Associate Professor
Nikki Turner
Academic General Practitioner
Wellington

Current Issues re Vaccinations - What’s New? - Concurrent Workshop Repeated
Friday, 21 June 2013
Start 4:30pm
Start 5:35pm
Duration: 55mins
Duration: 55mins
Sigma
Sigma
Current issues with vaccination: what's new?

Nikki Turner
University of Auckland
June 2013
<table>
<thead>
<tr>
<th>Vaccine-Preventable Disease</th>
<th>Estimated Annual Average Cases&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Estimated Annual Average Deaths&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Peak Cases&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Peak Deaths&lt;sup&gt;e&lt;/sup&gt;</th>
<th>Vaccine Date(s), y&lt;sup&gt;f&lt;/sup&gt;</th>
<th>Most Recent Postvaccine Reported No. Cases, 2006&lt;sup&gt;g&lt;/sup&gt;</th>
<th>Most Recent Postvaccine Reported No. Deaths, 2004&lt;sup&gt;h&lt;/sup&gt;</th>
<th>Prevaccine Estimated Annual No. vs Most Recent Reported No. (% Reduction) Cases</th>
<th>Prevaccine Estimated Annual No. vs Most Recent Reported No. (% Reduction) Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>21053 (1936-1945)</td>
<td>1822 (1936-1945)</td>
<td>30508 (1938)</td>
<td>3065 (1936)</td>
<td>1928-1943</td>
<td>0</td>
<td>0</td>
<td>21053 (100)</td>
<td>1822 (100)</td>
</tr>
<tr>
<td>Mumps</td>
<td>162344 (1963-1968)</td>
<td>39 (1963-1968)</td>
<td>212932 (1964)</td>
<td>50 (1964)</td>
<td>1940s, 1967</td>
<td>6584</td>
<td>0</td>
<td>155760 (95.9)</td>
<td>39 (100)</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200752 (1934-1943)</td>
<td>4034 (1934-1943)</td>
<td>265269 (1934)</td>
<td>7518 (1934)</td>
<td>1914-1941</td>
<td>15632</td>
<td>27</td>
<td>185120 (92.2)</td>
<td>4007 (99.3)</td>
</tr>
<tr>
<td>Poliomyelitis, acute</td>
<td>19794 (1941-1950)</td>
<td>1393 (1941-1950)</td>
<td>42033 (1949)</td>
<td>2720 (1949)</td>
<td>1955, 1961-1963, 1967</td>
<td>0</td>
<td>0</td>
<td>19794 (100)</td>
<td>1393 (100)</td>
</tr>
<tr>
<td>Poliomyelitis, paralytic</td>
<td>16316 (1951-1954)</td>
<td>1879 (1951-1954)</td>
<td>21269 (1952)</td>
<td>3145 (1952)</td>
<td>1955, 1961-1963, 1967</td>
<td>0</td>
<td>0</td>
<td>16316 (100)</td>
<td>1879 (100)</td>
</tr>
<tr>
<td>Smallpox</td>
<td>29005 (1900-1949)</td>
<td>337 (1900-1949)</td>
<td>110672 (1920)</td>
<td>2510 (1902)</td>
<td>1798</td>
<td>0</td>
<td>0</td>
<td>29005 (100)</td>
<td>337 (100)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Footnote letters correspond to Box 1.
• Current challenges with VPDs
• Influenza
• Pregnancy vaccination
• Healthcare worker vaccination
• Types of vaccines
• Private market vaccines
• Future of the national schedule
• Immunisation coverage
• Communication issues
Current challenges
Mrs B is 79, she has had an annoying cough for a few weeks, worse at night, comes in bouts, a little moist, no fever, overall pretty well in herself but she is fed up with coughing

- Hx: stable CHF, IHD, diabetes
- FHx: lives with daughter’s family
- non smoker
Figure 2: Pertussis notifications and hospitalisations by calendar month-year since 1998 up to 28 February 2013

Ref: ESR 2013
Clinical Case Definition of pertussis for surveillance purposes (reproduced from Cherry et al. 2012)

- **Cough and coryza with no or minimal fever PLUS:**
  - Whoop OR
  - Apnea OR
  - Posttussive emesis OR
  - Cyanosis OR
  - Seizure
  - Pneumonia
  - Close exposure to an adolescent or adult (usually a family member) with a prolonged afebrile cough illness.

- **Paroxysmal cough with no or minimal fever PLUS:**
  - Whoop OR
  - Apnea OR
  - Posttussive emesis
  - Seizure
  - Worsening of symptoms at night
  - Pneumonia
  - Close exposure to an adolescent or adult (usually a family member) with a prolonged afebrile cough illness.

- **Nonproductive, paroxysmal cough of ≥2 weeks duration without fever PLUS:**
  - Whoop OR
  - Apnea OR
  - Sweating episodes between paroxysms
  - Posttussive emesis
  - Worsening of symptoms at night
• **How to test**
  – PCR
  – Pref within 7 days
  – not serology

• **When to test**
  – Diagnosis to guide management

• **Who to test**
  • Infants <12 months
  • Pregnant women, partic last trimester
  • Household contacts
  • Children in ECC
  • Occupations: ECC staff, HCWs, US!

• **Notifiable**
Rx

• To reduce transmission
• May not alter course of illness
• Non-infectious after 5d Rx or >3 weeks cough

• Infants/children < 45kg:
  – azithromycin 10mg/kg D1, 5mg/kg day D2-5
    (alt: erythromycin 10mg/kg qid 14d)

• All else:
  – erythromycin 400mg qid 14d OR
  – azithromycin 500mg D1, 250mg D2-5

REF bpac.org.nz/BPJ/2013/March/pertussis.aspx
Pertussis control

• Unable to eradicate from whole community
• Most severe in younger children
  – Main target of immunisation strategies
• KEY: High coverage and timeliness of delivery
• Other strategies
  – Immunising older children
  – Immunising adults
  – Cocoon strategies
  – Immunising pregnant women
FLU
NZ medical experts brace for arrival of deadly flu
NZ Herald Jan 15, 2013

Flu infections sweep America hospitalizing thousands and leaving 18 children dead of complications, and it's going to get worse...
MailOnline Feb 20 2013

Flu reaches epidemic level in U.S., says CDC
Jan 2013

India swine flu 2013: Over 700 cases this year
Feb 25, 2013 HealthIndia

'Dirty Brits are world's worst flu spreaders'
Daily Telegraph Oct 2012
“We’d love to come but the flu mongers have paralyzed us with fear.”
Consultation rates – 2007 to 2012

Figure 1. Weekly consultation rates for ILI in New Zealand, 2007–2012

Ref: ESR 2012
Recent TIV vaccine efficacy and effectiveness studies conducted in adults under 65 years of age. 
*Adapted from Plotkin 6th edition 2012 and updated.*

<table>
<thead>
<tr>
<th>Study</th>
<th>Population age</th>
<th>Study design</th>
<th>Study years</th>
<th>Outcomes and VE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jefferson 2010 [74]</td>
<td>16-65</td>
<td>Meta-analysis</td>
<td>NA</td>
<td>30% (17%-41%) VE against ILI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>73% (CI 54%-84%) VE against influenza symptoms</td>
</tr>
<tr>
<td>Osterholm 2012 [74]</td>
<td>18-65 years</td>
<td>Systematic review and meta-analysis</td>
<td>N/A</td>
<td>59% (CI 51%-67%) VE against influenza</td>
</tr>
<tr>
<td>Monto 2009 [75]</td>
<td>18-49</td>
<td>RPCT</td>
<td>2007-2008</td>
<td>68% VE against LCI</td>
</tr>
<tr>
<td>Beran 2009 [76]</td>
<td>18-64</td>
<td>RPCT</td>
<td>2006-2007</td>
<td>62% VE against LCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>67% VE against vaccine matched strains</td>
</tr>
<tr>
<td>Jackson 2010 [77]</td>
<td>18-49</td>
<td>RPCT</td>
<td>2005-6 2006-7</td>
<td>49% VE against CCI</td>
</tr>
<tr>
<td>Barrett 2011 [78]</td>
<td>18-49</td>
<td>RPCT</td>
<td>2008-2009</td>
<td>78% VE against matched, CCI</td>
</tr>
</tbody>
</table>
Recent TIV vaccine efficacy and effectiveness studies conducted in infants and children.
*Adapted from Plotkin 6th edition 2012 and updated.*

<table>
<thead>
<tr>
<th>Study</th>
<th>Population age</th>
<th>Study design</th>
<th>Study years</th>
<th>Outcomes and VE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jefferson 2012</td>
<td>Under two years</td>
<td>Systematic review</td>
<td>N/A</td>
<td>Insufficient data to support VE</td>
</tr>
<tr>
<td>Cochran 2010</td>
<td>6-23 months</td>
<td>Retrospective cohort</td>
<td>2003-2006</td>
<td>76% VE against LCI 2005-6 No effectiveness in 2003-4 or 2004-5</td>
</tr>
<tr>
<td>Heinonen 2010</td>
<td>9 months to 3 years</td>
<td>Prospective cohort</td>
<td>2007-2008</td>
<td>66% VE against ILI</td>
</tr>
<tr>
<td>Kelly 2011</td>
<td>6-59 months</td>
<td>Case-control</td>
<td>2008</td>
<td>58% VE against medical visits;</td>
</tr>
<tr>
<td>Vesikari 2011</td>
<td>6-71 months</td>
<td>RPCT</td>
<td>2007-8 and 2008-9</td>
<td>43% (CI 15-61%) VE against PCR-confirmed influenza</td>
</tr>
<tr>
<td>Jefferson 2012</td>
<td>Under 16 years</td>
<td>Systematic review and meta-analysis</td>
<td>N/A</td>
<td>59% (41% - 71%) efficacy against LCI 36% (24% - 46%) effectiveness against ILI</td>
</tr>
</tbody>
</table>
2013 Vaccine strains

- A/California/7/2009 (H1N1)pdm09-like virus (15 μg HA per dose)
- A/Victoria/361/2011 (H3N2)-like virus (15 μg HA per dose) new strain
- B/Wisconsin/1/2010-like virus (15 μg HA per dose) new strain
Vaccines

• **TIV (trivalent inactivated vaccines)**
  – The only current NZ vaccines
  – QIVs on the way

• **Adjuvanted**
  – Expected to have stronger immune response
  – Was used effectively in some pandemic vaccines
  – Likely better immune response in elderly, young children
  – Safety issues – local reactions, ?narcolepsy

• **LAIV (Live Attenuated Intranasal)**
  – Broader immune response
  – Likely better for children
  – ?safety issues in children <2 yrs
  – Likely better for herd immunity
  – To be introduced to UK all children > 2, 2014
Strategies

- Targeted Individual protection
- Pregnancy – individual protection and fetal/infant protection
- Cocoon protection (not funded)
  - Infants
  - Elderly
  - High risk patients
Hospitalisation by age

Hospitalized Influenza Cases among ADHB and CMDHB residents  30 April - 30 Sept 2012

SHIVERS data 2012
Hospitalisation by ethnicity

Hospitalised Influenza Cases among ADHB and CMDHB residents 30 April - 30 Sept 2012

Cases/Incidence per 100,000

- Maori
- Pacific
- Asian
- European + other
- Unknown

SHIVERS data 2012
And by socio-economic status

Hospitalised Influenza Cases among ADHB and CMDHB residents
30 April - 30 Sept 2012

Number/Percentage

0 20 40 60 80 100 120

Upper (1-3) Middle (4-7) Lower (8-10)

NZDep2006 Status by decile

SHIVERS data 2012
Clinical Symptoms more likely to be associated with diagnosis of flu in hospital admissions

- SHIVERS data

<table>
<thead>
<tr>
<th>Symptom</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sore throat</td>
<td>1.51 (1.13-2.01)</td>
</tr>
<tr>
<td>Headache</td>
<td>1.88 (1.37-2.58)</td>
</tr>
<tr>
<td>Aching muscles</td>
<td>1.4 (1.03-1.9)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1.49 (1.09-2.08)</td>
</tr>
</tbody>
</table>
FLU VACCINE CATEGORIES

- H1N1 Flu
- Nasal Flu Mist
- Regular Flu
- Needle Injection

- High Risk
  - Over Age 65
  - Under Age 2
  - Priority Jobs
  - Health Staff

- Low Risk
  - Ages 2-49

- High Dose
  - Pregnant

ANY QUESTIONS?
Pregnancy and Vaccination
**Flu vaccine**
- Start of flu season

- Reduces maternal morbidity/mortality
- Reduces fetal mortality
  - Reduces fever
- Reduces flu in newborn
  - Ab protective for around 8 weeks
  - 91% effective in reducing flu in infants

**Pertussis-containing vaccine**
- 28 to 38 weeks gestation

- Reduces maternal morbidity
- Reduces risk of transfer to newborn
- Some passive protection to newborn
  - Higher Ab transfer if later in pregnancy
Effectiveness of flu vaccine given during pregnancy in preventing hospitalisation for flu in infants

91% effective

<table>
<thead>
<tr>
<th>Measure</th>
<th>Subjects aged &lt;6 months</th>
<th>Subjects aged ≥6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%) of case infants; no. (%) of control infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother was vaccinated</td>
<td>2 (2.2); 31 (19.9)</td>
<td>1 (4.6); 2 (5.6)</td>
</tr>
<tr>
<td>Mother was not vaccinated</td>
<td>89 (97.8); 125 (80.1)</td>
<td>21 (95.5); 34 (94.4)</td>
</tr>
<tr>
<td>Vaccine effectiveness (95% CI), %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>90.7 (59.9–97.8)(^a)</td>
<td>−41.4 (−2257.3 to 91.5)(^b)</td>
</tr>
<tr>
<td>Adjusted(^c)</td>
<td>91.5 (61.7–98.1)(^a)</td>
<td>...</td>
</tr>
</tbody>
</table>

**NOTE.** CI, confidence interval.

\(^a\) \(P = .001\).

\(^b\) \(P = .809\).

\(^c\) The adjusted model for subjects aged <6 months retained vaccination of household contacts and prematurity.

Benowitz I, Esposito DB, Gracey KD, Shapiro ED, Vazquez M. Influenza vaccine given to pregnant women reduces hospitalization due to influenza in their infants. Clinical Infectious Diseases 2010 Dec 15;51(12):1355-61.
Pertussis: Transplacental maternal antibodies

- Efficiently transferred
- Cord blood from infants whose mothers vaccinated during or before pregnancy have higher titres
- Half life of maternal Abs in infant ~6 weeks
- Effectiveness of these Abs in preventing disease not yet known
- Vaccinated woman likely protected herself and not transmit to infant
- Optimise transfer by vaccinating late 2\textsuperscript{nd} or early 3\textsuperscript{rd} trimester as circulating Abs peak after 14 days then decline.


Safety of Tdap in pregnant women

- Pregnancy registers established by manufacturers
  - sanofi pasteur (Adacel®) and GSK (Boostrix®)

- Data from passive reporting systems evaluated
  - VAERS
  - The few serious events unlikely to be caused by the vaccine

- No elevated frequency or unusual patterns of AEFI in pregnant women
  - Delivery after 20 weeks' gestation is preferred to minimise the risk for any low-frequency adverse event and the possibility that any spurious association might appear causative.
HealthCare Professional Vaccination?
How are we doing in New Zealand?

Influenza vaccination of hospital staff by DHB in 2012

• Vaccination is a duty one assumes in becoming a healthcare provider

• Mandating vaccination is consistent with professional ethics, benefits many, including those who must rely on HCW to protect them, maintains a stable workforce......
• HCWs who have direct patient contact should consider it their responsibility to provide the highest standard of care which includes influenza vaccination.

• In the absence of contraindications, refusal of HCWs who have direct patient contact to be immunized implies failure in their duty of care to patients.
BC 2012 Policy

- Fall 2012 HCW in BC must be vaccinated against influenza as a condition of service
- If unable/unwilling must wear a mask
  - throughout influenza season
  - while in facilities where patient care is given
  - includes physicians, RNs, students, volunteers and contracted workers
  - regardless of reason for not immunising
Protect ourselves and others
- our ethical obligations to our patients

• Am I vaccinated as a health professional?
  – Flu
  – Pertussis
  – Measles
  – Hepatitis B
  – MMR
  – Varicella
Vaccines are not all the same
Vaccines against encapsulated bacteria
Hib, pneumococcal, meningococcal

**Polysaccharides**
- 1970s technology
- Don’t work effectively in children <2 years
- Primarily B cell response only:
  - low affinity Ab production only
- No immune memory generated
  - No induction of T cells
  - Cannot boost immunity
  - Hyporesponsiveness with repeated doses
  - No effect on carriage

Pneumovax23
Mencevax ACWY, Menomune ACYW135

**Conjugates**
- Newer technology
- Effective in children < 2 years
- Immune memory and maturation due to induction of T-cells
  - High affinity Abs
  - Potential to boost (secondary response)
  - Effective in carriage reduction

HiB
Synflorix, Prevenar13
NeisVac, Meningitec, Menactra
Pneumococcal Vaccines

- **PCV10: Synflorix® - Routine childhood programme**
  - Contains the 7 types (4,6B,9V,14,18C,19F,23F) and extra types 1,5,7F
  - conjugated to Protein D (non-typable H influenza)

- **PCV13: Prevenar 13® - High risk children**
  - Contains the 7 types (4,6b,9v,14,18c,19f,23f) and extra types 1,3,5,6A,7F,19A
  - conjugated to CRM197 (non-toxin diphtheria)

- **23 PPV: Pneumovax®23 – high risk adults / children**
  - A polysaccharide vaccine
  - Less immunogenic, shorter duration of immunity
  - Poorly immunogenic in kids under 3 years
Incidence rates of invasive pneumococcal disease by serotype, in children aged less than five years, New Zealand, 1998 – 2007
(NB prior to introduction of PCV vaccine)
Private Market Vaccines
• Cory has been brought in for his 6 week immunisations. His Mum wants to give him all the full protection she can. Should she have the ‘better’ pneumococcal vaccine that she was told about in her antenatal group.
What would I currently recommend to patients?
Cost versus effectiveness: balance...not simple

- Rotavirus 2 doses 6 and 10 weeks
- Varicella
  - 2 dose from 9m or ?one dose at a year of age (assume wild boosting)
  - Adolescents/adults with no history of disease 2dose
- Meningococcal
  - Conjugate C 2+1, or single dose >1 year
  - Conjugate C or quadrivalent at mid teenager
- Pertussis and influenza: pregnancy (funded)/cocoon
  - Occupational Tdap/flu
- HPV boys
- At risk occupations/travellers – hepatitis B, hepatitis A
Private market vaccines to consider

<table>
<thead>
<tr>
<th>Patient</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>Rotavirus vaccine</td>
</tr>
<tr>
<td></td>
<td>Meningococcal C conjugate vaccine</td>
</tr>
<tr>
<td>Older infants/toddlers</td>
<td>Varicella, meningococcal conjugate</td>
</tr>
<tr>
<td>Adolescents/young adults</td>
<td>4-valent Meningococcal conjugate (polysaccharide cheaper for short duration immunity)</td>
</tr>
<tr>
<td>Cocoon protection</td>
<td>Pertussis and influenza</td>
</tr>
<tr>
<td>MSM</td>
<td>HPV</td>
</tr>
<tr>
<td>Boys/young men</td>
<td>HPV</td>
</tr>
<tr>
<td>Elderly</td>
<td>Pneumococcal conjugate + polysaccharide</td>
</tr>
<tr>
<td>You</td>
<td>Pertussis and influenza</td>
</tr>
</tbody>
</table>
Rotavirus

- Death rare
- 1 in 43 children hospitalised by 5 yrs in NZ
- For each hospitalisation 8 children seen in primary care
- > 90% children have RV by 3 yrs
  - no strong ethnic or se gradient, a universal bug!
- Vaccine 85% efficacy against RV hospitalisation
  - 2 doses 4 weeks apart, complete by 24 weeks
  - $100 (currently) - $160 course exc GST and delivery

Grimwood K, Lambert SB. Hum Vaccine 2009;5:57–69
Meningococcal disease rates by age group, 2007–2011

From: *The Epidemiology of Meningococcal disease in New Zealand in 2011* ESR June 2011
## Distribution of strain types among meningococcal disease cases 2011

<table>
<thead>
<tr>
<th>Strain group</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group B</td>
<td>62</td>
</tr>
<tr>
<td>P1.7-2,4</td>
<td>37</td>
</tr>
<tr>
<td>Other group Bs</td>
<td>25</td>
</tr>
<tr>
<td>Group C</td>
<td>38</td>
</tr>
<tr>
<td>P1.5-1,10-8</td>
<td>27</td>
</tr>
<tr>
<td>Other group Cs</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
</tr>
<tr>
<td>Group Y</td>
<td>3</td>
</tr>
<tr>
<td>Group W135</td>
<td>2</td>
</tr>
<tr>
<td>Non-groupable</td>
<td>1</td>
</tr>
</tbody>
</table>

From: *The Epidemiology of Meningococcal disease in New Zealand in 2011* ESR June 2011
Meningococcal vaccines

Currently only private market and outbreak use in NZ

- **Polysaccharides** – A, C, Y, W-135
  - Ineffective in younger children
  - Short duration of immunity
  - Possible hyporesponsiveness with multiple use

- **Conjugates** – C, Quadrivalent
  - Effective in younger children
  - Herd immunity effects

- **B vaccine**.....close

  (NB unlikely to be any individual protection left now in NZ community from MeNZB vaccine)
Varicella vaccines

• **Why use**
  - >90% children catch varicella
  - 150-200 hospitalisations/year (2/3 otherwise healthy)
    - 1-2 long term disability
    - Death occasional
    - Skin sepsis rates

• **When to start**

• **1 dose or 2?**
  - Wild boosting in NZ current context

• **Role of MMRV (not yet available in NZ)**
  - 12-23 months: = 1 extra febrile seizure for every 2300 doses over MMR + Varicella vaccine.

Klein et al Pediatrics July 27 2010
Shingles - Zostavax

• **VE**
  - Zoster reduction 51%
  - Post herpetic neuralgia reduction 67%

• **Contraindications**
  - Anaphylaxis to any components, neomycin
  - Immunodeficiency/ immunosuppressed
  - Pregnancy
  - Active untreated Tb

• **Who to advise**
  - Elderly ..... 

Aims
  - Keep independent living
  - Reduce increased frailty with onset of zoster
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Protects against</th>
<th>Manufacturer</th>
<th>Price per dose(^1)</th>
<th>Number of doses required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adacel(^*)</td>
<td>pertussis, tetanus and diphtheria</td>
<td>Sanofi-Pasteur</td>
<td>$25.00</td>
<td>1 dose as a booster&lt;br&gt;Can be offered to adults for pertussis protection</td>
</tr>
<tr>
<td>Boostrix™</td>
<td>pertussis, tetanus and diphtheria</td>
<td>GSK</td>
<td>$25.00</td>
<td>1 dose as a booster&lt;br&gt;Can be offered to adults for pertussis protection</td>
</tr>
<tr>
<td>Gardasil(^*)</td>
<td>human papillomavirus 6,11,16 and 18</td>
<td>CSL</td>
<td>$128.50</td>
<td>3 doses for females 9-45 yrs and males 12-15 yrs&lt;br&gt;NB funded for girls born after 1.1.90</td>
</tr>
<tr>
<td>Intanza(^*)</td>
<td>Influenza</td>
<td>Sanofi-Pasteur</td>
<td>$150/10</td>
<td>Intradermal vaccine</td>
</tr>
<tr>
<td>IPOL(^*)</td>
<td>polio</td>
<td>Sanofi-Pasteur</td>
<td>$35.32</td>
<td>1 dose as a booster</td>
</tr>
<tr>
<td>Meningitec(^*)</td>
<td>meningococcal disease group C</td>
<td>Pfizer (Wyeth)</td>
<td>$75.00</td>
<td>3 doses before 12 months or 1 dose if given after 12 months</td>
</tr>
<tr>
<td>NeisVac-C™</td>
<td>Meningococcal disease group C</td>
<td>Baxter</td>
<td>$43.00</td>
<td>2 doses before 12 months or 1 dose after 12 months</td>
</tr>
<tr>
<td>Menactra(^*)</td>
<td>Meningococcal disease groups A,C,Y, W135</td>
<td>sanofi-aventis</td>
<td>$89.95</td>
<td>Single dose aged 2 – 55 years&lt;br&gt;Booster dose ever 5 years if risk continues</td>
</tr>
<tr>
<td>Mencevax™ ACWY</td>
<td>meningococcal A, C, W(_{135}) and Y</td>
<td>GSK</td>
<td>$30.00</td>
<td>1 dose. Do not use before 2 years</td>
</tr>
<tr>
<td>Menomune™ ACYW-135</td>
<td>meningococcal A, C, W(_{135}) and Y</td>
<td>Sanofi-Pasteur</td>
<td>$30.00</td>
<td>1 dose. Do not use before 2 years</td>
</tr>
<tr>
<td>Pneumovax(^*)23</td>
<td>pneumococcal disease</td>
<td>MSD</td>
<td>$40.00</td>
<td>1 dose. Do not use before 2 years</td>
</tr>
<tr>
<td>Prevenar 13(^*)</td>
<td>pneumococcal disease</td>
<td>Pfizer (Wyeth)</td>
<td>$168.20</td>
<td>1 dose if given after 2 years&lt;br&gt;NB funded for children born after 1.1.08</td>
</tr>
<tr>
<td>Rotarix(^*)</td>
<td>rotavirus</td>
<td>GSK</td>
<td>$80.00</td>
<td>2 doses (before 24 weeks)</td>
</tr>
<tr>
<td>Varivax(^*)</td>
<td>varicella (chickenpox)</td>
<td>MSD</td>
<td>$50.00</td>
<td>1 dose 12 months-12 years or 2 doses if given from 13 years</td>
</tr>
<tr>
<td>Varilrix™</td>
<td>varicella (chickenpox)</td>
<td>GSK</td>
<td>$50.00</td>
<td>1 dose 9 months-12 years or 2 doses if given from 13 years</td>
</tr>
<tr>
<td>Zostavax™</td>
<td>Varicella (zoster)</td>
<td>MSD</td>
<td>$172.42</td>
<td>1 dose from 50 years</td>
</tr>
</tbody>
</table>
NZ Immunisation Schedule

? the future....
Vaccines: What is next............

• Always the possibility of future flu pandemics
• Next vaccines recommended for the schedule
  – Rotavirus
  – Varicella
• To consider after that
  – Meningococcal Vaccines
    • Conjugates C and quadrivalent
    • B
  – Better flu vaccines: live attenuated (kids), adjuvanted (elderly)
  – HPV for boys/men
  – Shingles vaccines (over 50 yrs)
  – Pertussis vaccines in older age groups
Delivery issues....

- MMRV versus monovalent Varicella
- ?extra injections in 15 month visit or
- ?an extra visit in Year two
- Adult vaccination schedule ?
- ?Children and annual flu vaccination (LAIV)
Slightly more distant horizon

• Better adjuvants
• Delivery mechanisms
  – More intranasal eg live influenza vaccine
  – Aerosol eg measles, rubella
  – Oral eg transgenic plants
  – Transcutaneous eg hepB, anthrax
  – More thermostable
• New targets.....
Fully Immunised at age of 2 years
2007 to 2012

<table>
<thead>
<tr>
<th>Year</th>
<th>2007</th>
<th>2008</th>
<th>Dec-09</th>
<th>Dec-10</th>
<th>Dec-11</th>
<th>Dec-12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunised</td>
<td>78%</td>
<td>82%</td>
<td>85%</td>
<td>88%</td>
<td>92%</td>
<td>91%</td>
</tr>
</tbody>
</table>
Why are we improving

• Commitment at all levels – national target
• Feedback loops – DHBs and PHOs
• General Practice engagement and confidence
  – More focus, higher priority
  – Less missed opportunities

• SYSTEMS
  – Early ENROLMENT! - and follow up
  – Precalls/recalls/audits
  – PMS/NIR
  – Providers to OIS : effective interface

• Confident health sector spills over to confident public
  – Less anti-science in the media
Areas to continue focus: Missed opportunities
True contraindication

• Anaphylaxis to any component of the vaccine
• Acutely unwell: high fever, toxic etc

Immunocompromised with a live vaccine (MMR, Varicella)
Evolving neurological conditions with pertussis
Anaphylaxis to egg with flu vaccine
False....

• MMR vaccine causes autism
• Egg allergy cannot vaccinate with MMR
• Availability of single vaccines eg tetanus
• 3 injections at 15 months is too hard
• Can’t vaccinate while breast feeding
Typologies

- Nuturers – children at low risk of disease
- Fearfuls – experience emotionally distressing
- Vulnerables – barriers to access
- Unwell - child poor health
- Rejectors - opposed

Litmus: Immunisation Audience Research, Feb 2011
Communication challenges
Anecdote trumps science any day
hero, victim and villain

“He plunged the needle into my son and I watched his soul leave his body”
Jenny McCarthy
Loss of confidence in vaccination...

Whooping Cough Incidence in England and Wales (1965-1995)

- Disease Incidence per 100,000
- Pertussis Vaccination Coverage (%)

- 81% Pertussis vaccine concerns publicized
- 31% Outbreaks of pertussis
- 93%
International Examples leading to reduction in coverage

• Polio vaccine and contraceptives – Nigeria 2004
• Multiple sclerosis and HepB vaccine – France
• Pertussis vaccine and brain damage internationally 1980s

• MMR and autism – UK, 1998…..
Lack of understanding of immunology

- Baby’s system is too young
- Overloaded immune systems
- Skewering of the immune system
- Too many antigens in each vaccine
Myth: Vaccines reactions are underreported

Adverse Event reporting via CARM is for signal generation for anything new or unexpected e.g. febrile convulsions and Fluvax

- is not designed to account for all adverse events

Active surveillance occurs internationally in many different formats

e.g. vaccine safety data links - matching hospital records, GP records to imms records; prevalence studies; case control; independent reviews
US Vaccine Safety Datalink Group

Ray et al PIDJ 2006


“In this study of more than 2 million children DTP and MMR vaccines were not associated with an increased risk of encephalopathy after vaccination”.

Vaccinated people slightly **less likely** to have allergic disease

Vaccinated babies **less likely** to die of cot death

Vaccinated people **no more** likely to develop:

- Autism
- Diabetes
- Multiple sclerosis...

In the 1970s a swine flu vaccine used in the USA had an increased risk of Guillain-Barre Syndrome

- One brand of 2009 influenza vaccine associated with 2 cases per 1 million doses in older adults.
- Influenza infection is associated with GBS

**MMR 1/30,000 ITP**

A recent monovalent adjuvanted flu vaccine was associated with an increase in narcolepsy (not used in NZ)
Coincidence vs. Causality

“Regardless of what the research tells us, I know what I saw.”

Dr. Kathy Pratt, April 25th, 2001, during a hearing by the Office of Government Reform to investigate MMR and autism
The importance of knowing background rates of disease in assessment of vaccine safety

If a cohort of 10 million individuals was vaccinated with a hypothetical vaccine, the medical events that would be expected to occur within 6 weeks post hypothetical vaccine dose:

- **21.5 cases of Guillain-Barré Syndrome**
- **5.75 cases of sudden death**

In a cohort of 1 million vaccinated pregnant women, within **1 day** of hypothetical vaccination:

- **397 would be predicted to have a spontaneous abortion**

Paediatric Vaccines Research Review

Welcome to the latest edition of Paediatric Vaccines Research Review, a quarterly New Zealand publication bringing you some of the most important paediatric vaccine research from around the world. The Review provides summaries of 10 recent studies, each accompanied by a comment from either Dr. Nikki Turner or Helen Petousis-Harris on why it is important and how it can potentially affect practice. The Review also provides website links to the abstract or fully published paper so you can make your own judgements. Highlights this month include reassuring data of the safety of the influenza vaccine in pregnant women, impressive results from a study of the quadrivalent HPV vaccine in males, and exciting signs that intranasal PCV7 vaccine might suppress asthma.

If you have colleagues within New Zealand who would like to receive Paediatric Vaccines Research Review, please send us their contact email and we will include them next time. We hope you find this edition interesting and look forward to hearing your comments.

Kind regards,

Dr Chris Ianlaid
Medical Advisor, Research Review
christianlaidresearchreview.co.nz

Improving timely childhood immunizations through pay for performance in Medicaid-managed care

Authors: Chin AI et al

Summary: This study evaluated the impact of a pay-for-performance (P4P) programme designed to reward timely immunization delivery to 2-year-olds. In 2003, the Hudson Health Plan (a not-for-profit Medicaid-focused managed care plan) introduced a scheme whereby it paid $10 for each fully immunized, 2-year-old. Immunization rates within Hudson Health Plan were at a higher rate than those in comparison health plans. Supplementary analyses found that children with chronic conditions were more likely to be fully immunized during the study period as a result of the programme. In conclusion, a P4P programme can improve childhood immunization rates.

Comment: Payment for performance (incentives) has been shown internationally to be effective in many contexts in healthcare. However, in immunisation there is limited research published on effective strategies and design. This study capitalised on a natural experiment in New York State, USA where one healthcare plan offered providers large financial remuneration and administrative support for timely immunisation rates, while others in the same region did not. These reimbursements amounted to 1%-29% above base reimbursement for the care of 0- to 2-year-olds. It is no surprise that this was effective, however it was modest. Importantly it did not also incentivise disparities. However the question for now would be whether this is the best use of a considerable amount of resources and how effective interventions of this nature would be if they were of a lesser amount? MT

http://dx.doi.org/10.1111/j.1446-7391.2010.01160.x

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www.immune.org.nz
EXTRA SLIDES
Long term follow up of vaccines

• Difficult to follow up large cohort of millions long term. (very large numbers required for rare risks)
• Instead use a mixture of methods
  – Hypothesis generate i.e. do vaccines cause cot death
  – No one study answers all your questions
  – Beware of poorly designed studies creating bias
  – Several studies, range of methods such as
    • Case-control studies
    • Cohort studies
    • Prospective
    • Retrospective
    • Cross-sectional
• For example - all these these have been used to explore and reject the hypothesis that MMR causes Autism
Examples of safety evaluation

- Vaccine safety datalinks
  - E.g. encephalopathy MMR, wPertusisis
  - US CDC and HMOs collaboration
    - autism/MMR, rotavirus/intussusception, hepB/MS, thiomersal
- Matching hospital records to immunisation records
  - UK MMR/autism
- Prevalence studies
  - MMR autism, Denmark, whole birth cohort
- Case control
  - neurological damage and pertussis vaccine (UK)
- Independent reviews e.g. IOM reviews
  - Thiomersal, multiple antigens, influenza vaccine / neurological disorders
Influenza in pregnancy - risk to mother

• Excess hospital admissions in healthy pregnant women
  – Similar to non pregnant women with comorbidities
• Excess hospital admissions in women with co-morbidities
• Increases with gestation
• More vulnerable during pandemics
  – 1918, 27% case fatality rate
  – 1957, ½ deaths in young women who were pregnant
  – 2009, 13% of all deaths from H1N1 were pregnant women

Influenza in pregnancy - risks to fetus

1. Infection and fever
   - Associated with congenital abnormalities

2. Associated with increased risk of cancer
   - Neoplasms of lymphatic and haematopoietic tissue 1957 Asian influenza
   - Neuroblastomas

3. Increased risk of general complications

Influenza vaccine in pregnancy - effectiveness

- Immunogenicity of TIV
  - Similar to non pregnant women

- 28% efficacy against febrile illness in pregnant women

- High transplacental transfer of maternal Ab
  - Half life 43-53 days
  - Protective for around 8 weeks (61%)


Influenza vaccine in pregnancy – safety

• Several studies and no indication of increased risk to fetus e.g.:
  – 2291 vaccinated in cohort of 51000 no evidence for excess of childhood malignancies (Heinonen 1973)
  – 41 vaccinated in cohort of 517 no excess physical or neurological, perinatal complications, no serious events (Deinard 1981)
  – 1006 vaccinated and 1495 unvaccinated, no adverse events Also passive reporting systems
    • i.e. UK Yellow Card reporting 1994-2004

Neonatal outcomes - RCT

- 340 pregnant women randomised to TIV or PPV-23
- During period with circulating influenza maternal influenza vaccination associated with
  - Fewer small for gestational age infants
  - Increase in mean birth weight
  - Less incidence of fever and respiratory illness in mother

Children/Adults high risk: pre or post splenectomy

- Vaccines now being offered:
  - Prevenar 13® (children up to 18 years only)
  - Act-HIB™
  - Pneumovax® 23
  - Menomune ACYW135

NB Prevenar 13® and Act-HIB™ are only licensed to 5 years of age, giving to older children and adults is currently outside of licensure. While there are not expected to be any safety concerns, it is important to give full informed consent.
Targeted programmes

- BCG for high risk infants
  - List of high-incidence countries:
    - [www.moh.govt.nz/immunisation](http://www.moh.govt.nz/immunisation)

- Neonatal hepatitis B and HBIG for infants of hepatitis B carrier mothers

- Influenza for those at high risk

- Pertussis for pregnant women 28-38 weeks

- Pneumococcal programme for high risk children

- Splenectomised older children/ adults

- MMR 2 doses all unvaccinated adults born after 1969
Pneumococcal high risk children: 0 - 18 yrs

• Offer PCV13 followed by 23PPV
• Up to 5 years of age: (59 months)
  – On immunosuppressive therapy or radiation therapy
  – Primary immune deficiencies
  – HIV
  – Renal failure or nephrotic syndrome
  – Immune suppressed following organ transplantation
  – Cochlear implants, intracranial shunts
  – CSF leaks
  – On corticosteroids at least 2mg/kg/day prednisone (or 20mg a day) >2 weeks
  – Chronic pulmonary disease
  – IDDM
  – Down Syndrome
  – Pre or post-splenectomy or functional asplenia
  – Preterm infants born at under 28 weeks
• 6 – 18 years:
  – Pre or post-splenectomy or functional asplenia