Childhood Vaccines: What’s new?

Jim Buttery

Monash Children’s Hospital
Monash University
SAEFVIC
Disclosures

Through employer- Monash Health- No personal compensation or payment:

Served on DSMB: Seqiris

Investigator on clinical trials:
Novavax, Merck, Seqiris, MedImmune

Member TGA Advisory Committee on Vaccines
### AUSTRALIAN STANDARD VACCINATION SCHEDULE
(November 1996)

#### July 2018

**AGE**

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>VACCINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>6 weeks</td>
<td>Diphtheria, tetanus, pertussis, <em>Haemophilus influenzae</em> type b, hepatitis B, polio</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
</tr>
<tr>
<td></td>
<td>Rotavirus</td>
</tr>
<tr>
<td>4 months</td>
<td>Diphtheria, tetanus, pertussis, <em>Haemophilus influenzae</em> type b, hepatitis B, polio</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
</tr>
<tr>
<td></td>
<td>Rotavirus</td>
</tr>
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</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
</tr>
<tr>
<td></td>
<td>Rotavirus</td>
</tr>
<tr>
<td>12 months</td>
<td>Meningococcal ACWY</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
</tr>
<tr>
<td></td>
<td>Measles, mumps, rubella</td>
</tr>
<tr>
<td></td>
<td>Diphtheria, tetanus, pertussis</td>
</tr>
<tr>
<td></td>
<td>Measles, mumps, rubella, varicella</td>
</tr>
<tr>
<td></td>
<td><em>Haemophilus influenzae</em> type b</td>
</tr>
<tr>
<td>12 months†</td>
<td>Diphtheria, tetanus, pertussis, <em>Haemophilus influenzae</em> type b, hepatitis B, polio</td>
</tr>
<tr>
<td>18 months</td>
<td>Meningococcal ACWY</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
</tr>
<tr>
<td></td>
<td>Measles, mumps, rubella</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
<td><em>Haemophilus influenzae</em> type b</td>
</tr>
<tr>
<td>4 years</td>
<td>Diphtheria, tetanus, pertussis</td>
</tr>
<tr>
<td></td>
<td>Human papillomavirus (2 doses)</td>
</tr>
<tr>
<td></td>
<td>Meningococcal ACWY</td>
</tr>
<tr>
<td>Years 10 - 11 (In 2018)</td>
<td>Diphtheria, tetanus, pertussis</td>
</tr>
<tr>
<td></td>
<td>Human papillomavirus (2 doses)</td>
</tr>
<tr>
<td></td>
<td>Meningococcal ACWY</td>
</tr>
</tbody>
</table>
Lessons from history: schedule

“Its all about the antibody stupid”
Hib

UK: Booster dose added 2003

MenC

Post marketing studies of MCC vaccines in UK

- Short term protection high in all age groups (>=90%)
  - correlated well with immunological correlate (rSBA >=1:8)
- Protection declines over time in younger vaccinees
  - Remains high if vaccinated as older child / adolescent

<table>
<thead>
<tr>
<th>Age at vaccination</th>
<th>Within 1 year</th>
<th>More than 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (routine)</td>
<td>97 %</td>
<td>68 %</td>
</tr>
<tr>
<td>Toddlers (catch-up)</td>
<td>89 %</td>
<td>71 %</td>
</tr>
<tr>
<td>3 to 18 years</td>
<td>96 %</td>
<td>93 %</td>
</tr>
</tbody>
</table>


The Lancet

Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction

Caroline I. Trotter, PhD • Nick J. Andrews, MSc • Edward B Kaczmarski, FRCPath • Elizabeth Miller, FRCPath • Mary E Ramsay, FFPHM

Published: July 24, 2004 • DOI: https://doi.org/10.1016/S0140-6736(04)16725-1

Heath & Ramsay BMJ 2003
Australia: Pneumococcus

• Cases of 13vPCV vaccine failures in toddlers older than 12 months continue to occur at higher rates than seen in other countries that provide a booster dose of 13vPCV during the second year of life. These vaccine failures were children diagnosed with IPD due to serotypes covered in 13vPCV who had received three infant doses of 13vPCV (at 2, 4, 6 months of age). Although not all children who are vaccinated will be protected, the evidence shows that some children in Australia who have received three doses of 13vPCV in accordance with the current schedule are not being adequately protected beyond the first year of life.

• Other countries that provide a dose of 13vPCV during the second year of life are seeing greater benefits from herd immunity than is currently being achieved in Australia. This is reflected in a lower number of IPD cases due to vaccine serotypes among unvaccinated children and adults. The experience in other countries shows that by providing better protection during the second year of life, Australia also has the potential to reduce the risk of unvaccinated individuals getting IPD due to the serotypes in the 13vPCV.
Australia Pneumococcus 2018

NIP schedule changes July 1 2018- FAQ’s

1. Do all 12-month old’s receive a Prevenar 13® even if they’ve previously received 3 doses in their infant schedule?

All children 12-months of age from July 1 2018 will be offered a Prevenar 13®. If a child has previously received 3 doses in their infant schedule they are not required on the AIR to have a 4th dose at 12-months, but to reduce the risk of invasive pneumococcal disease it is clinically recommended and safe to do so.
Lessons from history: schedule

“Its all about the antibody stupid”

Conjugate vaccines need a dose in or after the 2\textsuperscript{nd} year of life
Meningococcal disease has a case fatality rate of approximately 10%, however more deaths are caused by septicaemia than by meningitis.

Meningococcal Epidemiology Victoria
Meningococcal notifications

Meningococcal infections notified in Victoria, 1936-2012

Number of notified cases

Year


2054701, 2450000, 2930000, 3220000, 3520000, 3750000

700

600

500

400

300

200

100

0


3500000

3000000

2500000

2000000

1500000

1000000

500000

0

Cases

VIC Population

Courtesy Lucinda Franklin/Kath Taylor, DHHS Victoria
Meningococcal immunity

Meningococcal vaccine history Aust

1970’s Polysaccharides developed incl ACWY
1991 MenACWY PS 1\textsuperscript{st} recommendation (Haj)
2001 1\textsuperscript{st} Men C conjugate licensed
2003 Funded MenC program (12m)
2010 Hib- MenC registered
2011 1\textsuperscript{st} Men ACWY conjugate registered
2013 1\textsuperscript{st} Men B (4vMenB) registered
2017 Men ACWY conj jurisdictions funded yr10-12
2017 one Men ACWY conjugate age lowered to 2m
Invasive meningococcal disease
Serogroup and Year
Victoria: 2000 to 2017

MenCCV 12mo dose (from Jan 2003) catch-up 1-19yo's (2003-2006)

Courtesy Lucinda Franklin, DHHS Victoria
Victoria Adolescent program: Meningococcal ACWY conjugate

Began term 2 2017

All young people aged 15 to 19 years
  – between 18 April 2017 and 31 December 2017

1 dose Menactra

Secondary school program
  - Also available from GPs or local council community immunisation service
<table>
<thead>
<tr>
<th>Age</th>
<th>Disease</th>
<th>Vaccine brand*</th>
<th>Reconstitute</th>
<th>Site given</th>
<th>Route given</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>Measles-mumps-rubella</td>
<td>Priorix* or M-M-R-II*</td>
<td>✔</td>
<td>Anterolateral thigh</td>
<td>Priorix SC /IM, M-M-R-II SC</td>
</tr>
<tr>
<td></td>
<td>Meningococcal ACWY</td>
<td>Nimenrix</td>
<td>✔</td>
<td>Deltoid</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
<td>Prevenar 13</td>
<td>✗</td>
<td>Deltoid</td>
<td>IM</td>
</tr>
</tbody>
</table>
4CMenB

GpB PS- polymer of sialic acid:
• chemically identical to polysaccharides found in human tissues during development
• (2→8)-α-Neu5Ac as a self antigen of humans
• potential cause of immunopathology
Recommendations

Based on their higher disease risk, 4CMenB is recommended for:

- Infants and young children, particularly those aged <24 months
- Adolescents aged 15 to 19 years
- Children and adults with medical conditions that place them at a high risk of IMD, such as functional or anatomical asplenia or complement component disorders (see Chapter 4.10 of *The Australian Immunisation Handbook*, 10th edition)
- Laboratory personnel who frequently handle *Neisseria meningitidis*.

4CMenB is also recommended for all children and young adults who wish to reduce their risk of MenB IMD.

Table 1. Recommended schedule of 4CMenB by age group

<table>
<thead>
<tr>
<th>Age at commencement of vaccine course</th>
<th>Primary immunisation</th>
<th>Interval between primary doses</th>
<th>Age for booster dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months*</td>
<td>3 doses, delivered at ~2*, 4 and 6 months of age; (intervals ~2 months, at least 1 month)</td>
<td>12 months</td>
<td></td>
</tr>
<tr>
<td>3 to 5 months</td>
<td>3 doses</td>
<td>1–2 months</td>
<td>12 months</td>
</tr>
<tr>
<td>6 to 11 months</td>
<td>2 doses</td>
<td>2 months</td>
<td>12 months, or 2 months after previous dose, whichever is later</td>
</tr>
<tr>
<td>12 months to 10 years</td>
<td>2 doses</td>
<td>2 months</td>
<td>No booster required†</td>
</tr>
<tr>
<td>11 years and above‡</td>
<td>2 doses</td>
<td>1–2 months</td>
<td>No booster required†</td>
</tr>
</tbody>
</table>

* 4CMenB is registered for use in persons ≥2 months of age; however, the 1st dose of 4CMenB may be administered as early as 6 weeks of age to align with the NIP infant schedule.
† The need for a booster dose for this age group is as yet uncertain.
‡ There are currently no data on the use of 4CMenB in individuals aged over 50 years, however, based on first principles, ATAGI recommends that 4CMenB can be used in older persons who are at high risk of IMD.

MenB: Known unknowns

Will it work?
- Modified serology says yes
- Early effectiveness data encouraging

Will it provide herd immunity?
- Reduction in NP carriage 12.6% (−15.9%, 34.1%)

Will protection last?

Will there be “escape strains”?

Will it increase fever/ febrile convulsions?
- Yes / No

Will Australians follow paracetamol advice?
- Will that change febrile seizure risk anyway?
Two-dose vaccine effectiveness was 82.9% (95% CI 24.1–95.2) against all MenB cases.
Safety (UK)

• Routine 3 doses paracetamol (?compliance)
• No increase in Febrile Seizure presentations
  • HPA
Life is like a box of chocolates

Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhoea in New Zealand: a retrospective case-control study

Dr Helen Petousis-Harris, PhD, Janine Paynter, PhD, Jane Morgan, MD, Peter Saxton, PhD, Barbara McArdle, MCE, Prof Felicity Goodyear-Smith, MD, Prof Steven Black, MD

Published: 10 July 2017
Antenatal vaccination
Effectiveness of maternal pertussis vaccination in England: an observational study

Gayatri Amirthalingam, Nick Andrews, Helen Campbell, Sonia Ribeiro, Edna Kara, Katherine Donegan, Norman K Fry, Elizabeth Miller, Mary Ramsay

<table>
<thead>
<tr>
<th>Infants &lt;3 months of age</th>
<th>Percentage of cases vaccinated</th>
<th>Average matched coverage* †</th>
<th>Vaccine effectiveness‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination at least 7 days before birth</td>
<td>15% (12/82)§</td>
<td>62%</td>
<td>91% (84 to 95)</td>
</tr>
<tr>
<td>Vaccination at least 7 days before birth with coverage reduced by a relative 20%</td>
<td>15% (12/82)§</td>
<td>49%</td>
<td>84% (71 to 93)</td>
</tr>
<tr>
<td>Infants &lt;3 months of age by timing of maternal immunisation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccination at least 28 days before birth</td>
<td>14% (10/69)¶</td>
<td>63%</td>
<td>91% (83 to 95)</td>
</tr>
<tr>
<td>Vaccination 7–27 days before birth</td>
<td>3% (2/72)‖</td>
<td>19%</td>
<td>91% (70 to 96)</td>
</tr>
<tr>
<td>Vaccination 0–6 days before or 1–13 days after birth</td>
<td>3% (2/68)**</td>
<td>5%</td>
<td>38% (−95 to 80)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infants &lt;2 months of age</th>
<th>Percentage of cases vaccinated</th>
<th>Average matched coverage* †</th>
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<tr>
<td>Vaccination at least 7 days before birth with coverage reduced by a relative 20%</td>
<td>15% (11/71)</td>
<td>49%</td>
<td>82% (67 to 90)</td>
</tr>
</tbody>
</table>

Data are % (n/N), %, or % (95% CI). * Average matched coverage is the average of the matched population coverage estimates for all cases included in the analysis. † For cases in which the mother matched to zero coverage, that case was dropped from the analysis because it did not contribute information. ‡ Vaccine effectiveness calculated on the basis of matched coverage on each individual, not with average matched coverage. § 90 cases minus one case vaccinated within a week of birth and seven cases matched to zero coverage. ¶ 90 cases minus three cases vaccinated at other times before birth and 18 cases matched to zero coverage. ‖ 90 cases minus 11 cases vaccinated at other times before birth and seven cases matched to zero coverage. ** 90 cases minus 12 cases vaccinated at other times before birth and ten cases matched to zero coverage.

Table 4: Effectiveness of maternal pertussis vaccine by infant age at onset and timing of vaccination
~50% reduction in HIV negative mothers and infants to 6 months
Similar protection in HIV +ve mothers- no clear protection in HIV exposed infants
Strategies to implement maternal vaccination: A comparison between standing orders for midwife delivery, a hospital based maternal immunisation service and primary care

Improving

83 % recommended dTap
78% recommended influenza

Midwives more safety concerns
RSV

Paramyxovirus
RNA- stable antigenically
F- fusion protein
G protein- types A & B
Clinical RSV

<2yo
ALRI: (25-40%)
Bronchiolitis
Pneumonia

URTI

Asymptomatic
RSV epidemiology

Paediatric Seasonality of Detected Respiratory Pathogen

Natasha Ching JPCH 2018
RSV in adults

Adult Seasonality of Detected Respiratory Pathogen

Annually in the US, in adults 65 and older

RSV Infections: 2,400,000
Medical Interventions: 900,000
Deaths: 14,000

Natasha Ching JPCH 2018
Vaccine hesitancy

Eve Dubé, Institut National de Santé Publique du Québec, Canada
Disease/Vaccine lifecycle

Modified from Chen et al
Increased hesitancy was associated with:

- 1st time mothers
- decreased confidence in the schedule (p < 0.001)
- decreased trust in child’s doctor (p < 0.0001)
- decreased perceived protection from disease (p < 0.05)
- and increased decisional conflict on all measured subscales (p < 0.0001).
Countering antivaccination attitudes

Zachary Horne\textsuperscript{a,1,2}, Derek Powell\textsuperscript{b,1}, John E. Hummel\textsuperscript{a}, and Keith J. Holyoak\textsuperscript{b}

RCT
315 participants
Assigned to:
• Disease risk stories and images
• Autism myth correction info
• Control information

Vaccine Attitude Pre-test Score

PNAS | August 18, 2015 | vol. 112 | no. 33 | 10321–10324
Vaccine communication: RCT
Vaccine hesitancy

At MVEC we strongly encourage people to seek answers to their questions and to be well informed with evidence based information. We know that nearly half of all parents have some concerns about immunising their children, ranging from minor concerns to more serious degrees of vaccine hesitancy.

There is a lot of information available to people, particularly on the internet, which can be quite overwhelming. However, we know that health care providers, particularly GPs, nurses and paediatricians, are the most frequently accessed resources for immunisation information for parents and the most trusted. We also know that providing information alone is not enough to address parents concerns about immunisation and we would encourage them to speak with their health care provider as well as accessing information from recommended websites or online. (see Resources)

MVEC is committed to providing up-to-date information to help address questions about immunisation, appreciating that this information needs to be in multiple formats and cover a broad range of queries.

Below is a selection of reliable resources that can help in the decision-making process.

Resources

Immunisation - [Get The Facts About Immunisation](http://www.mvec.vic.edu.au/immunisation-references/vaccine-hesitancy/)

NCIRS SARAH project – [Support and resources to assist hesitant parents with vaccination](http://www.mvec.vic.edu.au/immunisation-references/vaccine-hesitancy/)

Better Health Channel [Victoria]- [Immunity for community](http://www.mvec.vic.edu.au/immunisation-references/vaccine-hesitancy/)

Department of Health [Canberra] [Immunisation resources- myths and realities](http://www.mvec.vic.edu.au/immunisation-references/vaccine-hesitancy/)

MVEC: [MMR vaccine and autism](http://www.mvec.vic.edu.au/immunisation-references/vaccine-hesitancy/)

Children's Hospital of Philadelphia Vaccino Education Centro (USA)

The Vaccine Confidence Project
Clamour for vaccines as measles outbreak kills nearly 1,000 children in Madagascar
Washington is under a state of emergency as measles cases rise
Acknowledgements

Monash Immunisation
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Sushena Krishnaswamy

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Nigel Crawford