

MENINGITIS – WHAT’S NEW?

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CONFLICTS OF INTEREST

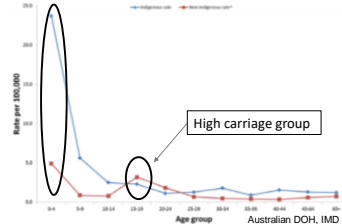
- Educational travel grant - Gilead

MORE DISEASE, MORE VACCINES

- 1. Invasive meningococcal disease rare but rising**
 - Mostly due to serogroups W & Y (MenW, MenY)
 - More atypical presentations, severe disease
 - Serogroup B remains common
- 2. New meningococcal vaccines available**
 - New infant & adolescent programs – targeting MenW & MenY
 - Serogroup B vaccine – recommended, unfunded

INVASIVE MENINGOCOCCAL DISEASE: HIGHEST IN <2 YO AND 15-19 YO

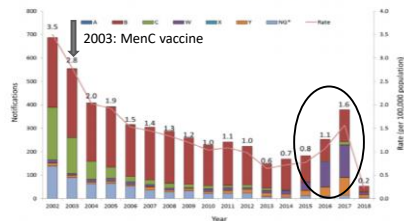
Figure 3. Notification rates of IMD, Australia, 2002 to 2018 YTD^a, by indigenous status and age group



Australian DOH, IMD Surveillance Report, 31/03/18

MENINGOCOCCAL SEROGROUPS W AND Y: ON THE RISE

Figure 1. Cases and rates of IMD, Australia, 2002 to 2018 YTD^a, by serogroup



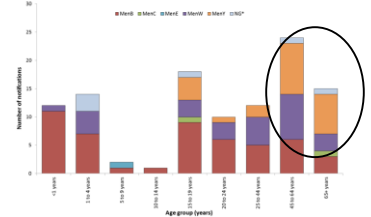
Australian DOH, IMD Surveillance Report, 31/03/18

^a Data from the NNISDS with a diagnosis date up until 31 March 2018. Data was extracted on 23 April 2018.

SEROGROUPS W AND Y: OLDER PATIENTS

- Similar pattern seen in UK
- Subsequent spread to preschool children, adolescents

Figure 3. Notifications of IMD, Australia, 1 January to 30 June 2018, by serogroup and age group



Australian DOH, IMD Surveillance Report, 30/6/18

SEROGROUP W: HIGHER FATALITY RATE

- Nearly all MenW in Australia = hypervirulent clonal complex 11 (CC11)
- Endemic in UK
- MenW case fatality rate: 9.3%
- Compared to 5% for MenB and MenY



Australian DOH, IMD Surveillance Report, 31/3/18

SEROGROUP W: ATYPICAL PRESENTATIONS

- 80% typical
 - Septicaemia and/or meningitis
- 20% atypical
 - Septic arthritis
 - Pneumonia
 - Epiglottitis



Commun Dis Intell 2017;40(4):E454-E459.

SEROGROUP W: GASTROENTERITIS-LIKE PRESENTATION

- Up to 50% predominant GI symptoms, no rash
 - Diarrhoea
 - N/V, abdominal pain
- 25% initially diagnosed as gastroenteritis
- Diarrhoea associated with increased case fatality
- Australia (2018) – 15% MenW p/w gastroenteritis

Presentation with gastrointestinal symptoms and high case fatality associated with group W meningococcal disease (MenW) in teenagers, England, July 2015 to January 2016

Wongkittakorn J, Kelly A, Brown J, Haxton M, Wilson M, Stubbins M, et al. Presentation with gastrointestinal symptoms and high case fatality associated with group W meningococcal disease (MenW) in teenagers, England, July 2015 to January 2016. *Emerg Infect Dis* 2016;22(12):pii=30175. Australian DOH, IMD Surveillance Report, 30/6/18

Euro Surveill 2016;21(12):pii=30175; Australian DOH, IMD Surveillance Report, 30/6/18

MEN ACWY VACCINE: BASICS

- Conjugate vaccine: 80-85% efficacy
 - Also effective against carriage
- Brand names: Nimenrix, Menveo, Menactra
- UK: Year 9 students & new university students - 2015
 - High risk group & reservoir
 - 69% reduction in MenW 1st year
- Australia: NIP for 12 mo; state adolescent programs started 2017



Emerg Infect Dis 2017;23(7):1184-1187.

MEN ACWY VACCINE: RECOMMENDATIONS

- All < 2yo – now on NIP
- All 15-19 yo – single dose
- 20 – 24 yo – single dose
 - Who live in close quarters OR Current smokers
- ATSI: 2 mo – 19 yo – dosing age-dependent
- Patients at increased risk of IMD (e.g. asplenia) – dosing age-dependent



MEN ACWY VACCINE: NATIONAL IMMUNISATION PROGRAM (NIP)

- Men ACWY vaccine (Nimenrix) replaced Men C vaccine at 12 months from 1 July 2018
 - HiB vaccine moved to 18 months
 - 6 month Prevenar moved to 12 months
- Nimenrix funded for NIP for Year 10 students & adolescent catch-up 15-19 yo from April 2019

MEN ACWY VACCINE: THE FINE PRINT



- **Menveo and Nimenrix can be given from 6 weeks**
- **Menveo or Nimenrix preferred in ≥ 2 yo**
 - Higher antibody responses
 - Longer duration of immunity
- **Do not administer Menactra with Prevenar 13**
- **Infant dosing schedule may differ from PI**

MEN ACWY VACCINE: CURRENT SHORTAGES

- **Menveo**
 - Unavailable until 2019
- **Menactra**
 - Used in state-based adolescent programs
 - Unavailable until 2019
- **Nimenrix – no current shortage**

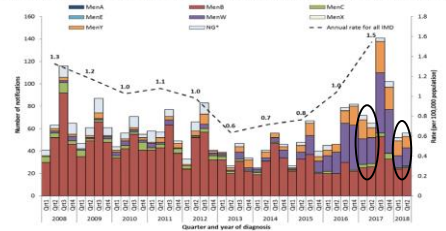
TGA Medicine Shortages Information Initiative, accessed 3/11/18

MEN ACWY VACCINE: STATE PROGRAMS

State	Target Population
WA	1 – 4 years; Year 10 students; 15-19 years
QLD	Year 10 students; 15-19 years
VIC	Year 10 students; 15-16 years; MSM
NSW	Year 10-11 students; 15-19 years
ACT	Year 10 students; 16-19 years
TAS	6 weeks – 21 years
SA	Aboriginal in Eyre & Far North, Flinders & Upper North: 1- 19 years
NT	1 – 19 years

SEROGROUP W: ARE WE WINNING?

Figure 1. Quarterly cases and annual rate of IMD, Australia, 1 January 2008 to 30 June 2018 by serogroup



Australian DOH, IMD Surveillance Report, 30/6/18

SEROGROUP W: ARE WE WINNING?

Meningococcal W confirmed as strain behind death of Hobart teenager
Teenager was 'sent home with painkillers' before dying of meningococcal

The Tasmanian teenager who died from meningococcal disease this month had the W strain of the bacteria, health authorities say.

Griffith Hospital has launched an investigation into the death of a 19-year-old woman who was reportedly sent home from the hospital with painkillers before being re-admitted and diagnosed with meningococcal.

Melanie Hadden died on the Central Coast Hospital of meningococcal last week.

The lab confirmed the meningococcal W strain, the Central Coast Local Health District (CCLHD) confirmed on Facebook.



SEROGROUP B: REMAINS COMMON

- **2017**
 - Serogroup B: 36%
 - Serogroups W & Y: 56%
- **2018 through 30/6/18**
 - Serogroup B: 45%
 - Serogroups W & Y: 46%

Australian DOH, IMD Surveillance Reports, 30/6/18 & 31/12/17

MEN B VACCINE: BASICS

- **Recombinant vaccine** – ‘reverse vaccinology’
- **Brand names:** Bexsero (≥ 6 weeks), Trumenba (≥ 10 yo)
- **On UK schedule for infants since 2015**
- **Australia:** unfunded except South Australia

MEN B VACCINE: RECOMMENDATIONS

Australian
Immunisation
Handbook

- **All <2 yo** – *dosing age-dependent*
- **All 15 – 19 yo** – two doses
- **20 – 24 yo** – two doses
 - Who live in close quarters OR Current smokers
- **ATSI: 2 mo – 19 yo** – *dosing age-dependent*
- **Patients at increased risk of IMD** (e.g. asplenia) – *dosing age-dependent and brand-dependent*

MEN B VACCINE: ISSUES TO DISCUSS WITH PARENTS

- **Efficacy**
 - ‘Promising; standard vaccine in UK’
- **Safety**
 - ‘High rates of fever (preventable)’
- **Cost**
 - ‘Currently unfunded - \$500 for infants’

MEN B VACCINE: EFFICACY ESTIMATED TO BE HIGH

- **UK vaccine efficacy:**
 - **83%** - after two doses (2,4 months)
 - **94%** efficacy against predicted strain coverage
- **Australia:** estimated **76%** MenB strain coverage
- **Not serogroup specific**
 - May offer protection against MenW

Vaccine 2015;33:2629-36; Lancet 2016;388:2775-2782

MEN B VACCINE: DURATION, EFFECT ON CARRIAGE UNCLEAR

- **Duration of protection** - unclear
 - **Infants:** circa 3 yo (after primary infant + 12 month booster course)
 - **Adolescents:** unknown
- **Reduction of pharyngeal carriage** - uncertain
 - Of public health (not individual) importance

JCVI 2014; Lancet 2014;384:2123-31

MEN B VACCINE: HIGH RATES OF FEVER IN INFANTS

Table 2. Proportion (%) of infants reporting fever within 7 days after at least 1 of the 3 infant doses of 4CMenB, by vaccine recipient group

Axillary temperature	Routine vaccines only	4CMenB only	Concurrent vaccines (routine + 4CMenB)
$\geq 38^{\circ}\text{C}$	23–36%	26–41%	51–62%
$\geq 39^{\circ}\text{C}$	3–4%	4–8%	10–15%

ATAGI 2014

MEN B VACCINE:

PROPHYLACTIC PARACETAMOL <2 YO

- **Paracetamol recommended with vaccination**
 - No reduction in immunogenicity

Table 3. Proportion (%) of infants reporting fever with vs without prophylactic paracetamol

Temperature	Proportion of infants reporting fever	
	With prophylactic paracetamol	Without prophylactic paracetamol
Within 7 days after a dose of 4CMenB		
≥38.5°C	39%	69%
≥39.5°C	3%	8%
Within 6 hours of 1st dose of 4CMenB at 2 months of age*		
≥38.5°C	<15%	>40%
≥39.5°C	Substantially lower with the use of prophylactic paracetamol*	

* Values estimated from graphs provided as summary of the clinical study results³

ATAGI 2014

MEN B VACCINE: <2 YO DOSING SCHEDULE

Age at start of vaccine course	MenB vaccine brand	Dose requirements for healthy people (without any medical conditions associated with increased risk of invasive meningococcal disease)	3+1		OR		2+1	
			Age at first dose	Primary immunisation	Interval between Primary Doses	Booster		
0-5 weeks to 6 months	Bexsero	4 doses (8 weeks between doses; 4th dose at 12 months of age)	Infants, 2 months & 4 months	Two doses (8 weeks apart) of 0.5 ml	Not less than 6 months	Yes, 1 dose in the second year of life from the age of 12 months or age, with an interval of at least 6 months between the primary series and booster dose ¹		
6-11 months	Bexsero	3 doses (8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age or 8 weeks after 2nd dose, whichever is later)		Three doses (each of 0.5 ml)	Not less than 1 month			
12-23 months	Bexsero	2 doses (8 weeks between doses)						

Australian Immunisation Handbook

Bexsero PI

MEN B VACCINE: AVAILABILITY AND COST

- **Private prescription – \$120-140 per dose**
 - Infant vaccination = c. \$500
 - Some private health funds provide rebate
- **Previous shortage now resolved**
- **South Australia:**
 - Years 10-12: 'B Part of It' study
 - From 2019: Year 10 students, 17-20 yo
 - From Oct. 2018: 6 weeks – 12 months, with catch-up for 12 months – 3 yo



MORE DISEASE, MORE VACCINES

1. **Invasive meningococcal disease rare but rising**
 - i. Mostly due to serogroups W & Y (MenW, MenY)
 - ii. More atypical presentations, severe disease
 - iii. Serogroup B remains common
2. **New meningococcal vaccines available**
 - i. New infant & adolescent programs – targeting MenW & MenY
 - ii. Serogroup B vaccine – recommended, unfunded

THE FUTURE

- i. **Men B vaccine**
 - i. On NIP for all infants & adolescents?
 - 'Health Minister Greg Hunt has encouraged GSK to apply for PBAC approval next year.'
 - GSK awaiting 'B Part of It' study results.
 - ii. State-based programs instead?