

Newsletter

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Hot Topics 1

Festschrift for Professor Margaret Burgess AO

In honour of the retirement of our director Margaret Burgess, NCIRS held a Festschrift on February 5th-6th 2004. The themes of the event were Vaccines for the 21st Century and Congenital & Neonatal Infections. International guests attended the Festschrift, as well as over 180 colleagues and co-workers from across Australia. A full summary of the presentations over these two fascinating days will be available on the NCIRS website soon.

Day One Presentations

Session One: Congenital rubella in Australia 1941-2004: Prof Margaret Burgess

Margaret described the important role researchers in Australia and especially those from the Royal Alexandra Hospital for Children have played in the story of rubella in pregnancy.

Rubella - the global picture: Prof Felicity Cutts

Professor Cutts discussed the global burden of rubella and congenital rubella syndrome (CRS) and estimates of the level of vaccination coverage required in each country to achieve herd immunity.

Rubella vaccination has been reported to be cost saving in both developing and developed countries. However, Professor Cutts cautioned that this doesn't mean infant vaccination should be introduced in all countries. Infant vaccination shifts the average age of infection upwards and

may increase the risk of infection in women of child-bearing age (and the risk of CRS) so it should only be introduced if sufficient coverage can be achieved.

Vaccines in the 21st Century: Prof Stanley Plotkin

Emeritus Professor Stanley Plotkin reflected on the history of vaccination and outlined his perception of six revolutions in vaccine development. Particular challenges and trends in vaccination in 2004 described by Professor Plotkin included the need for new combination paediatric and adult vaccines, the rise of adolescent vaccines; and trends in new vaccination targets such as for hospitalised patients, for pregnant women, against bioterrorism threats and against chronic infections. The main threats to vaccination in the 21st Century are issues of cost, supply, ensuring safety and anti-vaccinationism. Professor Plotkin reflected that we are in the golden age of vaccine development, in which it is feasible to produce any antigen we want for use in a vaccine, but that we currently lack sufficient knowledge of pathogenesis and immunology to choose the best antigens and methods of vaccination.

Session Two: The Australian Contribution to Vaccine Research

Historical background: Prof Sir Gustav Nossal

Professor Sir Gustav Nossal outlined the history of vaccine development in Australia from World War 1 to the present.

Vaccine trials in Australia: Prof Terry Nolan

Professor Terry Nolan outlined the recent history of vaccine trials in Australia from the 1980's until today. A range of governmental initiatives in the 1980's paved the way for increased trials and the broad range of subsequent vaccines successfully trialled was highlighted. Australia is an attractive site for industry sponsored trials. The road ahead promises new vaccines trialled by enthusiastic and dedicated researchers.

CRC for Vaccine Technology: Professor Anne Kelso

The Collaborative Research Centre for Vaccine Technology was established in 1993 with the aim of maximising the economic and social benefits of publicly funded vaccine research and design through collaboration between researchers, government and industry. In the past decade, the CRC has taken many novel ideas and transformed them into potential commercially successful products and along the way considerably enhanced the numbers of commercially aware PhD students and research managers in Australia.

The contribution of Prof Margaret Burgess:

Professor Kim Oates summarised the early years of Professor Margaret Burgess' professional life, starting with Margaret attending Fort Street Girls' High School through to her gaining a MD in 1971. A/Prof Peter Shaw and Dr Mary Bergin then summarised Margaret's involvement with the Oncology Department at Royal Alexandra Hospital for Children, Sydney. From 1972 until 1995, her work was shared between clinical work in the Oncology Department and research into vaccine preventable diseases.

In 1995, she became the Director of the Centre for Immunisation Research (CIR). In 1997, under her leadership, the Centre was successful in securing the Commonwealth's tender to become the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS).

A/Professor Peter McIntyre wrapped up the session with an impressive list of Margaret's achievements as Director of CIR/NCIRS. In 1998 Margaret became Professor of Paediatrics and Preventive Medicine from the

University of Sydney. She was awarded an Order of Australia in 2003 for services to public health in Australia and overseas. She has been a member of various committees and working parties at the State, National and International levels such as the Australian Technical Advisory Group on Immunisation (ATAGI), Department of Health and Ageing and National Health and Medical Research Council and the Strategic Advisory Group of Experts (SAGE) to the Department of Vaccines and Biologicals, World Health Organization (1999-2002). She is a patron of the NSW Deaf Children's Association. Margaret has authored at least 185 peer-reviewed articles and numerous books and book chapters. Peter finished with a poem particularly well suited to 'our' Margaret - "To Margaret" by Charles Lamb (1775-1834).

To Margaret

Margaret, in happy hour
Christen'd from that humble flower
Which we a daisy call!
May thy pretty name-sake be
In all things a type of thee,
And image to thee in all.

Like *it* you show a modest face,
An unpretending native grace;
The tulip, and the pink,
The china and the damask rose,
And every flaunting flower that blows,
In the comparing shrink.

Of lowly fields you think no scorn,
Yet gayest gardens would adorn,
And grace, wherever set,
Home-seated in your lovely bower,
Or wedded - a transplanted flower-
I bless you, Margaret!

Charles Lamb (1775-1834)

Day Two Presentations

Day two of the Festschrift focused on vaccines for the prevention of congenital and neonatal infections. A detailed summary of all presentations from Day 2 can soon be found on the NCIRS website at

<http://www.ncirs.usyd.edu.au>

Hot Topic 2

Planning for Human Papillomavirus (HPV) Vaccines in Australia

On 12 Dec 03 NCIRS brought together representatives from eight Australian research groups currently involved in HPV research & both vaccine manufacturers with current HPV vaccine candidates. The objectives of the meeting were to identify information needs & research priorities to inform national vaccination policy decisions & secondly, to foster links between research groups.

During the meeting updates on vaccine development & trial results were discussed, with results to date indicating that the vaccines are effective in preventing persistent infection with targeted HPV types, induce high titres of protective antibody & are safe. Groups represented were; NCIRS, Dept of Microbiology & Infectious Diseases, Women's & Children's Hospital, Melbourne, Centre for Immunology and Cancer Research, University of Qld, Division of Microbiology & Infectious Diseases, PathCentre, Dept of Infectious Diseases & Immunology, University of Sydney, Research & Registers Division, The Cancer Council NSW, Screening Test Evaluation Program, School of Public Health, University of Sydney, Vaccine & Immunisation Research Group, Murdoch Children's Research Institute.

Group discussions were held to determine future priorities for HPV research in Australia as it pertains to vaccination. These were: (1) adequate local knowledge of age/sex/type specific burden of disease. This should particularly focus on women most at risk & include the burden of disease from genital warts (2) data collection for, & undertaking of, health economic analyses that would inform decisions about population use of HPV vaccines and about the target groups for vaccination (especially in relation to the impact on screening programs); and (3) the need to develop an understanding of communication & implementation issues relating to HPV immunisation of adolescents & the general population.

Recommendations in HPV research were:

1. Epidemiological data collection is a priority using modern assays/genotyping & representative sampling, preferably across Australia, but if necessary focussing on those groups with potentially most to benefit from vaccination (high risk groups).
2. Measure type specific HPV prevalence now, &

after vaccine introduction (replacement studies).

3. Assess current burden of illness & costs from cervical cancer, genital warts & other HPV related diseases.
4. Plan for impact of vaccination on cervical screening and disease burden including modelling. Start developing epidemiological and health economic models to assess where we should be focussing on getting "harder" Australian data.
5. A focus on collaboration to ensure securement and efficient expenditure of adequate research funding.
6. Education/communication strategy research.
7. Utilise standardised serological test interpretation once available.
8. Ongoing assessment of the importance of sequence variation in L1 HPV 16 & 18.

The group plans to reconvene in 2004 to discuss ongoing research, results and collaborations.

A list of references for this article is available on request.

Human Papillomavirus (HPV) and vaccination

HPV is the most common viral sexually transmitted infection, with estimates that up to 75% of people are infected at some time (Koutsky 1997). Whilst most infection resolves without symptoms, some HPV infections can persist & cause cancer. In particular, the role of HPV infection in causing cervical cancer, the 2nd most common cause of cancer in women worldwide, is undisputed. Approx. 470,000 cases of cervical cancer & 235,000 deaths occurred worldwide in 2000 (Ferlay, 2001). Most of this disease occurs in the developing world. Other HPV types cause skin warts & may cause other anogenital cancers, oral & laryngeal cancers.

In Australia, cervical cancer is the 11th most common cancer in women. Almost 800 new cases occur annually (7.1 per 100,000 women) with 262 deaths in 2001 (AIHW 03).

HPV exists as over 200 types but only some of these types cause cancer. International prevalence surveys of HPV types in invasive cervical cancer have shown that the most common types of HPV found in cancers are types 16 & 18 (Walboomers 1999, Clifford 2003). HPV 16 is the most common type in every country.

The recent development of vaccines that produce antibodies to protect against persistent infection with cancer causing HPV types holds promise for the primary prevention of both cervical cancer & its precursors. Vaccines against the cancer causing HPV types 16 & 18 & against 6 & 11 (which cause genital warts) are in current clinical trials. Early results are promising with vaccine providing 100% protection (95%CI 90-100%) against persistent infection with targeted HPV types (Koutsky 2002). These vaccines are likely to become available in the next few years. According to a recent meta-analysis of prevalence data, vaccinating against HPV16 & 18 could prevent over 70% of invasive cervical cancers worldwide (Clifford 2003).

NCIRS Pilot MMR Decision Aid

A web-based **Decision Aid** designed to assist parents to decide whether to vaccinate their children with the measles, mumps and rubella (MMR) vaccine is currently being piloted by NCIRS.

The decision aid contains information about vaccine risks and benefits in numerical and graphical format, clarifies parental values and encourages parents to consider the implications of their vaccination decisions.

Please encourage parents and caregivers to use this interactive information tool to assist them to make decisions about MMR vaccination. The decision aid is available on

www.ncirs.usyd.edu.au/decisionaid

Recent Journal Club topics

Should we afford universal conjugate pneumococcal vaccine?

There has been controversy and adverse publicity over the Government decision to fund pneumococcal conjugate vaccine for selected high-risk groups, but not for all children. Much of the controversy has centred around an unfavourable comparison with the Government decision to fund immunisation with the meningococcal C conjugate vaccine, including catch-up, for all children aged 1 to 17 years old.

In this presentation NCIRS Journal Club members discussed:

1. the basis for current funding recommendations by the Australian Technical Advisory Group on Immunisation (ATAGI),
2. the current mechanism for funding vaccine and alternatives,
3. the wisdom, or otherwise, of public criticism of the Government decision not to fund universal childhood pneumococcal conjugate vaccine, and
4. the best way to provide the best achievable immunisation schedule for Australian children.

Effectiveness of inactivated influenza vaccine in preventing acute otitis media in young children. A randomized controlled trial. A Hoberman, DP Greenberg, JL Paradise, et al JAMA 2003;290:1608-1616.

Use of influenza vaccine in young children is topical as the American Academy of Paediatrics has recently recommended it for all children 6-24 months of age based on high rates of hospitalisation for influenza in this age group. This study, which follows earlier ones showing a reduction of AOM in otitis-prone children and those attending day care (two groups which may be very similar), looked at children in primary care and in the community in Pittsburgh, USA.

The study showed that although a significant reduction in influenza could be shown (66% efficacy) this was limited to the year where there was high influenza activity. During this first year of the study, 16% of the children randomised to placebo developed influenza compared to 6% of vaccine recipients. However, no corresponding decrease in overall respiratory infection, otitis media, GP visits or hospitalisations could be shown in either year of the study.

This study highlights the fact that influenza prevention may not translate into an easily measurable impact in other important health outcomes where influenza is only a minor overall contributor to total disease burden like otitis media even in epidemic years. It also highlights the paradox that while the youngest children have the highest rates of flu injection they may have lesser vaccine responses. Reduced rates of AOM were only shown in the oldest children (19-24 months), similar to previous studies which mainly looked at older children.

Recent NCIRS Publications

- ◆ Gidding HF, MacIntyre CR, Burgess MA, Gilbert GL. The seroepidemiology and transmission dynamics of varicella in Australia. *Epidemiology and Infection* 2003;131:1085-9.
 - ◆ McIntyre P. Pneumococcal disease. In: Thomson N (ed). *The health of Indigenous Australians*. South Melbourne: Oxford University Press; 2003.
 - ◆ Butler JRG, MacIntyre P, MacIntyre CR, Gilmour R, Howarth AL, Sander B. The cost-effectiveness of pneumococcal conjugate vaccination in Australia. *Vaccine* 2004;22:1138-49.
 - ◆ Forrest JM, Burgess M, Donovan T. A resurgence of congenital rubella in Australia? *Communicable Diseases Intelligence* 2003;27:533-6.
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NCIRS-AIP Australian Immunisation Professionals (AIP)

NCIRS-AIP is an electronic email discussion group that has been set up for Australian immunisation professionals. The group facilitates communication between Australian immunisation practitioners, policy makers and researchers. It is modelled on a similar group in the United Kingdom.

Discussion items include;

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

The group is designed chiefly for professionals involved in immunisation in Australia, whether at the level of research, policy development or as immunisation providers. NCIRS welcomes into the group all Australian professionals, as well as professionals in other countries who wish to learn more about immunisation in Australia, and/or wish to communicate their experience with us. Subscribers to NCIRS-AIP receive regular international updates on immunisation news (news briefs) and weekly summaries and commentaries on recent papers presented and discussed at the NCIRS Journal Club.

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 or visit our website at <http://www.ncirs.usyd.edu.au/newsevents/index.html>

Commonly asked immunisation questions (and answers!)

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

Do you need to provide catch up if a baby missed their birth dose of hepatitis B vaccine?

The purpose of the birth hepatitis B is to reduce the chance of vertical transmission from mother to baby and to provide some protection from household transmission in the neonatal period. Prior to 8 days of age catch up should be provided to babies who miss out on their birth dose. After this age no catch up is required (provided the mother is HbsAg negative) and infants should commence their three-dose hepatitis B schedule at 2 months of age. Infants given hepatitis B vaccine in combination with Hib (PRP-OMP) (trade name Comvax) receive doses at 2,4 and 12 months of age. Infants given hepatitis B vaccine in combination with DTPa (trade name Infanrix-HepB) receive doses at 2,4 and 6 months of age.

Reference: *The Australian Immunisation Handbook 8th edition*, page 151.

Is it okay to proceed with the 2nd dose of chickenpox vaccine if a vesicular rash develops after the 1st dose (in those requiring two doses, ie. those aged 14 years and over)?

Maculopapular or papulovesicular rashes may

develop after varicella-zoster vaccination (in 6-10% of recipients.) Rashes with early onset (within two weeks of vaccination) are likely to be due to co-incidental wild type varicella-zoster virus, whereas rashes developing later are more likely to be vaccine related. In either case, the second dose can still be given - serology is not required.

References: *The Australian Immunisation Handbook 8th edition*, page 187. *American Academy of Pediatrics. Varicella Zoster Infections. In: Pickering LK, ed. Red Book: 2003 Report of the Committee on Infectious Diseases. 26th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2003:672-686.*

Sharrar RG, La Russa P, Galea SA, et al. The postmarketing safety profile of varicella vaccine. Vaccine 2000;19:916-23.

Can chickenpox vaccine be given at the same time as meningococcal C vaccine?

Varicella-zoster vaccine can be safely administered at the same time as other vaccines including MMR, DTPa, hepatitis B, Hib, polio and MenCCV, using separate syringes and injection sites. The vaccine should be administered by subcutaneous injection, preferably into the deltoid region. If the vaccine is not given at the same time as other live virus vaccines, in particular MMR, they should be given at least 4 weeks apart. This is due to the documented increase in breakthrough varicella infections in those who receive MMR vaccine within 28 days of receipt of varicella-zoster vaccine.

References: *The Australian Immunisation Handbook 8th edition*, page 185.

Centers for Disease Control and Prevention. Simultaneous administration of varicella vaccine and other recommended childhood vaccines - United States, 1995-1999. MMWR - Morbidity & Mortality Weekly Report 2001;50:1058-61.