Invasive Meningococcal Disease (IMD)
An update on prevention in Australia
Prof Robert Booy, NCIRS

Declaration of interests: RB consults to vaccine companies but does not accept personal payment
Invasive Meningococcal Disease

Caused by the bacterium *Neisseria meningitidis*\(^1\)

- Meningococci are classified into serogroups that are determined by the components of the polysaccharide capsule\(^1\)
  - Globally, 6 serogroups most commonly cause disease\(^2\)

A B C W X Y

- In Australia, three serogroups cause the majority of IMD\(^3\)

B W Y

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Invasive meningococcal disease (IMD) in Australia

• Overall, the national incidence of invasive meningococcal disease (IMD) in Australia is low
• From 2003 to 2013, there was a large decrease in the number AUS notifications: 99% drop in Men C!
  - after the introduction of 2003 meningococcal C (Men C) dose at 12 months to National Immunisation Program (NIP) – catch-up vacc’n 2-19 year olds (herd immunity <1 & >20yrs)
• & reduced smoking +improved SES:
  55% drop in Men B! Without a vaccine program
• However, in recent years the rate of IMD has increased: 2017 had the highest rate in 10 years
• Men W and Y now important in older adults
Notifications of invasive meningococcal disease, Australia, 1992-2017, by year, all serogroups

- 2013-2017: 4 yrs
- 2017: 383 cases
- Highest number of cases since 2006
- 2018: 281 cases
- 2019: ? fewer

- 3rd Age peak 60-64 yrs
- W and Y

Nat’l Men C program from 2003

Adapted from National Notifiable Diseases Surveillance System

Meningococcal disease by age, NSW, 2018

Breakdown by age bands

Age group (years)

Number of Notifications

Men B

Men Y & W

NSW Health - [Accessed Feb 2019]
https://www1.health.nsw.gov.au
Introduction of Men C vaccine to NIP

99% C change; 55% B change

Australia, 1997 - 2017, by year and bacterial serogroup

Adapted from the Annual reports of the meningococcal surveillance program\(^1\) and the Department of Health, 2017\(^2\)

Note: “Other” includes other serogroups not singled out, cases where meningococcal isolates could not be identified, other isolates not grouped and cases where serogroup was not known.

1. Annual reports of the Australian Meningococcal Surveillance programme, 1997-2016

Why 2017 so bad?
Meningococcus
Sequence type 11 (cc 11)

- Associated with C and later W strains (some B)
- Hyper-invasive: greater mortality/morbidity; more outbreaks

C disease: teens/young adults
W disease: Babies, young adults, older adults
Wider presentations eg arthritis, pneumonia, epiglottitis, gastro
“Spacing Out” in the Prevention of Military Epidemics of Cerebro-Spinal Fever.

By Captain J. A. Glover, M.D., D.P.H., R.A.M.C.

We were crowded enough to cause a pestilence among us. — Defoe.

The main etiological factors producing military outbreaks of cerebro-spinal fever appear to be six—namely:

1. **Season**—the first quarter of the year.
2. **Severe weather** of all kinds and particularly sudden variations, east winds, and intense cold.
3. **Antecedent epidemics of influenza.**
4. **Causes temporarily lowering resistance,** such as antityphoid inoculation, fatigue, strenuous training, nostalgia, railway journeys, and the strangeness of barrack life to the new recruit.
5. **Overcrowding.**
6. **A high carrier rate** of epidemic strains of the meningococcus in the population at risk.

Large flu year in 2017 in Australia
The Association of Meningococcal Disease with Influenza in the United States, 1989–2009

Jessica Hartman Jacobs¹, Cécile Viboud², Eric Tchetgen Tchetgen¹,³, Joel Schwartz¹,⁴, Claudia Steiner⁵, Lone Simonsen²,⁶, Marc Lipsitch¹,⁷*

• In 19 of 20 seasons, influenza peaked ≤2 weeks before IMD
• peaks were highly correlated in time (ρ = 0.95; P < .001).
• H3N2 and H1N1 peaks were highly synchronized with IMD
• pandemic H1N1, B, and respiratory syncytial virus were not
• over 20 years, 12.8% (95% CI, 9.1–15.0) of IMD attributable to ‘flu in preceding weeks
during the height of ‘flu season, weekly attributable fractions reach 59%.
• vaccination against meningococcal disease is the most important prevention strategy
• influenza vaccination could provide further protection

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0107486
Symptoms are difficult to diagnose at early onset and develop rapidly\(^1,2\)

Medical intervention often does not occur until late

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**13-24 HOURS**

**POTENTIALLY LETHAL**

Most progressed from non-specific initial symptoms to close to death within 24 hours

- Neck pain and stiffness
- Hemorrhagic rash
- Floppy muscle tone\(^#\)
- Bulging fontanelle\(^*\)
- Photophobia
- Confusion and delirium\(^^\)
- Seizure

\(\sim 13\) hours - Median time to first hospitalisation\(^*\)

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**8 – 12 HOURS**

\(~8\) hrs – Median time to first GP consultation\(^*\)

- Cold hands and feet
- Abnormal skin colour
- Breathing difficulty
- Increased thirst
- Diarrhoea

\(^*\)in infants < 1 year

\(^#\)in children < 5 years

\(^^\)in children > 1 year

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**0-7 HOURS**

**NON SPECIFIC SYMPTOMS**

- Fever
- Irritability
- Nausea or vomiting
- Poor appetite or feeding
- Drowsiness
- Headache\(^^\)
- Sore throat
- Thirst
- Leg pain
- General aches

\(^\wedge\)in children > 1 year

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Meningococcal disease can be deadly and devastating\textsuperscript{1-3}

- Significant morbidity and mortality despite early diagnosis and appropriate medical treatment
  - \textbf{\~10\% of cases} are fatal\textsuperscript{1,2} (more in older adults)

- \textbf{1 in 5 survivors} of IMD (all serogroups) have permanent sequelae\textsuperscript{1,2}

- Child survivors may experience major sequelae eg limb amputations, seizures and hearing loss\textsuperscript{3}
  - \textbf{\~30\%} experience other deficits such as psychological disorders, digit amputations and unilateral hearing loss\textsuperscript{3}

- Google Eliza Meningococcal

\textsuperscript{1.} Meningococcal meningitis factsheet No 141. World Health Organization website. \url{http://www.who.int/mediacentre/factsheets/fs141/en/}
IMD has a higher case fatality rate compared with other VPDs rapid and deadly!!


IMD = invasive meningococcal disease VPDs = vaccine preventable diseases
Most cases in NSW, QLD, Vic

1. Adapted from the National Notifiable Diseases Database Surveillance System and Australian Government (accessed 10 Feb 2019).
Hence, state-based approaches.
IMD in Australia:
Breakdown by State or Territory, 2018

Rate per 100,000 population per year: overall Australian notification rate 1.1 per 100,000
Smallest populations but highest incidences

<table>
<thead>
<tr>
<th>ACT</th>
<th>NSW</th>
<th>NT</th>
<th>QLD</th>
<th>SA</th>
<th>TAS</th>
<th>VIC</th>
<th>WA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.9</td>
<td>4.4</td>
<td>1.2</td>
<td>2</td>
<td>2.1</td>
<td>0.8</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Adapted from the Department of Health, 2018

*NG includes where meningococcal isolates could not be identified (‘not groupable’), other isolates not grouped and where serogroup was not known. 0.5 0.9 4.4 1.2 2 2.1 0.8 1.5

Australia-wide, 1 January to 30 September 2018

Breakdown by age

Data were extracted from the NNDSS on 1 August 2018, by diagnosis date.

Nb <1 year & 15-24 years  B = #1
Cf 25-64 years W & Y common
By 5 yr bands, highest no. 0-5 yrs,
then 15-19 yrs
then 60-64

#Data were extracted from the NNDSS on 1 August 2018, by diagnosis date.

Invasive Meningococcal Disease National Surveillance Report – 1 April to 30 September 2018 - [Accessed Jan 2019]
IMD notification rates, Australia

By Indigenous status and age group, 2002-2018 YTD#

- OUTBREAK 2017 nt MenW cc11
- OUTBREAK 2017 MenC MSM ST11

Incidence X5 in young indigenous!

#Data from the NNDSS with a diagnosis date up until of 31 March 2018. Data was extracted on 23 April 2018.

^Non-Indigenous includes case reported as non-Indigenous and not stated.

National/State-based MenACWY vaccination programs¹

Target adolescents, due to highest carriage rate and high disease rate

Brand of meningococcal ACWY vaccine used varies

Commonwealth took over April 2019

A school-based program for adolescents in Year 10 aged 14–16 years; and

An ongoing GP-based catch up for adolescents 15–19 years of age who have not received the vaccine through the schools programs

States and Territories may also implement additional programs or on an as-needed basis
MenY IMD

AUSTRALIA:
increase in MenY

2000-2010: ~3% of all IMD cases annually (range 1.3% to 4.6%)

2017:
75 cases
20% of notifications

2016: 40 (17%)
2015: 22 (12%)
2014: 12 (7%)

WGS IMD 2017 MDU: MenY cc23
tight clustering suggesting local transmission, spread
(unpublished data courtesy Ben Howden)
**NIP childhood schedule From 1 July 2018**

*Changes then and now*

<table>
<thead>
<tr>
<th>Age</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>Hepatitis B&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>2 months</td>
<td>DTPa-IPV-HBV/Hib</td>
</tr>
<tr>
<td>(from 6 weeks of age)</td>
<td>PCV13</td>
</tr>
<tr>
<td>4 months</td>
<td>DTPa-IPV-HBV/Hib</td>
</tr>
<tr>
<td>6 months</td>
<td>DTPa-IPV-HBV/Hib</td>
</tr>
<tr>
<td>12 months</td>
<td>MenACWY</td>
</tr>
<tr>
<td>18 months</td>
<td>Hib</td>
</tr>
<tr>
<td></td>
<td>MMRV</td>
</tr>
<tr>
<td></td>
<td>PCV13</td>
</tr>
<tr>
<td>4 years</td>
<td>DTPa-IPV</td>
</tr>
</tbody>
</table>

<sup>a</sup> Hepatitis B vaccine: Should be given to all infants as soon as practicable after birth. The greatest benefit is if given within 24 hours, and must be given within 7 days.

<sup>b</sup> Rotavirus vaccine: First dose must be given by 14 weeks of age, the second dose by 24 weeks of age.
Australian Immunisation Handbook (AIH):
Meningococcal vaccination recommendations

* Refer also to NCIRS meningococcal fact sheet & FAQs
Recommendations

All infants, children and adults

Any person from 6 weeks of age who wants to protect themselves against meningococcal disease is recommended to receive MenACWY vaccine and MenB vaccine

Infants and children

Infants and children aged <2 years are strongly recommended to receive MenACWY vaccine

Infants and children aged <2 years are strongly recommended to receive MenB vaccine
### Adolescents

- Healthy adolescents aged 15–19 years are strongly recommended to receive MenACWY vaccine

### Aboriginal and Torres Strait Islander people

- Aboriginal and Torres Strait Islander people aged 2 months to 19 years are strongly recommended to receive MenACWY vaccine

- All Aboriginal and Torres Strait Islander people aged 2 months to 19 years are strongly recommended to receive MenB vaccine
People with medical conditions that increase their risk of invasive meningococcal disease

- People with medical conditions that increase their risk of invasive meningococcal disease are strongly recommended to receive MenACWY and MenB vaccines

Laboratory workers

- Laboratory workers who frequently handle Neisseria meningitidis are strongly recommended to receive MenACWY and MenB vaccines

Travellers

- People who travel to areas where meningococcal disease is more common, or who travel to mass gatherings such as the Hajj, are strongly recommended to receive MenACWY vaccines
Young adults living in close quarters

Adolescents and young adults living in close quarters are strongly recommended to receive MenACWY and MenB vaccines

Smokers

Adolescents and young adults who are current smokers are strongly recommended to receive MenACWY and MenB vaccines
Meningococcal vaccines

The National Immunisation Program (NIP), state programs & private vaccines

**Meningococcal C**
- Introduced to the NIP in 2003
- Drastic reduction in disease

**Meningococcal A,C, W & Y**
- Introduced to the NIP July 2018 to replace MenC +Hib at 12 months (Hib at 18 mths)
- All states & territories except SA had adolescent programs*
  - From April 2019, MenACWY vaccination of adolescents was introduced to the NIP
  - Private prescription ≥ 6 weeks of age

**Meningococcal B**
- Not currently on the NIP
  - Oct 2018, SA program for those aged 0-4 years
  - 2019 program for 15-20 year olds
  - Private prescription in all other states for ≥ 2 months of age

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*The specifics of each program varies, including the brand of vaccine used. Please refer to your state or territory health department for more details. Note: some programs may have now ended.
Men B vaccine PI update:
Approved dosing schedules for Bexsero in Australia

Administer by **deep intramuscular injection**, preferably in the anterolateral aspect of thigh in infants or deltoid muscle region of upper arm in older subjects

<table>
<thead>
<tr>
<th>Dosage:</th>
<th>Primary immunisation</th>
<th>Minimum interval between primary doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants 2-5 months*</td>
<td>2 doses, 3 doses</td>
<td>≥ 2 months, ≥ 1 month</td>
<td>Second year of life (≥6 months post primary series)</td>
</tr>
<tr>
<td>Infants 6-11 months</td>
<td>2 doses</td>
<td>≥ 2 months</td>
<td>Second year of life (≥2 months post primary series)</td>
</tr>
<tr>
<td>Toddlers 12 months - 23 months</td>
<td>2 doses</td>
<td>≥ 2 months</td>
<td>Need not established</td>
</tr>
<tr>
<td>Children (≥2 years), Adolescents &amp; Adults^</td>
<td>2 doses</td>
<td>≥ 1 month</td>
<td></td>
</tr>
</tbody>
</table>

*The safety and efficacy of the vaccine in infants <8 weeks have not been established. No data available
^The safety and efficacy of the vaccine in individuals above 50 years of age have not been established

1. Bexsero Product Information
Bexsero update: Real world experience

UK
Introduction of national vaccination campaign (2+1 schedule)
10 months after program introduction → 50% reduction in MenB cases in vaccine-eligible infants

Canada
Regional vaccination campaign in Saguenay–Lac-Saint-Jean, Quebec and vaccination during a MenB outbreak at Acadia University, Nova Scotia

USA
Vaccination during MenB outbreaks at Princeton University, University of California at Santa Barbara, and Santa Clara University

Infants >2mths

Adolescents

Breaking news! 80% protection in Portugal for Men B

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1. Watson P and Turner D. Vaccine 2016;34:875–880
3. Bexsero PI
UK PHE MenB vaccination program

• 74% reduction in Men B disease in the vaccinated cohort

• Men B program has prevented ~ 250 cases

• Men ACWY program has prevented ~ 50 cases

• No safety signals identified from 5 million doses administered
UK Safety Experience with Bexsero\textsuperscript{1,2}

Sep 2015-May 2017

~1.29 million infants vaccinated\textsuperscript{*}

Analysis of suspected adverse reactions:
- Passive surveillance (Yellow Card Scheme)
- Data analysis from the Clinical Practice Research Datalink (CPRD)

\textbf{Safety findings}

- 902 adverse reaction reports\textsuperscript{†}
  - Most common: local reactions (41%), fever (40%)
- No new safety signals identified
- Anticipated reactogenicity did not affect compliance with subsequent doses
- To date, UK experience shows 4CMenB has a favourable benefit–risk profile

The safety profile of 4CMenB was broadly as expected, with no serious safety concerns identified

- *1.29 million infants aged 2-18 months received a combined 3 million doses between Sep 2015 to May 2017
- † Mainly relating to fever (40%) and localised reactions (41%), and equates to 2429 adverse events

### Meningococcal recommendations

<table>
<thead>
<tr>
<th>Age group</th>
<th>Healthy Aboriginal and Torres Strait Islander people</th>
<th>Healthy non-Indigenous people</th>
<th>Special risk groups (including adolescent and young adult smokers and those living in close quarters; and laboratory workers)</th>
<th>Travellers to regions with an increased risk of exposure to MenACWY disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks–23 months</td>
<td>MenB and MenACWY&lt;sup&gt;a&lt;/sup&gt;</td>
<td>MenB and MenACWY&lt;sup&gt;a&lt;/sup&gt;</td>
<td>MenB and MenACWY&lt;sup&gt;a&lt;/sup&gt;</td>
<td>MenACWY&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>2–4 years</td>
<td>MenB and MenACWY</td>
<td>None</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
<tr>
<td>5–14 years</td>
<td>MenB and MenACWY</td>
<td>None</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
<tr>
<td>15–19 years</td>
<td>MenB and MenACWY</td>
<td>MenB and MenACWY</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
<tr>
<td>≥20 years</td>
<td>None</td>
<td>None</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
</tbody>
</table>
Vaccine recommendations

Any person aged 6+ weeks who wishes to protect themselves against meningococcal to have both MenACWY & MenB vaccines

These vaccines are strongly recommended for:

- Infants aged 6 weeks < 2 years
- Teens aged 15 - 19 years
- All indigenous aged 2 months – 19 years
- High risk conditions e.g. lab, crowded, smokers (15-24 years)
- Travellers e.g. “meningitis belt”, Hajj

All are considered high risk
Summary

- IMD is a rare, but potentially fatal disease
  - difficult to diagnose early due to non-specific symptoms
  - symptoms develop rapidly
  - even with appropriate medical treatment up to 10% of cases are fatal and up to 30% of survivors suffer from permanent sequelae

- Changing epidemiology has influenced changes to funded programs
  - MenACWY vaccine provided under NIP at 12 mth encounter: July 2018 (replaced MenC + Hib)
  - From April 2019, MenACWY vaccine now available on the NIP for 14-16 year old’s (catch-up program for those aged 15-19 years)

- In 2018 & many other years, MenB was the predominant serogroup in Australia, esp’ly children & young adults
  - 1 Oct 2018, SA introduced a State-based funded MenB program for infants and (from 1 Feb 2019) adolescents
  - In all other states MenB is available on private prescription

- ATAGI strongly recommend MenB and MenACWY vaccination for at-risk groups

- MenW and Y predominate in older adults; wider clinical presentations eg pneumonia, septic arthritis, epiglottitis
MenB OMP vaccine and Gonorrhoea prevention

- Case-control study Sex Health Clinic, 15–30 years
- estimated efficacy MeNZB against NG 31% (95% CI 21–39)
- adjusted for ethnicity, deprivation, geographical area, sex
- first vaccine that has shown any protection against N Gonorrhoea
- proof of principle can inform prospective NG vaccine development - new Australian study
## Quadrivalent ACWY meningococcal vaccines

Meningococcal A, C, W and Y conjugate vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Indication</th>
<th>Dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Menveo</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>≥2 months</td>
<td>&lt;6 months, 4 doses</td>
</tr>
<tr>
<td>GSK</td>
<td></td>
<td>7-23 months, 2 doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥2 years, 1 dose</td>
</tr>
<tr>
<td><strong>Nimenrix</strong>&lt;sup&gt;®3&lt;/sup&gt;</td>
<td>≥6 weeks</td>
<td>6-12 weeks, 3 doses</td>
</tr>
<tr>
<td>Pfizer</td>
<td></td>
<td>≥12 months, 1 dose</td>
</tr>
<tr>
<td><strong>Menactra</strong>&lt;sup&gt;®4&lt;/sup&gt;</td>
<td>≥9 months–55 years</td>
<td>9-23 months, 2 doses</td>
</tr>
<tr>
<td>Sanofi-Aventis</td>
<td></td>
<td>2-55 years, 1 dose</td>
</tr>
</tbody>
</table>

Generally well tolerated, with the most common side effects (>10%) typically associated with vaccination

- i.e. Injection site reactions, gastrointestinal upset, headache, fatigue. Not a complete list, refer to PI's for full details<sup>2-4</sup>

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2. Menveo Product Information, GSK
3. Nimenrix Product Information, Pfizer
4. Menactra Product Information, Sanofi-Aventis
# Meningococcal B vaccines\(^1\,-^2\)

Recombinant meningococcal B vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Indication</th>
<th>Antigen/s</th>
<th>Dosing schedule</th>
</tr>
</thead>
</table>
| **Bexsero\(^1\)**  
**GSK**        | ≥2 months  | • fHbp*  
• NadA\(^^\)  
• NHBA\(^#\)  
• NZ Por A P1.4: porin A | Variable, depending on age at first administration |
| **Trumenba\(^2\)**  
**Pfizer**     | ≥10 years  | • fHbp* subfamily A (A05)  
• fHbp *subfamily B (B01) | Variable, depending on patient risk of IMD          |

*Factor H Binding Protein  
^Neisseria Adhesin A protein (rbe)  
#Neisseria Heparin Binding Antigen fusion protein (rbe)

Bexsero and Trumenba are recombinant, **inactive** vaccines (ie. not live vaccines)

1. Bexsero Product Information GSK  
2. Trumenba Product Information, Pfizer  
Trumenba is a trade mark owned by Pfizer. Bexsero is a trade mark owned by or licensed to the GSK group of companies
Recommendations: Bexsero and Prophylactic Paracetamol, age < 2 years

Australian Technical Advisory Group on Immunisation (ATAGI)¹

1st DOSE*  
VACCINATE  
2 ADDITIONAL DOSES

• Prophylactic use of paracetamol reduces the incidence and severity of fever without affecting the immunogenicity of either Bexsero or routine vaccines (PCV-7 and DTP-IPV-HBV/Hib)²
• The effect of antipyretics other than paracetamol on the immune response has not been studied²

*15mg/kg paracetamol within 30 minutes prior to vaccination (or as soon as practicable after)  
^ATAGI recommends doses of paracetamol be given 6 hours apart.

2. Bexsero Product Information
Vaccine recommendations

Any person aged 6+ weeks who wishes to protect themselves against meningococcal to have both MenACWY & MenB vaccines.

These vaccines are strongly recommended for:

- Infants aged 6 weeks < 2 years
- Teens aged 15 - 19 years
- All indigenous aged 2 months – 19 years
- High risk conditions e.g. lab, crowded, smokers (15-24 years)
- Travellers e.g. “meningitis belt”, Hajj

All are considered high risk.
Menactra, Menveo, Nimenrix (ACWY)

- Age <2 years: no preference; Menveo & Nimenrix 2/12 start, Menactra start from 9/12 of age
- If 12-23/12 one dose Nimenrix, two doses of other 2; best not give a Tet Tox vaccine 1/12 before Nimenrix (carrier interference)
- Age 2+ years: single dose of any, Menactra less favoured – less antibody and declines more
- Menactra not given with PCV13 as less pneumo antibody, but can give PCV13 first then 1/12 gap to Menactra
- Menactra must be given with or one month before Dip Tox, to prevent carrier interference
Bexsero and Trumenba

- Bexsero = recombinant, multi-component, given from 6 weeks
- Trumenba = recombinant, bivalent, from 10 years
- No preference for either if age 10+ years
- Should not mix schedules – if aged 10+ give 2 doses of each
- *(Mixing is OK with MenACWY vaccines)*

*MenACWY and MenB vaccines are equally important from a clinical/public health perspective, but as yet only MenACWY is on the National Immunisation Program*
Bexsero dosing schedule changes

**2+1 schedule in infants:**
change to update dosing schedule for infants 2 through 5 months of age to allow for a 2+1 dose schedule

**0, 1 month schedule in children:**
change to support a 0, 1 month schedule in unvaccinated children 2 through 10 years of age. Currently it is a 0, 2 month schedule.

<table>
<thead>
<tr>
<th>Age at first dose</th>
<th>Primary Immunisation</th>
<th>Intervals between Primary Doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants, 2 months to 5 months*</td>
<td>Two doses each of 0.5 ml</td>
<td>Not less than 2 months</td>
<td>Yes, 1 dose in the second year of life, from the age of 12 months or later, with an interval of at least 6 months between the primary series and booster dose b</td>
</tr>
<tr>
<td>Infants, 6 months to 11 months</td>
<td>Two doses each of 0.5 mL</td>
<td>Not less than 2 months</td>
<td>Yes, 1 dose in the second year of life with an interval of at least 2 months between the primary series and booster dose b</td>
</tr>
<tr>
<td>Toddlers, 12 months to 23 months</td>
<td>Two doses each of 0.5 mL</td>
<td>Not less than 2 months</td>
<td>Need not established b</td>
</tr>
<tr>
<td>Children, 2 years to 10 years</td>
<td>Two doses each of 0.5 mL</td>
<td>Not less than 1 month</td>
<td>Need not established b</td>
</tr>
<tr>
<td>Adolescents (from, 11 years) and adults*</td>
<td>Two doses each of 0.5 mL</td>
<td>Not less than 1 month</td>
<td>Need not established b</td>
</tr>
</tbody>
</table>

* The first dose should be given no earlier than 2 months of age. The safety and efficacy of Bexsero in infants less than 8 weeks of age has not yet been established. No data are available.
Carriage of *N. meningitidis* in high school students

“B Part of It” study

- Professor Helen Marshall
- NHMRC Senior Research Fellow
- Senior Medical Practitioner and Director VIRTU, Women’s and Children’s Health Network
- Deputy Director, Robinson Research Institute, University of Adelaide

Preliminary results presented at IPNC, USA Sep 2018
IMD serogroup B notifications in adolescents in SA pre and post study implementation

No IMD in 35,000 study participants
Notifications of invasive meningococcal disease
Australia, 1991-2017, by year, all cases of IMD

2019: 17 cases YTD

Adapted from National Notifiable Diseases Surveillance System
IMD vaccine development

Conventional approaches have not been possible for MenB

\[ H_{influenzae}^1 \]
(1 pathogenic serotype)

\[ S_{pneumoniae}^2 \]
(23 pathogenic serotypes^)

\[ N_{meningitidis}^3 \]
(5 pathogenic serogroups)

INVASIVE DISEASE

Hib Glycoconjugate vaccine

Pneumococcal Glycoconjugate vaccine

Meningococcal Glycoconjugate vaccine

Capsule poorly Immunogenic\(^4,5\)

\(^23\) pathogenic serotypes, causing 90% of invasive disease in developed countries

Bexsero contains 4 antigenic components (4CMenB vaccine)

Identified using a “reverse vaccinology” approach

Bexsero = 3 recombinant surface-exposed protein antigens + OMV¹

NHBA: Neisseria Heparin-Binding Antigen + GNA fusion protein

OMV: NZ PorA P1.4: porin A

fHBP: factor H Binding Protein + GNA fusion protein

NadA: Neisseria adhesin A Protein

• Images are © Hurd Studios, 2012 and courtesy of GlaxoSmithKline
Bexsero Consists of 3 Protein Antigens and an Outer Membrane Vesicle (OMV)*

- **Multicomponent (4) Meningococcal Serogroup B Vaccine**
  - Has the potential to protect against the majority of MenB disease
  - Includes 4 antigen components

*OMV from a hyperendemic New Zealand Neisseria meningitidis serogroup B strain measured as amount of total protein containing the PorA P1.4.

\[\text{PorA}^\text{P1.4}\]  
\[\text{OMV}\]

\[\text{fHbp}^*\]  
\[\text{NadA}\]  
\[\text{NHBA}^*\]

\[\text{PorA} 1.4\]  
\[\text{(as part of OMV}^\dagger\text{)}\]

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*Fusion proteins; fHbp=GNA2091 and NHBA=GNA1030.  
†OMV from a hyperendemic New Zealand Neisseria meningitidis serogroup B strain measured as amount of total protein containing the PorA P1.4.  
fHbp=factor H–binding protein; NadA=Neisserial adhesin protein A; NHBA=Neisseria heparin–binding protein; PorA=porin A.
Bexsero approvals and recommendations

More than 20 million doses distributed worldwide since launch

**41 APPROVALS**
- EU/EEA: 31 countries (plus Andorra)*
- Other: Argentina, Australia, Brazil, Canada, Chile, Uruguay, USA

**19 CLINICAL RECOMMENDATIONS†**
- Australia, Austria, Belgium, Brazil, Canada, Cyprus, Czech Republic, France, Germany, Greece, Hungary, Portugal, Spain
- Andorra, Ireland, Italy, UK, USA (see below)

**9 NIPs**
- Andorra, Ireland, Italy, Lithuania, Malta, Portugal, UK: NIPs implemented
- USA: Category B national recommendation

NIPs, National Immunisation Programmes
*Bexsero approved across EU and EEA countries under a centralised procedure (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, UK; Andorra is not listed in EU SmPC, but follows the same approvals as Spain)
†Clinical recommendation in countries where Bexsero has been approved

Please refer to slide notes for references
Q1. Why has a new meningocococcus vaccine been introduced? (discuss changing serotypes, conjugate vs polysaccharide)

Q2. What meningococcal vaccinations are currently available?

Q3. Does the new meningocococcus vaccine protect travellers? Eg Middle East, Sub-saharan Africa, youths in dormitories in US

Q4. When should a booster for meningococcus be considered?

Q5. Should doctors suggest everyone be vaccinated for meningococcus?

Q6. Which immunosuppressed patients need vaccination for meningococcus?

Q7. Why does meningococcus become invasive?

Q8. What precautions are needed when vaccinating for meningococcus B? (can it be co-administered with other meningococcal vaccines, other vaccines generally? Paracetamol, watch for 30min after, warn re febrile convolution etc)
### Meningococcal recommendations

<table>
<thead>
<tr>
<th>Age group</th>
<th>Healthy Aboriginal and Torres Strait Islander people</th>
<th>Healthy non-Indigenous people</th>
<th>Special risk groups (including adolescent and young adult smokers and those living in close quarters; and laboratory workers)</th>
<th>Travellers to regions with an increased risk of exposure to MenACWY disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks–23 months</td>
<td>MenB and MenACWY&lt;sup&gt;a&lt;/sup&gt;</td>
<td>MenB and MenACWY&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>MenACWY&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>2–4 years</td>
<td>MenB and MenACWY</td>
<td>None</td>
<td>MenB and MenACWY</td>
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<tr>
<td>5–14 years</td>
<td>MenB and MenACWY</td>
<td>None</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
<tr>
<td>15–19 years</td>
<td>MenB and MenACWY</td>
<td>MenB and MenACWY</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
<tr>
<td>≥20 years</td>
<td>None</td>
<td>None</td>
<td>MenB and MenACWY</td>
<td>MenACWY</td>
</tr>
</tbody>
</table>

<sup>a</sup> MenACWY refers to the meningococcal serogroups A, C, W and Y.