NCIRS hosted a national Pneumococcal Vaccines Workshop on 30th July 2009 at the University of Sydney. Speakers included local as well as international experts on pneumococcal disease and vaccines. Four sessions were held to address current issues in controlling pneumococcal disease with vaccination.

A) Conjugate vaccines – present and future

Professor Philippe De Wals from Quebec, Canada, summarised the epidemiological evidence that schedules using a primary course of 2 (Quebec) or 3 doses (USA) of 7-valent pneumococcal conjugate vaccine (7vPCV) followed by a booster (the “2+1” and “3+1” schedules, respectively) were both effective in reducing invasive pneumococcal disease (IPD), community acquired pneumonia and acute otitis media (AOM) in children, and provided herd immunity protection against IPD in other age groups. However, serotype replacement in IPD and AOM occurred progressively.

Professor Peter McIntyre showed that impacts on IPD, ear disease (measured by myringotomy tube insertion) and pneumonia hospitalisation comparable to that observed in North America were observed in Australia, where a high vaccine coverage was achieved rapidly, employing a “3+0” schedule together with an initial catch-up program. The herd immunity effect was also similar.

Dr Jan Poolman from GSK described the results of the clinical development of the new 10-valent vaccine (10vPCV) that uses the diphtheria mutant toxoid CRM197 as the conjugating protein. Dr Luis Jodar from Wyeth described the development of the new 13-valent vaccine (13vPCV) that uses the diphtheria mutant toxoid CRM197 as the conjugating protein, as used in the current 7vPCV.

The potential benefits and limitations of these 2 vaccines in immune protection against some additional pneumococcal serotypes and in reducing ear diseases were discussed by these 2 speakers and the panel.

B) Pneumococcal vaccines in high incidence populations

Associate Professor Vicki Krause reviewed the epidemiology of IPD among Indigenous children living in regions with high IPD incidence, and especially the NT, in particular from the perspective of impact of the 23-valent pneumococcal polysaccharide vaccine (23vPPV) booster dose, recommended at age 18–24 months for children in high incidence regions. She concluded that there is no clear compelling evidence of benefit or harm of this dose, but there is suggestive evidence of augmentation of protection against 7vPCV serotypes and a lower than expected incidence of IPD due to serotype 19A in Indigenous children attributable to the 23vPPV booster program.

The importance of re-evaluating the use of 23vPPV in Indigenous children as a matter of priority was highlighted in a presentation by Dr Kerry-Anne O’Grady based on a study exploring the protective effectiveness of pneumococcal vaccines against hospitalised acute lower respiratory infections in children aged 5–23 months in the NT. Protective effect of 7vPCV against pneumonia hospitalisation was not observed, but there was an apparent increase in risk in all cause pneumonia following 23vPPV. Possible explanations including immune hypo-responsiveness, and directions for further research to clarify the possible causes, were proposed.

Professor Kim Mulholland presented data showing that 23vPPV was an effective booster for 7vPCV immunised children in Fiji, but responses to subsequent exposure to pneumococcal antigens were blunted, and boosting was best for 1-dose 7vPCV recipients.

The clinical significance of this, as well as the relevance of the Fiji data to NT children, are yet unclear. Plans to address these issues are underway.
Associate Professor Amanda Leach presented the design and rationale of a study to determine the effect of a combined schedule using the forthcoming 10vPCV and 13vPCV, and comparing with homogenous schedules of either. Immunogenicity, nasopharyngeal carriage and otitis media outcomes will be measured.

Dr Peter Richmond presented preliminary findings of a study conducted in Papua New Guinea, on various schedules of 7vPCV that commence early in life.

Early PCV schedules of 0, 1, 2 months and 1, 2, 3 months of age were shown to be immunogenic, well tolerated and able to prime for immunologic memory. Findings suggested that neonatal 7vPCV might provide earlier protection against some serotypes and delay onset of moderate and severe pneumonia in infants.

The panel speakers then discussed the roles and the future of 23vPPV booster in high-risk children and the rationale for the use and choice of newer conjugate vaccines based on epidemiological and immunogenicity data.

C) Pneumococcal vaccines in adults

Mr Rob Menzies reviewed some overseas and Australian epidemiologic data and studies on the effectiveness of the 23vPPV in adults. He concluded that there was some limited evidence of modest beneficial impact of 23vPPV for non-Indigenous adults, and that the impact of 23vPPV was unclear among Indigenous adults in Australia, noting the many confounders that affect the estimation of the vaccine’s efficacy. The issue of low coverage of 23vPPV in Indigenous adults aged <50 years, the group in which most cases of IPD occur, was highlighted.

Professor Raina MacIntyre presented data showing the lack of clear benefit of PCV over PPV in the elderly, but an encouraging proportion (29–57%) of frail elderly patients were able to mount an acceptable or strong immune response against some pneumococcal serotypes, despite them being considered a vulnerable population. Frailty rather than age was found to better correlate with the immune response to vaccination.

D) Surveillance and diagnostics

Professor De Wals portrayed the surveillance and evaluation systems in Quebec, in the Canadian context, including surveillance for pneumococcal diseases, vaccine coverage, and adverse events, and highlighted areas of deficiencies.

Ms Heather Cook described IPD surveillance activities in Australia undertaken by the Enhanced IPD Surveillance Working Group since 2000. Key surveillance results were shown, and important achievements were highlighted, including the establishment of a comprehensive dataset with serotype information available on 90% of isolates, and an enhanced data subset that also contains information on the clinical presentations, medical risk factors and vaccination history of cases, and microbiological details of isolates.

Associate Professor Amanda Leach reviewed several important overseas and Australian carriage studies, and discussed the use of carriage surveillance in monitoring the epidemiology of bacterial and viral pathogens including pneumococcus, especially regarding serotype replacement in carriage and disease.

Professor Lyn Gilbert highlighted the value of PCR as a highly sensitive, specific and rapid method for pneumococcal disease diagnosis (including serotyping) and surveillance.

Some presentations from the workshop are available on the NCIRS website at www.ncirs.usyd.edu.au
The second Indigenous Immunisation Research Workshop held by NCIRS occurred at the University of Sydney on July 31. While the room was ‘Baltic’ a few lively debates helped keep the blood pumping. After a call to ‘Acknowledgement of Country’ by Adam Hill on his didgeridoo, the workshop commenced with a ‘report card’ approach of the national highs and lows of Indigenous immunisation from Rob Menzies, which identified the many benefits and achievements to date. The remaining issues identified were coverage for vaccines targeted at Indigenous people and timeliness for all vaccines.

We then heard from Dr Geetha Issac-Toua from the Office for Aboriginal and Torres Strait Islander Health about their priorities for Indigenous immunisation. Dr Jenny Hunt, representing Aboriginal Community Controlled Health Services, raised items such as the importance of accreditation of Aboriginal Health Workers to immunise.

An enlightening session discussing the ‘Indigenous researcher’ started with a reflection from Dr Sandra Eades about her entry into research and her unplanned decision to move away from clinical practice. Ms Diane Walker showcased ‘Supporting Indigenous researchers: a practical guide for supervisors’, a very impressive resource which can be downloaded freely from the Cooperative Research Centre for Aboriginal Health. (http://www.crcah.org.au/publications/downloads/supervisors_guide1.pdf)

Dr Jonathan Carapetis provided an update on the activities of the NHMRC Centre for Clinical Excellence in Child and Adolescent Immunisation (Immunise CCRE).

He highlighted the value of non-Indigenous postgraduate students in research while realising the need to retain more Indigenous people and providing ways to enhance recruiting processes for Indigenous researchers.

During a session addressing alternate ways to conduct research, Mr James Ward presented a project that used innovative technology to get completed surveys from an Indigenous youth cohort. This technology, Personal Digital Assistants (PDA), resulted in 293 surveys being collected on the one day of a rugby ‘knockout’, with the unheard of happening, 16–30 year olds queuing to fill in a survey! Definitely a device to think about for future projects.

A personal highlight for me was an update of the PneuMum project by Sarah Moberly who stepped in for Ross Andrews. Sarah presented a study of maternal immunisation with polysaccharide pneumococcal vaccine during the third trimester of pregnancy or shortly after delivery. We heard about the resulting increased antibody levels in maternal blood and breast milk post vaccination and, while these are very early results and we need to see what the impact is on otitis media, it seemed to have a very positive outlook.

While I believe that this was a very successful day, I do think that in the future we will be ready to dedicate more time so that this event can accommodate community level presentations and feedback.

Presentations from this workshop will soon be available on the NCIRS website at www.ncirs.usyd.edu.au
Professor Charles Helms was farewelled recently by colleagues at NCIRS as he returned home to the USA.

Dr Helms, a Professor in the Carver College of Medicine at the University of Iowa and Medical Director of Clinical Quality, Safety and Performance Improvement at the University of Iowa Hospital and Clinics, won a Fulbright Scholarship to Australia in 2008. This is a prestigious cultural and educational exchange program between Australia and the USA. His research was aimed at assessing the impact of the policy of documenting health care worker vaccination implemented in New South Wales in 2006.

Under the NSW Directive, employers in the government sector must have documentation of vaccination for all consenting health care workers, as they may be at risk of acquiring and transmitting vaccine preventable diseases in the course of their work. Work restrictions may apply to staff if they have not received the required vaccines.

“Worldwide, this is a unique opportunity to study the impact of a policy with mandatory health care worker vaccination provisions. Other countries, like the United States, are wrestling with difficult issues of health care worker immunisation and patient safety,” Professor Helms commented. Fifty-eight in depth interviews took place, and Professor Helms also commented on how impressed he was with the calibre and dedication of the people working within the NSW Health public hospital system.

Over the past six months, Professor Helms has interviewed a range of policy-makers and stakeholders in NSW and has reviewed all publicly available data. He is preparing a full report of his findings assessing the implementation and impact of the NSW Health policy directive “Occupational assessment, screening and vaccination against specified infectious diseases”.

Some recent publications


Complete list available at www.ncirs.usyd.edu.au
New research on anti-viral drugs for swine flu & seasonal flu

The Immunisation Research Department at The Kids Research Institute at Westmead is inviting people, including parents, to join two new studies examining Tamiflu® and Relenza® for the treatment of flu.

“We are working in accident and emergency as well as directly with some GP practices to diagnose and treat adults and children aged more than five years who have influenza,” said Professor Robert Booy who is Head of Clinical Research at NCIRS.

Study 1
An unblinded, randomised study looking for resistance in influenza A/H1N1 2009 under standard or double dose oseltamivir treatment.

Objectives
The main purpose of this study is to assess the frequency of emergence of oseltamivir resistant viruses, and their virological characteristics, in patients treated with standard or double dose oseltamivir (Tamiflu®) for influenza caused by A/H1N1 2009 (‘swine flu’) and other human influenza viruses during periods of high transmission.

Design
Unblinded, randomised study

Interventions and follow-up
Patients with clinical symptoms indicative of influenza, who present within 48 hours of the onset of fever during confirmed influenza activity in the community, will be randomised to receive immediate treatment with oseltamivir at a standard age-appropriate dose or a double dose, both given twice daily for 5 days. Patients will have baseline viral samples taken for typing and oseltamivir sensitivity at the start of the study. Testing will be done again after treatment (around day 5).

Number of patients
A total of 125 subjects (aged 5 years and above)

Timing of the study
1 July 2009 to 28 February 2010

Study 2
An unblinded, randomised study looking for resistance in influenza A/H1N1 2009 to oseltamivir or zanamivir.

Objectives
The main purpose of this study is to assess the frequency of emergence of oseltamivir or zanamivir resistant viruses, and their virological characteristics, in patients treated with oseltamivir or zanamivir for influenza caused by A/H1N1 2009 (‘swine flu’) and other human influenza viruses during periods of high transmission.

Design
Unblinded, randomised study

Interventions and follow-up
Patients with clinical symptoms indicative of influenza, who present within 72 hours of the onset of fever during confirmed influenza activity in the community, will be randomised to receive immediate treatment with oseltamivir or zanamivir according to standard age-appropriate dose. Patients will have baseline viral samples taken for typing at the start of the study. Viruses will be tested for oseltamivir and zanamivir sensitivity and this will be done again on completion of treatment (after about 5 days).

Number of patients
A total of 120 subjects (aged 5 years to 50 years)

Timing of the study
1 July 2009 to 31 December 2009

For more information, please telephone Research Nurse Elizabeth Clarke and her team:
02 9845 1430
0418 209 323
0423 799 226
Recent Journal Club Presentations

Seize the moments: missed opportunities to immunize at the family practice level

Turner N, Grant C, Goodyear-Smith F, Petousis-Harris H. Family Practice 2009; 26: 275

Missed opportunities (MOs) are an important factor contributing to incomplete immunisation. This study described the frequency and characteristics of MOs within a New Zealand primary healthcare setting and estimated their effect on incomplete immunisation. It involved an audit of medical records of randomly selected children aged less than 2 years from 62 practices in Auckland, New Zealand. The study found that MOs occurred in 97% of practices. The MOs were more common with acute illness visits and contraindications for immunisation were present in 5% of visits. In addition, children with MO visits were 3 times more likely to be incompletely immunised. This audit concluded that MOs to vaccinate children occurred in most practices and that directives should focus on the practitioner and the practice system to reduce MOs.

Presented by Dr Aditi Dey, Epidemiologist, NCIRS

Socioeconomic impact of influenza on healthy children and their families


The findings of this Italian study are very relevant to Australia at this point of time, especially considering the impact of swine flu among young children. While scientists and the community are extremely concerned about the clinical implications of swine flu, researchers should also bear in mind that children and their household contacts can be affected severely in terms of quality of life, and lost school or work days. This study demonstrated that children with influenza tend to have longer durations of fever and absenteeism from day care or school when compared with those without influenza (p<0.0001). The household contacts of children with influenza also had more medical visits, missed work or school days, and the need for help at home to take care of sick children (p<0.0001). Having seen the significant socioeconomic impact brought by influenza to families, the authors emphasised the need to introduce programs to vaccinate children in order to protect the children themselves, as well as their household contacts. They also suggested that economic modelling of influenza immunisation programs should be done.

Presented by Maria Chow, Research Assistant, NCIRS

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