CVU:

What’s new?

2nd December 2013

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Outline

1. MMRV
2. Hib-MenC
3. HPV for boys
4. TIV recommendations for 2013
5. What's new at RCH?
Two versions of the NIP schedule card were included:
- Current to 30 June 2013
- New NIP schedule from 1 July 2013

New layout – includes 5 parts
### The NIP as of July 2013

<table>
<thead>
<tr>
<th>Age</th>
<th>Disease</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>Hepatitis B</td>
<td>H-B-Vax II Paediatric</td>
</tr>
<tr>
<td>2, 4, 6 months</td>
<td>Dip, tet, pertussis, hepatitis B, polio, <em>Hib</em> Pneumococcal Rotavirus</td>
<td>Infanrix <em>hexa</em> Prevenar 13 RotaTeq</td>
</tr>
<tr>
<td>12 months</td>
<td>Measles, mumps, rubella, <em>Hib</em>, meningococcal C</td>
<td><strong>M-M-R II / Priorix Menitorix</strong></td>
</tr>
<tr>
<td>18 months</td>
<td>Measles, mumps, rubella, chickenpox</td>
<td>Priorix-Tetra</td>
</tr>
<tr>
<td>4 years</td>
<td>Diphtheria, tetanus, pertussis, polio Measles, mumps, rubella</td>
<td>Infanrix IPV M-M-R II / Priorix</td>
</tr>
</tbody>
</table>
## The NIP as of July 2013

<table>
<thead>
<tr>
<th>Age</th>
<th>Disease</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-13 years</td>
<td>Hepatitis B</td>
<td>H-B-Vax II Adult</td>
</tr>
<tr>
<td>12-13 years or year 7</td>
<td>Chickenpox, Human papillomavirus</td>
<td>Varivax / Varilrix Gardasil</td>
</tr>
<tr>
<td>14-15 years or year 9</td>
<td>Human papillomavirus</td>
<td>Gardasil</td>
</tr>
<tr>
<td>15-16 years or year 10</td>
<td>Diphtheria, tetanus, pertussis</td>
<td>Boostrix</td>
</tr>
</tbody>
</table>
1. MMRV
Measles, mumps, rubella and chickenpox (varicella)

Immunisation information

The National Immunisation Program provides free combined MMRV vaccine for protection against measles, mumps, rubella and chickenpox (varicella) to children at 18 months of age.

Measles
Measles is a serious and highly contagious viral disease that causes fever, runny nose, cough and sore red eyes,
MMRV

- From 1 July 2013 new measles-mumps-rubella-varicella (MMRV) vaccines available
  - Given as 2nd dose of measles-containing vaccine at 18 months of age
  - Brings forward 2nd dose of MMR (from 4 years)
- MMRV not recommended in adolescents ≥14 years
Priorix-Tetra vs Priorix

When reconstituted, both pink and packaging the same – take care!
MMRV

Why?

• Earlier protection: 95% respond to dose 1; additional 2-5% respond to dose 2

• Improve varicella coverage
  • 2009: varicella coverage is lowest of all paediatric vaccines with only 81.8% of children vaccinated by 24 months of age
    • Hull, CDI 2011 35(2)132-140

• Reduce the number of injections
  • only 1 needle at 4 years now
Measles

- A “heat seeking missile for the un-immunised”
- A number of measles cases in Australia this year (to 7 Nov 2013 from NNDSS)
  - 112 cases from five jurisdictions: Qld (35), Vic (30), NSW (28), WA (10) and SA (9)
  - median age 21 years of age, with a range of 0-51 years.
- Based on vaccination status data:
  - 47% not vaccinated: including 4 infants < 1 year
  - 6% partially and 10% fully vaccinated
  - 40% unknown vaccination status
- Most cases of measles in Australia are either imported or import-related but 1/3 cases related to a cluster which commenced in Victoria with unknown primary source
Measles

Figure 1: Notifications of Measles, Australia, 2007-2013, by Diagnosis Week
Measles

Figure 2: Notifications of Measles (n=112), Australia, 2013, by Vaccination Status and Age Group

- Not vaccinated
- Partially vaccinated
- Vaccinated
- Unknown

Age Distribution and Vaccination Status

Murdoch Childrens Research Institute

Varicella

- Varicella introduced at 18 months onto NIP Nov 2005
- VZV vaccine prevents 85% of varicella
  - 97% protection against moderate/severe disease
  - 15% breakthrough cases
- Marked decrease in congenital and neonatal varicella cases
  - 1997-1999 data compared with 2006-09: CVS: 0.8/100,000 live births p.a c/w 0.19/100,000 in 2006-7
  - 0 cases 2008-9

MMRV – immunogenicity and safety

- Immunogenicity: equivalent to MMR + V
  - Increased mumps titer
  - No evidence for interference

- Safety:
  - Fever 1 in 5
    - More fever when MMRV given as dose 1 of MMR vaccine vs MMR + V separately
    - Similar fever rates when MMRV given as dose 2 vs MMR alone
Table 3. Analysis of reported incidence of any and grade 3 solicited symptoms from pooled studies.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dose 1: Priorix-Tetra</th>
<th>Dose 2: Priorix-Tetra</th>
<th>Dose 1: Priorix + Varilrix</th>
<th>Dose 2: Priorix</th>
<th>p &lt; 0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N= 2206</td>
<td>N= 574</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>≥ 38.0°C</td>
<td>1349</td>
<td>61.15</td>
<td>263</td>
<td>45.82</td>
</tr>
<tr>
<td></td>
<td>&gt; 39.5°C</td>
<td>247</td>
<td>11.20</td>
<td>43</td>
<td>7.49</td>
</tr>
<tr>
<td></td>
<td>≥ 38.0°C Rel</td>
<td>867</td>
<td>39.30</td>
<td>164</td>
<td>28.57</td>
</tr>
<tr>
<td></td>
<td>&gt; 39.5°C Rel</td>
<td>137</td>
<td>6.21</td>
<td>22</td>
<td>3.83</td>
</tr>
<tr>
<td>Rash</td>
<td>any</td>
<td>448</td>
<td>20.31</td>
<td>94</td>
<td>16.38</td>
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<tr>
<td></td>
<td>measles/rubella like</td>
<td>110</td>
<td>4.99</td>
<td>27</td>
<td>4.70</td>
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<tr>
<td></td>
<td>varicella-like</td>
<td>24</td>
<td>1.09</td>
<td>2</td>
<td>0.35</td>
</tr>
<tr>
<td>Pain</td>
<td>Any</td>
<td>209</td>
<td>9.47</td>
<td>50</td>
<td>8.71</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>2</td>
<td>0.09</td>
<td>0</td>
<td>0.00</td>
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<tr>
<td>Redness</td>
<td>Any</td>
<td>596</td>
<td>27.02</td>
<td>157</td>
<td>27.35</td>
</tr>
<tr>
<td></td>
<td>&gt; 20 mm</td>
<td>5</td>
<td>0.23</td>
<td>0</td>
<td>0.00</td>
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<tr>
<td>Swelling</td>
<td>Any</td>
<td>186</td>
<td>8.43</td>
<td>46</td>
<td>8.01</td>
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<tr>
<td></td>
<td>&gt; 20 mm</td>
<td>7</td>
<td>0.32</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>N= 2173</td>
<td>636</td>
<td>29.27</td>
<td>179</td>
<td>31.68</td>
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<tr>
<td></td>
<td>≥ 38.0°C</td>
<td>68</td>
<td>3.13</td>
<td>21</td>
<td>3.72</td>
</tr>
<tr>
<td></td>
<td>&gt; 39.5°C</td>
<td>55</td>
<td>2.44</td>
<td>19</td>
<td>3.40</td>
</tr>
<tr>
<td></td>
<td>≥ 38.0°C Rel</td>
<td>351</td>
<td>16.15</td>
<td>85</td>
<td>15.04</td>
</tr>
<tr>
<td></td>
<td>&gt; 39.5°C Rel</td>
<td>36</td>
<td>1.66</td>
<td>9</td>
<td>1.59</td>
</tr>
<tr>
<td>Rash</td>
<td>any</td>
<td>249</td>
<td>11.46</td>
<td>59</td>
<td>10.44</td>
</tr>
<tr>
<td></td>
<td>measles/rubella like</td>
<td>23</td>
<td>1.06</td>
<td>9</td>
<td>1.59</td>
</tr>
</tbody>
</table>
Post vaccination outpatient fever visits among 12- to 23-month-olds according to vaccine received: VSD study population, 2000–2008.
MMRV – febrile convulsions

Risk post dose 1 MMRV for 12-23 months:

- Post dose 1: 2 fold risk of febrile seizures 7-10 days post MMRV
  - (RR 1.98 (95% CI 1.43-2.73) compared to MMR + V  
    Klein et al Pediatrics 2010
- 1 additional seizure for every 2300 doses MMRV given
- All MMR vaccines have a fever and seizure risk compared to V alone
Post vaccination seizures among 12- to 23-month-olds according to vaccine received: VSD study population, 2000–2008.
MMRV – febrile convulsions

Risk post Dose 2

- No direct data for MMRV dose 2 at 18 months (only at 4-6 years)  
  Klein et al Pediatrics 2012 VSD 4-6yo
- Risk estimated to be 1:86,750
  - lower limit of 95% CI 1: 15 500

Therefore can rule out with 95% confidence a risk greater than 1 febrile seizure per 15 500 MMRV doses and 1 per 18 000 MMR + V doses
**FIGURE 1**
Postvaccination seizures among 4- to 6-year-olds by vaccine received, VSD study population 2000–2008.

**TABLE 3** Confirmed Febrile Seizures 7–10 Days after Vaccination Among 4- to 6-Year-Olds: 2000–2008

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Confirmed Febrile Seizures Post-Vaccination Days 7–10</th>
<th>Per Total Doses (95% CI)</th>
<th>Per 100 000 Doses (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMRV</td>
<td></td>
<td>1 per 86 750 (1 per 3 426 441, 1 per 15 570)</td>
<td>1.2 (0.03, 6.4)</td>
</tr>
<tr>
<td>MMR + Varicella</td>
<td></td>
<td>0 per 67 438 (0, 1 per 18 282)</td>
<td>0 (0, 5.5)</td>
</tr>
</tbody>
</table>
MMRV - summary

MMRV not recommended as 1st dose of measles-containing vaccine in children <4 years

- Fever risk higher when MMRV given dose 1
- Febrile convulsion risk of MMRV given at 18 months extremely small (no greater than 1 in 15 500)
- Will provide earlier protection against measles
  - Aim 95% coverage dose 1; 90% dose 2
- Improve varicella coverage
MMRV - summary

• Subcut or IM injection
• Priorix given at 12 months
  • If children have received varicella at 18 months, will still be given MMR at 4 years (until end of 2015)
• Children with egg allergy, including anaphylaxis, can be safely given MMR or MMRV vaccine
• 2nd dose of monovalent varicella vaccine not funded on NIP but can be given to minimize chance of breakthrough disease
2. Hib-MenCCV
Hib-MenCCV (Haemophilus influenza type b and Meningococcal C)

- 4th booster dose of Hib vaccine given in combination with meningococcal group C vaccine at 12 months
- Introduced July 1 2013
- No specific safety concerns
- Menitorix® replaces 2 injections
  - Hiberix®
  - NeisVac-C®
- reduces the number of injections needed at 12 months of age from three to two
Menitorix®

General catch up principles in children < 10 years of age

- Menitorix® can be used for catch-up vaccinations for either MenC or Hib in children <10 years of age, if required
- Administering ‘extra’ dose(s) of either Hib or MenCCV is acceptable - benefits of catch-up greater than any potential increase in adverse events due to additional dose(s) of either vaccine
Menitorix® - catch up

- Prioritise Infanrix hexa®, Prevenar 13® and MMR vaccines over menC vaccine in a child >12 months
  - low incidence of meningococcal serogroup C disease
- co-administration of Menitorix® with other Hib-containing vaccines, such as Infanrix hexa® acceptable if no suitable alternative vaccine(s) or schedules
  - Increase in AEs or reduction in immunogenicity of concomitantly administered vaccine antigens unlikely
  - DTPa-IPV can be considered but require access to monovalent paediatric hepatitis B vaccine
  - do not give the un-reconstituted component of Infanrix hexa® (DTPa-hepB-IPV antigens) to avoid Hib PRP-T antigen
Menitorix® - catch up

• limited evidence on the use of Menitorix® in adolescents and adults
  • vaccination of adolescents and adults against Hib and menC is not routinely recommended
• If a dose of MenCCV is required for a person ≥10 years of age ie unimmunised household or sexual contact
  • Menitorix® acceptable
  • Alternatively, use the 4vMenCV (Menactra® and Menveo®)
  • preferred over quadrivalent meningococcal polysaccharide vaccines (Mencevax ACWY® and Menomune®)
  • none of the available meningococcal vaccines are funded under the NIP for these uses
3. HPV for boys
HPV

- Highly contagious virus that can cause HPV-related cancers and disease, including genital warts
  - Responsible for >99.7% cervical cancer
  - 4 out of 5 people will have a HPV infection at some point in their lives - often asymptomatic

- **HPV types**
  - >100 types in humans and > 40 affect the anogenital mucosa
  - 15 designated as “high risk”
HPV types

- **16 and 18**: causative agents in 70-80% of all cervical cancers; account for about 90% of all HPV attributable cancers in men
  - Cause cancers of the vulva and vagina, anus, penis and oropharynx
- **6 and 11**: ‘low-risk’ (for cancer) - associated with 90% of genital warts
HPV vaccine

- HPV introduced in girls in 2007
- 3 dose schedule: 0, 2 and 6 months
- **GARDASIL®**
  - protection against four HPV genotypes (6, 11, 16, 18)
  - most effective when three doses given before first sexual contact/initial exposure to HPV
  - Longer term studies – vaccine highly immunogenic and efficacious after 8.5 years
    
    Olsson SE, Vaccine 2007; (25): 4931-7

- Females - still need regular Pap tests
- **HPV Register** – notify to reduce the risk of duplicate doses being given or vaccination courses not being completed.
HPV for boys

Why?

• Provide protection against a range of HPV-related cancers and disease
• Help protect the almost 30% of Australian females who remain unvaccinated (1)
• prevent up to an additional 24% of new HPV infections if similar coverage to female program (2)
• Genital warts (2004-2009):
  • decrease of approx 59% in young Australian females and 28% in heterosexual males, especially young males, due to herd immunity (3)
• More expected with the male program

1. (HPV register, data at January 2011); 2. (Smith MA, The predicted impact of HPV vaccination on male infections and male HPV-related cancers in Australia. Vaccine 2011; 29: 9112 – 22); 3. (Donovan B, Quadrivalent human papillomavirus vaccination and trends in genital warts in Australia: analysis of national sentinel surveillance data. Lancet 2011; 11: 39-44)
HPV for boys

• Vaccination recommended for:
  • Females aged 9–18 years (optimally at 11–13 years)
  • Males aged 9–18 years (optimally at 11–13 years)

• From February 2013:
  • Males aged 12-13 included in school-based national HPV program
  • Males aged 14-15 years eligible to receive the vaccine through a catch-up program in 2013 and 2014
Immunize Australia HPV site

Information, answers to common questions and a range of downloadable resources about the HPV school-based vaccination program for parents, students and health professionals.
Rollout of HPV School Vaccination Program

Year levels to be immunised

HPV - safety

- 7 million doses Gardasil administered in Australia
  - number of suspected adverse events reported very low
- Majority mild: headache, injection site reactions (pain, swelling, and/or redness at the injection site), nausea, dizziness, fatigue/lethargy, fever and malaise
- Syncope/syncopal seizures – common
  - Pain/adolescent propensity
- Utricaria: reported but true hypersensitivity uncommon
- Anaphylaxis: similar to other vaccines
HPV

Mass psychogenic response to human papillomavirus vaccination

Jim P Buttery, Simon Madin, Nigel W Crawford, Sonja Elia, Sophie La Vincente, Sarah Hanieh, Lindsay Smith and Bruce Bolam

Cervical cancer associated with human papillomavirus (HPV) affects approximately 1000 Australian women each year, causing about 300 deaths. The newly licensed HPV vaccines Gardasil (CSL Limited), a quadrivalent vaccine (4vHPV), and Cervarix (GlaxoSmithKline Vaccines), a bivalent vaccine (2vHPV), induce protection against the two most common strains of HPV, which cause 70% of all cervical cancers.

The quadrivalent HPV vaccine was included in the government-funded National Immunisation Program from April 2007 for females aged 12–26 years. The initial phase targeted secondary schools, vaccinating girls aged 12–17 years in Years 7, 10, 11 and 12. This program was conducted by local government vaccination teams in Victoria.

The reactogenicity of 4vHPV reported in clinical trials was acceptable, with serious adverse events following immunisation (AEFI) reported in less than 0.1% of vaccine recipients. In Australia, AEFI are reported to the Adverse Drug Reactions Unit separate entrances and exits for vaccinees, and a single class queued at any one time. Importantly, the entire school was built around a central quadrangle, with each of the 26 symptomatic girls taken to the sick bay being led through there in view of all classrooms.

Discussion

Without evidence of an organic aetiology or similar reports of AEFI elsewhere after the initiation of population vaccination with 4vHPV using the same vaccine batch, it is highly likely that this cluster was the result of a psychogenic response to mass vaccination in a school setting. With the implementation of a community-wide immunisation program, mass school programs are highly cost-effective and most effective for maximal coverage. However, similar psychogenic responses are well documented.

Mass psychogenic illness has been defined as “the collective occurrence of a constellation of symptoms suggestive of organic disease, but without demonstrable underlying pathology.”

HPV introduction in boys 2013: NO mass psychogenic response and prospective collection of adverse events
4. Influenza recommendations 2013
• 70% children contract the virus during pandemic years (compared with 10-30% adults)

• Amongst other vaccine-preventable diseases, flu is the leading cause for hospitalisations in children <5 y.o.

Courtesy of Influenza Specialist Group (ISG)
Risk of influenza in previously healthy children

• Neurological complications
  • 9.7% of all children admitted with influenza had a neurological complication (1)
  • 45% of these were previously healthy children with no medical risk factors
  • 50% cases in children <5 years
  • Only 60% presented with the triad of cough, coryza and fever and 12% had no respiratory symptoms: think of Flu!
  • Only 14% children with pre-existing medical conditions had had the flu vaccine and 10.9% overall

• Early diagnosis and antiviral medication should be considered in hospitalised children and those children at high risk of complications

Influenza

Handbook - Information added on:

• Intradermal vaccines
• Age specifications for each vaccine brand
• Fluvax (CSL) *not* for children aged <10 years
• Benefits of vaccination in Pregnancy
• Children (especially aged ≥6 months and <5 years)
• Immunocompromised
Recommendations

Now recommended for
• Staff in early childhood education/care
• Pork industry workers
• Persons at increased risk of complications from influenza infection expanded to include:
  • Obesity (BMI ≥30)
  • Down syndrome (all persons)
  • Alcoholism (as a chronic illness)
TIV recommendations 2013

- The trivalent influenza vaccine (TIV) contained 2 new strain changes in 2013:
  - A/California/7/2009 (H1N1)-like virus
  - A (H3N2): an A/Victoria/361/2011 (H3N2)-like virus
  - B/Wisconsin/1/2010-like virus

- In 2014: WHO recommended 2 new strain changes
  - An A/California/7/2009 (H1N1) - like virus
  - An A/Texas/50/2012 (H3N2) - like virus
  - A B/Massachusetts/2/2012 - like virus
Influenza 2013

2013 influenza
- commenced from a higher than usual inter-seasonal level
- short in duration and moderate in intensity
- 40% fewer total notifications compared with 2012
- overall influenza A was the predominant influenza virus type
- Pandemic Influenza A(H1N1)pdm09: 15% of overall notifications, compared to <1% of notifications in 2012
- influenza B higher than in recent years.
Routinely notified cases of laboratory-confirmed influenza (rate per 100,000 population) by age group and sex, Victoria, 1 January to week ending 27 October 2013
# Dosing guidelines by age

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
<th>Number of doses in the 1st year the vaccine is received</th>
<th>Number of doses in subsequent years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 months</td>
<td>Not recommended (poor immune response)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>&gt; 6 months to &lt; 3 years</td>
<td>0.25ml</td>
<td>2 4-weeks apart</td>
<td>1</td>
</tr>
<tr>
<td>&gt; 3 years to 9 years</td>
<td>0.5ml</td>
<td>2 4-weeks apart</td>
<td>1</td>
</tr>
<tr>
<td>&gt; 10 years</td>
<td>0.5ml</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
TIV and PCV13 in children < 6 years

• In 2011:
  • USA - an increase of febrile convulsions in children 12-24 months having Prevenar13® and Trivalent Influenza Vaccine (TIV) at the same time.
  • ATAGI recommendation is to consider separating these vaccines by 3 days
  • RCH: we recommend that children < 6 years should have these two vaccines separated by a minimum of 3 days
Two doses of TIV if immunosuppressed

- As there were 2 TIV strain changes in 2013
  - we are recommended 2 doses a minimum 4-weeks apart for immunocompromised and special risk patients of all ages (> 6-months)
Influenza vaccine and egg allergy

Recommendations:

• non-anaphylactic reactions to egg:
  • safe to administer under medical supervision as a single dose, with a 30-minute observation period (instead of 15 minutes)

• history of egg anaphylaxis: refer to an Allergy clinic ie SAEFVIC
Summary

• Young children are at risk of contracting and being hospitalised from influenza
  • Universal influenza vaccination should be supported
  • influenza can have serious consequences and be fatal in previously well children
5. What's new at RCH?
BCG clinics

- Funded at RCH and MMC
  - Increase in BCG vaccine requests since restriction of BCG vaccine clinics in Victoria in September 2012
  - Designated BCG clinics at RCH (Nov 2013) and MMC
  - Children < 12 months who intend to travel to high TB areas and who require limited other travel vaccines or travel advice
  - Approx 6-12 patients on a Tuesday morning, follow-up at 6 months (earlier of concerns); referral of siblings and parents if needed
Telehealth

- SAEFVIC offers telehealth for rural and regional patients
  - Usually Tuesday morning clinic at RCH
  - Very convenient for families
  - Provide clinical assessment and recommendations with vaccines being given by usual provider if possible
Thank you

- Any questions
  - SAEFVIC at RCH and MMC
  - RCH Immunisation service and Monash Immunisation