many religious organisations (that may oppose abortion) have supported the use of vaccination by coming to an understanding of the scientific process involved, and because of the enormous public health benefit of immunisation.

USA CDC website: http://www.cdc.gov/nip/vacsafe/concerns/gen/humancell.htm

5. A not so common but interesting question?

A child developed a patch of hair growth at the site of a recent vaccination. Has this reaction been previously reported?

Hypertrichosis (non sexual and non-androgen-dependent additional hair growth) has been associated with local trauma, malnutrition, eczema, thrombophlebitis, pretrialmyxedema, arthritis, corticosteroids, diazoxide and phenytin. Localised hypertrichosis has rarely been reported following vaccination with BCG, smallpox, diphtheria, tetanus and measles vaccines. It may be related to traumatic vaccination or the deposition of exogenous material such as aluminium or neomycin in the dermis. Hair loss and skin pigmentation have also been reported. Our local experience with such cases is that over time, usually some months, the hair falls out.

Pembroke A et al. Unusual cutaneous reactions following diphtheria and tetanus immunization. Clinical & Experimental Dermatology 1979; 43: 345-348

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