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Welcome to the latest issue of Paediatric Vaccines Research Review.

Highlights this month include evidence that NZ children would definitely benefit from the introduction of a rotavirus vaccine (and a varicella vaccine for that matter), but the world really does need better pertussis vaccines. We have also included a local study that found troubling ethnic disparities in paediatric pneumonia admissions, and more evidence supporting maternal influenza vaccination.

We hope you find this issue interesting and look forward to hearing your comments.

Kind regards,

Associate Professor Nikki Turner and Dr Helen Petousis-Harris
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Effectiveness of monovalent and pentavalent rotavirus vaccine

Authors: Cortese M et al

Summary: This study measured the vaccine effectiveness (VE) of the 2-dose monovalent rotavirus vaccine (RV1) and the 3-dose pentavalent vaccine (RV5) against rotavirus disease resulting in emergency department care. Children were included if they presented to hospital with diarrhoea of ≤10 days' duration and were born after RV1 introduction. Stools were collected and immunisation records were obtained. Overall, 165 rotavirus-case subjects and 428 rotavirus-negative controls were included. In children aged ≥8 months, VE of RV1 and RV5 was calculated to be 91% and 92%, respectively. The VE of RV1 against G2[P[4] disease was 94%, and against G1[P[8] disease was 89%. RV1 effectiveness was sustained among children aged 12–23 months. In conclusion, RV1 and RV5 were both highly effective against severe rotavirus disease.

Comment (NT): The US has been using rotavirus vaccine since 2008. Of interest in this study was that the vaccine effectiveness measure for children who had received only one dose of RV1 (Rotarix®) was 53%, albeit with very wide confidence intervals. Both rotavirus vaccines (Rotarix®, the monovalent and Rotateq®, the pentavalent) are highly effective in the real world. They reduce rotavirus disease resulting in hospitalisation or visits to ED by over 90%, sustained up until two years of age and there appears little difference between them in performance. Of note, the monovalent is performing well against genotype G2[P[4], for which there had been some earlier concerns in Latin American studies. Additionally, effectiveness was similar for children who were given a mixed series of one of each type of rotavirus vaccine. These US results are very similar to European results and NZ can be confident that the real world experience for both these vaccines bears out the clinical trial data. Our children can definitely benefit from the introduction of a rotavirus vaccine!

http://pediatrics.aappublications.org/content/132/1/e25

Long-term effectiveness of varicella vaccine

Authors: Baxter R et al

Summary: This 14-year prospective study evaluated varicella incidence and vaccine effectiveness in Kaiser Permanente Northern California members. 7585 children who were vaccinated with varicella vaccine in their second year of life in 1995 were followed up for breakthrough varicella and herpes zoster (HZ) through 2009. Of these children, 2826 received a second dose in 2006–2009. Incidences of varicella and HZ were estimated and compared with rates from the prevaccine era. The average incidence of varicella was 15.9 per 1000 person-years, which was 9- to 10-fold lower than the incidence in the prevaccine era. Vaccine effectiveness did not appear to wane with time, and was 90% at the end of the 14-year study period. Most varicella cases were mild and occurred early after vaccination; there were no reports of varicella after a second dose. Cases of HZ were mild, and rates were 39% lower in vaccinated children than during the prevaccine era. The average incidence of HZ was 3.8 per 1000 person-years, which was 10-fold lower than the incidence in the prevaccine era. Vaccine effectiveness did not appear to wane with time, and was 90% at the end of the 14-year study period. Most HZ cases occurred early after vaccination, with the rate being 90% lower than the prevaccine era. The vaccine also appears to decrease the incidence of zoster, with this study suggesting a 40% decrease but the true impact may be even higher as historic measurements of zoster prior to vaccine introduction were not accurate, and likely to be underestimated. The Americans are way ahead of us in progress in varicella disease prevention – they have excellent data and excellent disease control. NZ take note, this is another vaccine we should be using.

Comment (NT): This is the largest and longest follow-up study of varicella vaccine. The US has been using the varicella vaccine since 1985 and a two-dose regime since 2006. The results are excellent; there is no sign of waning immunity since introduction of the vaccine with no increasing incidence of breakthrough cases. Most breakthrough cases were mild and in the earlier years of this study demonstrating this is more likely to be due to early vaccine failure (when there were still high rates of circulating disease) and not evidence of waning immunity. The vaccine also appears to decrease the incidence of zoster, with this study suggesting a 40% decrease but the true impact may be even higher as historic measurements of zoster prior to vaccine introduction were not accurate, and likely to be underestimated. The Americans are way ahead of us in progress in varicella disease prevention – they have excellent data and excellent disease control. NZ take note, this is another vaccine we should be using.

http://dx.doi.org/10.1542/peds.2012-3303
Effectiveness of pertussis vaccines for adolescents and adults

Authors: Baxter R et al

Summary: This case-control study assessed the effectiveness of reduced acellular pertussis (Tdap) vaccines in adolescents and adults. All polymerase chain reaction (PCR)-confirmed cases of pertussis in Kaiser Permanente Northern California members aged ≥11 years were included. The Tdap vaccination status of PCR positive cases was compared with that of 2 control groups: people testing negative for pertussis by PCR and closely matched people from the general Kaiser Permanente Northern California population. A total of 668 PCR-positive cases, 10,098 PCR-negative controls, and 21,599 Kaiser Permanente Northern California matched controls were evaluated. Tdap vaccination rates were calculated to be 24.0% in PCR-positive cases and 31.9% in PCR-negative controls (p<0.001). The adjusted estimate of effectiveness of Tdap vaccination against pertussis was 53.0% in the comparison with PCR controls, and 64.0% in the comparison with Kaiser Permanente controls. In conclusion, Tdap vaccination was moderately effective at preventing PCR-confirmed pertussis in adolescents and adults.

Comment (NT): Pertussis is currently NZ’s biggest vaccine-preventable disease challenge. Acellular pertussis vaccines are less reactogenic than the old whole cell vaccines but overall probably less effective and with earlier waning of protective immunity. Adult Tdap vaccines have been developed to boost immunity for older children, adolescents and adults particularly to reduce disease spread back to the most vulnerable age group i.e. infants. Previous studies of booster doses in adolescence have been limited by low numbers of cases. This study, while having the limitations inherent in case-control design, does have the numbers to demonstrate ‘moderate’ effectiveness of an adolescent booster, with approximately a half to two-thirds of those vaccinated having protection against PCR-positive pertussis compared with approximately a half to two-thirds of those vaccinated having protection against PCR-negative pertussis (p<0.001). The study is a welcome addition to the evidence on the effectiveness of Tdap vaccines in adolescents and adults.

Reference: BMJ2013;347:f4249
http://www.bmj.com/content/347/bmj.f4249

The association between physicians’ and patients’ preventive health practices

Authors: Frank E et al

Summary: This study used objectively measured health care indicators to investigate the association between physicians’ personal health practices and those of their patients. Eight indicators of quality of health care (screening and vaccination practices) were assessed for primary care physicians (n=1488) and their adult patients (n=1,886,791) in Israel’s largest health maintenance organisation (the physicians were also patients in this health care system). For all 8 indicators, patients whose physicians were compliant with the preventive practices were more likely to also have undergone these preventive measures than patients with noncompliant physicians (p<0.05). For example, among patients whose physician had received the influenza vaccine, 49.1% of eligible patients received flu vaccines compared with 43.2% of patients whose physicians did not receive the vaccine. In conclusion, there was a consistent, positive relation between physicians’ and patients’ preventive health practices.

Comment (NT): Do we practice what we preach? This papers backs up our gut feeling that this actually really matters. I want to know that a mechanic treats their own car the same as mine. How often have you been asked ‘did you vaccinate your own children’ or ‘do you use the flu vaccine?’ It seems reasonable that a patient would want to know we use the same vaccines for ourselves and our families that we want them to be using. It would seem somewhat hypocritical otherwise! The authors here call for ‘promoting physical health habits among physicians’ – I wonder how far we need to take this. Non-smoking and drug free seems very reasonable, but I get a little more nervous if someone drills into my variable eating and exercise habits.

http://www.cmaj.ca/content/185/8/649

Reducing children’s pain and distress towards flu vaccinations: a novel and effective application of humanoid robotics

Authors: Beran T et al

Summary: This study investigated the impact of an interactive humanoid robot on children’s pain and distress during influenza vaccination. 57 children (mean age 7 years) were randomised to a standard vaccination session or a session that also incorporated a robot that was programmed to use cognitive-behavioural strategies with them. Interaction with a robot during flu vaccination resulted in significantly less pain and distress in children according to child, parent, nurse, and researcher ratings. This is the first study to examine the effectiveness of child-robot interaction for reducing children’s pain and distress during a medical procedure and the results warrant further research on bedside robotics.

Comment (NT): Vaccinators, the Canadians have found the solution for you: solving the challenges of minimising distress during childhood vaccination with robotics! These techies used a talking humanoid robot that used distraction and blowing techniques for vaccinating a group of children aged between 4 and 9 years. A snip at the price of Canadian $12,000 per robot. The authors do caution against excessive enthusiasm with the need to consider the importance of its physical appearance, type of comment and actions it uses – this one looks very cute in the picture but I suspect a budget NZ number 8 wire one might have the opposite effect. Who wants to lobby the funders for this one…?

Reference: Vaccine 2013;31(25):2772-2777
http://dx.doi.org/10.1016/j.vaccine.2013.03.056

Independent commentary provided by Associate Professor Nikki Turner.
Nikki is a NZ-trained GP with background experiences also in paediatrics and public health. She has a specialty interest in immunisation both internationally and in NZ. Nikki currently works as the Director of the Immunisation Advisory Centre, a national public health programme based at the University of Auckland. She is an Associate Professor in the Dept of General Practice and Primary Care at the University of Auckland, has an honorary Senior Lecturer position for the University of Otago and works part time as a GP in Wellington.
For full bio CLICK HERE.

Independent commentary provided by Dr Helen Petousis-Harris.
Helen is Senior Lecturer in the Department of General Practice and Primary Health Care at the University of Auckland and the Academic Lead for Immunisation Research and Vaccinology at the Immunisation Advisory Centre. She has a PhD in Vaccinology and is particularly interested in factors associated with vaccine safety and reactogenicity. Other areas of research activity include social aspects of immunisation, immunisation coverage and epidemiology and clinical aspects of immunogenicity and reactogenicity.
For full bio CLICK HERE.
Impact of pneumococcal vaccine on hospital admission with lower respiratory infection in children resident in South Auckland, New Zealand

Authors: Vogel A et al

Summary: This study evaluated the impact of introduction of the pneumococcal conjugate vaccine 7 valent (PCV7) in June 2008 on admission rates for lower respiratory infection (LRI) for children in the Counties Manukau DHB. LRI admissions to any NZ hospital between August 2001 and July 2011 for children <2 years who were resident in Counties Manukau DHB were analysed. Data for the first-year after vaccine introduction (August 2008 to 31 July 2009) were omitted. Pneumonia (but not bronchiolitis) admissions were found to have declined gradually after 2001, and pneumonia admissions decreased further after PCV7 introduction in 2008. LRI admissions declined significantly after PCV7 introduction in Pacific children but not in Maori children. Maori and Pacific children had a 4- to 5-fold increased risk of LRI admission compared with European children. In conclusion, the introduction of PCV7 resulted in reduced hospital admissions for pneumonia in young children in the Counties Manukau DHB.

Comment (HPH): The ethnic disparities identified in this study are troubling. Lower respiratory tract infections (LTRIs) have many causes and it is possible that pneumococcal infection is responsible for a lower proportion of these cases in some ethnic groups compared with others. This is unlikely to be due to any variation in vaccine performance between ethnic groups, as invasive pneumococcal disease caused by PCV7 serotypes in children under 2 years has effectively ceased nationally and these serotypes are no longer a cause of LRI. It is likely factors such as overcrowding, poor housing conditions and access to primary health care still continue to be the major barriers to achieving more significant reductions in LRI for Maori and Pacific children. Although the effectiveness of pneumococcal vaccination is well demonstrated there are other important issues at play here, including timeliness of vaccination. NZ has made great improvements here but there is still a challenge particularly for Maori and Pacific children.

Further research exploring the role of vaccine exposure (vaccination status) and association with pneumococcal disease could help answer some of these questions. Sadly it appears that the burden of bronchiectasis and pneumonia in Counties Manukau DHB and presumably nationally may require broader strategies than just pneumococcal vaccine, particularly for Maori and Pacific children. However, improving the low timeliness of uptake of vaccine among these children may help.

Reference: NZ Med J 2013;126;1378

A randomized trial of candidate inactivated quadrivalent influenza vaccine versus trivalent influenza vaccines in children aged 3–17 years

Authors: Domachowske J et al

Summary: This study compared the efficacies of a candidate inactivated quadrivalent influenza vaccine (QIV) and a trivalent influenza vaccine (TIV) in healthy children. 2738 children aged 3–17 years were randomised 1:1:1 to receive QIV or 1 of 2 TIVs (either B/Victoria or B/Yamagata lineage). Haemagglutination-inhibition assay were performed 28 days after 1 dose in primed children and after 2 doses in unprimed children. Comparison of geometric mean titers and seroconversion rates for QIV vs TIV showed noninferiority against shared strains and superiority against alternate-lineage influenza B strains. QIV was highly immunogenic, with seroconversion rates of 91.4%, 72.3%, 70.0%, and 72.5% against A/H1N1, A/H3N2, B/Victoria, and B/Yamagata, respectively. Reactogenicity and safety of QIV was similar to that of TIV. In conclusion, compared with TIV, QIV showed superior immunogenicity for the additional influenza B strain without interfering with immune responses to shared strains.

Comment (HPH): Due to challenges in accurately predicting which influenza B lineage will be circulating in a given season the addition of a second B lineage is expected to improve seasonal influenza vaccine effectiveness. A US study using 10 years of data on the annual incidence of influenza-associated outcomes, virologic circulation, vaccine coverage and vaccine effectiveness assessed the potential public health impact of including a second B strain in the seasonal influenza vaccine and concluded a modest reduction in influenza-associated outcomes would result from the addition of the second influenza B lineage. Quadrivalent vaccines that add a second strain of B subtype in order to reduce the potential for vaccine mismatch are now licensed internationally and are expected to become available in NZ soon. The ability of a quadrivalent vaccine to perform better than a trivalent vaccine will depend on the vaccine match including the amount of influenza B in circulation that is different from that in the trivalent preparation. Since 2002, influenza virus strain surveillance in NZ has frequently recorded co-circulation of four antigenically distinct viruses: A (H1N1), A (H3N2), B/Yamagata lineage and B/Victoria lineage virus. The NZ influenza virus circulation pattern supports the introduction of quadrivalent vaccines which contain these four antigenically distinct influenza viruses.

Reference: J Infect Dis 2013;207(12):1878-1887
http://dx.doi.org/10.1093/infdis/jit091

Effectiveness of pneumococcal conjugate vaccine in infants by maternal influenza vaccination status

Authors: van Santen K et al

Summary: This study investigated the impact of maternal influenza vaccination on the effectiveness of the pneumococcal conjugate vaccine (PCV) in infants. A retrospective cohort study of 9,807 mother-infant pairs for infants born in June 2002 through December 2009 was evaluated. Exposure was assessed for receipt of PCV only, and the combination of PCV and maternal influenza vaccine (TIV). For medically attended acute respiratory infection (MAARI) in the first year of life, vaccine effectiveness was 39.6% for the combination of TIV and PCV and 29.8% for PCV only. For acute otitis media (AOM) in the first year of life, vaccine effectiveness was 47.9% for the combination of TIV and PCV and 37.6% for PCV only. In conclusion, the combination of maternal influenza vaccine and infant PCV confers greater protection from AOM and MAARI in the first year of life than PCV alone.

Comment (HPH): If there were not already enough very good reasons to vaccinate pregnant women with influenza here is another one. We already know that maternal infection with influenza can have not only catastrophic consequences to the pregnancy but also increase the risk of a range of non-communicable diseases in the infant later on in life including various neoplasms and psychiatric illnesses. Influenza infection can also increase the risk for secondary infection with Streptococcus pneumoniae and the risk for severe pneumococcal disease in previously healthy children is increased if preceded by influenza infection. There is evidence to support mechanical damage to the lungs by influenza infection and also alterations to the inflammatory response to the pneumococcus as a result of influenza infection. Both of these factors may underlie the relationship between these infections. As you would expect, the 2009 influenza pandemic had a significant impact on the rate of hospitalisations with pneumococcal pneumonia and reflected the variations in influenza activity. This information will certainly be helpful for pregnant women making decisions about influenza vaccination.

Reference: Pediatr Infect Dis J 2013; published online 12 Jul

www.researchreview.co.nz
Pregnancy dose Tdap and postpartum cocooning to prevent infant pertussis

Authors: Terranella A et al

Summary: This study compared the effectiveness of a booster dose of tetanus, diphtheria, and acellular pertussis (Tdap) vaccine during pregnancy with that of postpartum “cocooning” to prevent infant pertussis. The study used a cohort model reflecting US 2009 births and the Tdap schedule to simulate a decision and cost-effectiveness analysis of Tdap vaccination during pregnancy compared with postpartum vaccination with or without vaccination of other close contacts (i.e. postpartum cocooning). Pregnancy vaccination was found to be more effective than postpartum vaccination in reducing the annual infant pertussis incidence (reduced by 33% vs 20%), hospitalisations (reduced by 38% vs 19%) and deaths (reduced by 49% vs 16%). Additional cocooning doses in a father and 1 grandparent could avert a further 16% of cases. The cost per quality-adjusted life-year saved for pregnancy vaccination was less than postpartum vaccination ($414,523 vs $1,172,825).

Comment (HPH): Here is a useful contribution to the pertussis conundrum. Of the many challenges pertussis poses, one that that of correlates of infection, vaccination and protection. Firstly, we cannot estimate with any real degree of accuracy what proportion of the population is likely to be protected against pertussis infection and/or disease. Secondly, we cannot determine if immunity is naturally acquired or vaccine derived. Thirdly, when immunogenicity studies are carried out there are usually bloods taken at different time points and these are not always consistent between studies nor are they necessarily reflective of the maturation of the immune response — things can be missed. The authors here also argue that using geometric mean titre of pertussis antibodies (pooling all the individuals in the study and averaging them) is misleading as there is considerable variation between individuals and between natural infection and vaccine responses. For example, some people are protected for many years after vaccination while others only a couple and some not at all. I suspect that this could be an issue with other vaccine immunogenicity studies too such as hepatitis B and conjugate vaccines. In other words we only get a snapshot of one moment in time and it may not actually be the most informative moment and may not reflect most of the population. This novel approach enabled the prediction of antibody waning from both natural pertussis infection and vaccination, a very useful contribution to understanding.

Reference: Vaccine 2013;31(36):3732-3738
http://dx.doi.org/10.1016/j.vaccine.2013.05.073

A novel method for evaluating natural and vaccine induced serological responses to Bordetella pertussis antigens

Authors: Berbers G et al

Summary: This study used a novel method to analyse responses to pertussis vaccine compared with natural infection with Bordetella pertussis. A mathematical model was used to describe the time course of serum IgG antibodies against pertussis toxin (PT), filamentous haemagglutinin (FHA) and pertactin in 134 individuals vaccinated with four different pertussis vaccines at 4 years of age compared with the responses to natural infection with B. pertussis in individuals aged 1–8 years (n=44). Responses to PT after vaccination with the tested vaccines were smaller and tended to decay faster than those after natural infection. When present in vaccines, FHA and pertactin tended to produce higher peak levels than those in naturally infected patients, but they decayed faster. In conclusion, this model allows a better comparison of the kinetics of vaccine-induced and natural infection-induced antibody responses over a long follow-up period.

Reference: Vaccine 2013;31(36):3732-3738
http://dx.doi.org/10.1016/j.vaccine.2013.05.073

Midwifery Research Review

Midwifery Research Review is a new publication that contains a selection of recently published papers on research important to midwifery practise. Expert commentary is provided by Jackie Gunn who has been involved in leadership of midwifery education at AUT University for more than two decades. She is the National Educational Consultant on the NZ College of Midwives, of which she is a foundation member. Jackie has practised midwifery in tertiary and primary maternity units and also as an LMC midwife and has a particular interest in midwifery practices that support physiological pregnancy, childbirth and transition to parenthood processes, midwifery education, and development of midwifery practice.

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