Bacterial meningitis in children : rare, severe, mostly preventable What should GPs advise Australian parents in 2018?

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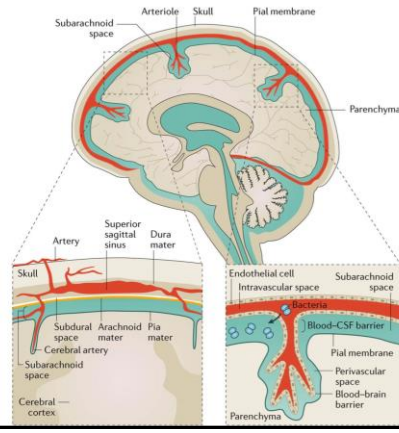
Overview

1. **Bacterial meningitis in children**
   - **Organisms**
   - **Death and long-term sequelae**
   - **Where are we now?**
2. **"Free" vaccines for meningitis**
   - **National Immunisation Program – changes July 1**
   - **Queensland - high school ACWY program**
3. **"Extra protection" - vaccines for private purchase**
   - **Ask and you shall receive**

No conflicts of interest

BACTERIAL MENINGITIS IN CHILDREN



Bacterial Meningitis 3

Effect of vaccines on bacterial meningitis worldwide

Peter B McIntyre, Katherine L O'Brien, Brian Greenwood, Diederik van de Beek

	Haemophilus influenzae	*Streptococcus pneumoniae*	*Neisseria meningitidis*
Cell wall	Gram negative	Gram positive	Gram negative
Capsular types	6 capsular types (a–f) Capsular type b in >90% Other capsular types can cause meningitis, especially type a; unencapsulated rarely	>90 capsular types Prominent serotype variation; by region, time period, and invasive potential Wide distribution of serotypes with high incidence	12 serogroups Most disease due to 6 serogroups (A, B, C, W135, X, Y) Unencapsulated meningococci predominate in carriage
Case severity	Meningitis more severe than other focal infections; in low-income countries pneumonia accounts for more severe infections than meningitis	Meningitis more severe than other focal infections	Sepsis and hypotension more severe than meningitis
Meningitis as a proportion of invasive disease	50%; higher where blood cultures not taken or unavailable	10%; higher where blood cultures not taken or unavailable and lower in adults	Higher in epidemic settings and with serogroup A
Age distribution	90% <5 years Age distribution shifted towards infants in high-incidence settings	Highest incidence <2 years and >75 years Age distribution shifted towards infants in high-incidence settings	Peaks in infants and adolescents Age distribution varies by serogroup and in epidemics

Incidence and Sequelae

- Hib most common, Pneumo most sequelae, Meningo most deaths

	Haemophilus influenzae type b[22]	*Streptococcus pneumoniae*[21]	*Neisseria meningitidis*[12,23]
Cases			
Highest incidence region (Africa)	46 (31–52)	38 (11–48)	>100 (endemic)* >1000 (epidemic)*
Lowest incidence region (Europe)	16 (12–22)	6 (5–9)	1–2 (endemic)† 2–10 (epidemic)†
Deaths			
Highest mortality region (Africa)*	31 (20–35)	28 (7–36)	..
Lowest mortality region (Europe)†	4 (3–6)	3 (1–7)	..
Morbidity			
Proportion of survivors with major long-term sequelae[1]	9·5% (7·1–15·3)	24·7% (16·2–35·3)	7·2% (4·3–11·2)

Arch Dis Child 2000;83:111–116

Twelve year outcomes following bacterial meningitis: further evidence for persisting effects

Keith Grimwood, Peter Anderson, Vicki Anderson, Lesley Tan, Terry Nolan

Table 1 Summary of impairments

	Meningitis subjects			Control subjects		
	Complications*					
	Yes (n = 49)	No (n = 60)	Total (n = 109)	(n = 96)	OR	95% CI
Summary						
No problems	26 (53%)	42 (70%)	68 (62%)	85 (89%)	0.2	0.1 to 0.4
One minor impairment	8 (16%)	8 (13%)	16 (15%)	6 (6%)	2.6	1.0 to 7.4
Significant impairment§	15 (31%)	10 (17%)	25 (23%)	5 (5%)	5.4	2.0 to 14.3

Significant long term sequelae
even in children who seem normal at discharge

BACTERIAL MENINGITIS – WORTH PREVENTING

IMPACT OF VACCINES GREATEST FOR HIB

Bacterial meningitis post vaccines:
Hib disappears, Pneumo reduces, Meningo varies

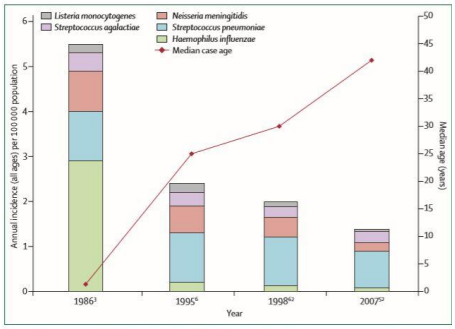
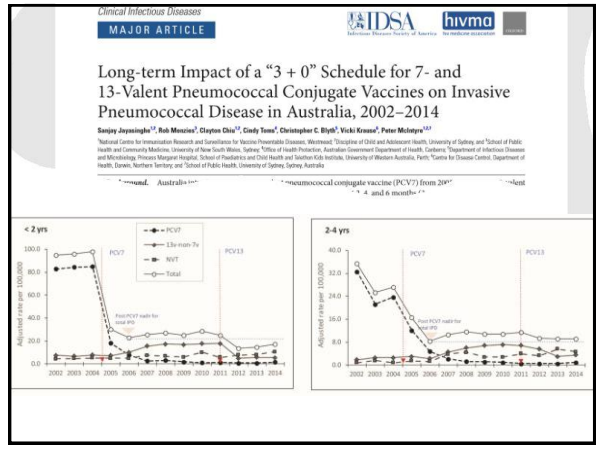


Figure 2: Prevalence of bacterial meningitis in the USA attributable to *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Streptococcus agalactiae*, and *Listeria monocytogenes*, 1986–2007[1,2]

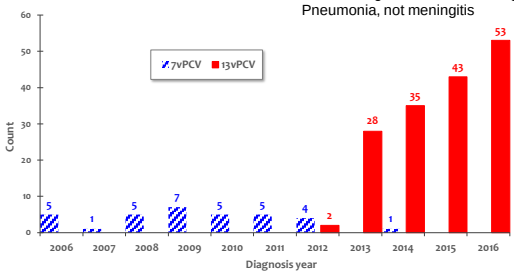
SITUATION IN 2018: PNEUMO AND MENINGO

Invasive Pneumococcal Disease: breakthrough cases



7vPCV & 13vPCV 3-dose breakthroughs: 2006-2016

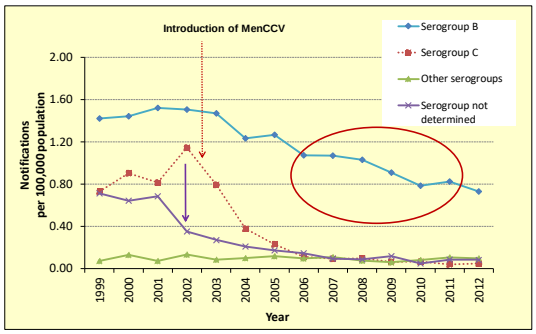
Breakthroughs > 12 months of age
Pneumonia, not meningitis



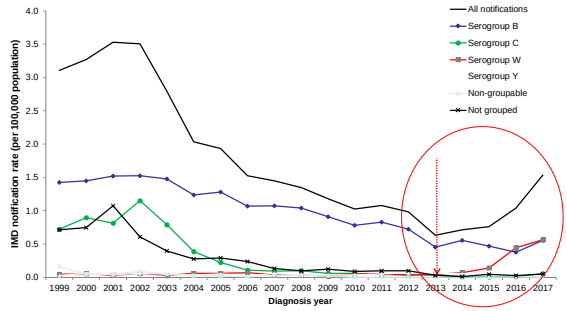
Data source: National Notifiable Diseases Surveillance System

Meningococcal disease – emergence of serotypes W and Y

Confirmed IMD cases, Australia 1999-2012



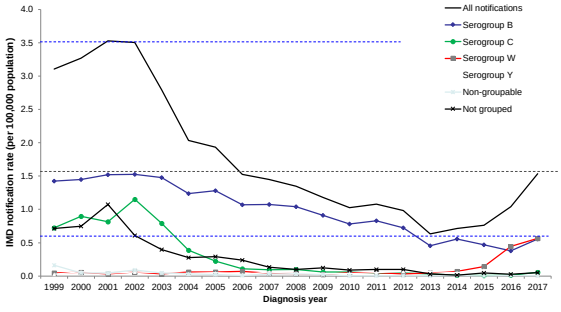
IMD notification rate by serogroup and year, 1999–2017



Trends are not shown for serogroups A (n=6) and X (n=2)

16

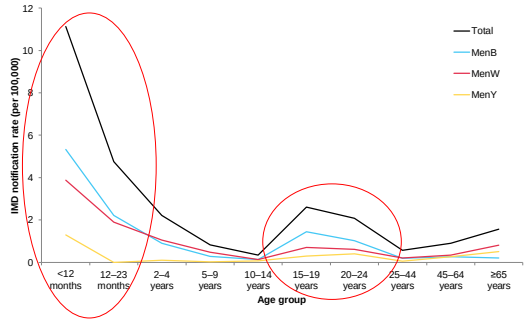
IMD notification rate by serogroup and year, 1999–2017



Trends are not shown for serogroups A (n=6) and X (n=2)

17

IMD notification rate by serogroup and age group, 2016-2017

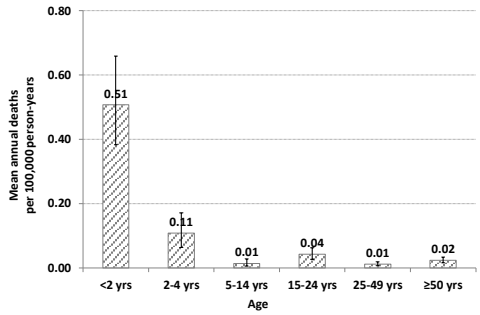


18

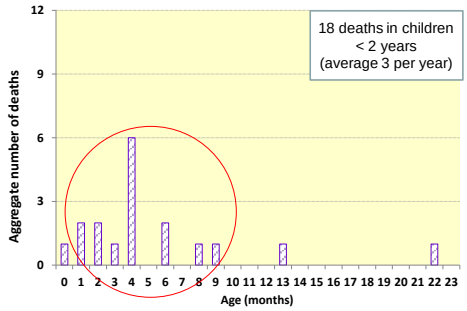
Meningococcal disease in infants

20

MenB death rates 1991-2011 by age group



Number of MenB deaths 2006-2011, by age in months (to <2 years)



IMD mortality and case fatality ratios, 2016–2017 (comparison with MenC 1999–2002)

Serogroup	Number of deaths	Number of cases	Case Fatality Ratio
MenB	10	229	4.4%
MenC	49	686	7.1%
MenW	23	247	9.3%
MenY	5	114	4.4%

23

Where are we in 2018?

- Hib meningitis
  - occasional cases in unvaccinated infants
- Pneumococcal meningitis
  - significant reduction
  - persistent cases due to non-vaccine serotypes
- Meningococcal meningitis and sepsis
  - Type B disease reduced significantly in absence of vaccine ➡ peak< 2 years; smaller adolescent
  - Type W and Y emerged; now approx. = type B

24

Hib, Pneumo and Meningo vaccines – changes July 1

- *Hib vaccine:*
  - hexavalent 2,4,6 months; 12 month booster to move to 18 months as Hib vaccine alone (current Hib-MenC)
- *Pneumococcal vaccine:*
  - 3rd dose to move to 12 months (2+1)
  - High risk kids (Aboriginal and medical conditions) continue 2,4,6 + 12 months
- *Meningococcal vaccines:*
  - MenACWY replaces MenC @ 12 months
  - Adolescent programs for meningococcal vaccination through high schools in Queensland since 2017
  - No MenB vaccine on NIP

25

THE FINE PRINT

Amendment to Immunisation Handbook

Table 1: Comparison of current and proposed ATAGI recommendations for 13vPCV schedules in children

Cohort		Schedule in previous recommendation*	Schedule in current recommendation
Children **without** underlying medical conditions associated with increased risk of IPD	All children in ACT, NSW, TAS or VIC	3+0 (2, 4 and 6 months)	2+1 (2, 4 and 12 months)
	Non-Indigenous children in NT, QLD, SA or WA		
	Aboriginal and Torres Strait Islander children in NT, QLD, SA or WA	3+1 (2, 4, 6 and 12–18 months)	3+1 (2, 4, 6 and 12 months)
All children **with** underlying medical conditions associated with increased risk of IPD (Attachment A)		3+1 (2, 4, 6 and 12 months)	3+1 (2, 4, 6 and 12 months)

2+1 pneumococcal vaccine and meningitis

- Most 3 dose breakthrough cases after 12 months
- Most pneumonia or empyaema
- Moving booster to 12 months will give stronger and more long-lasting protection with same number of doses

BUT….

- Meningitis mostly before 12 months
- Experience in UK with 2+1 suggests meningitis cases after 2 doses (between 4 and 12 months) could occur
- Like meningo, 2 dose meningitis breakthrough rare but serious

Important points about 2+1

- *Between July 1 and Dec 31 2018:*
  - Infants turning 12 months of age receive PCV13 dose @ 12 months; ie 4 doses (3rd dose @ 6 months)
  - Infants turning 6 months DO NOT get PCV 13 dose
  - No change with high risk babies inc Aboriginal
- *From Jan 1, 2019:*
  - 3rd dose at or slightly before 12 months – no delay!

Important points about Men ACWY

- *Between July 1 and Dec 31 2018:*
  - ACWY replaces Hib-Men C vaccine @ 12 months
  - Supplies expected soon – no definite date as yet
  - No catch up funded – high school programs continue
- *From January 1 2019:*
  - Cohort turning 18 months receives monovalent Hib vaccine @ 18 months with MMR-V and DTPa
  - Hib risk so low that no issue with delay to 18 months for Hib dose

EXTRA PROTECTION: VACCINES FOR PRIVATE PURCHASE

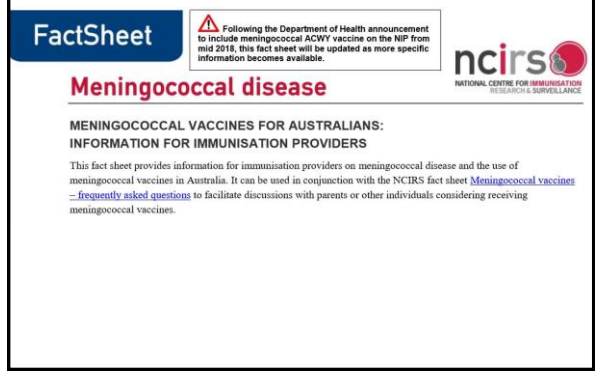
Extra vaccine options

- **PCV 13:**
  - Continue to have 3rd dose @ 6 months (4 doses)
  - Chemist Warehouse: N/A
- **Men ACWY:**
  - Infants: Additional doses from 6 weeks
  - Children who have previously received Men C
  - Chemist Warehouse: Nimenrix = $56
- **Men B:**
  - Infants: Additional doses from 6 weeks; older children
  - Chemist Warehouse: Nov 2017: $110

Vaccines against meningococcal disease – minimum doses by age group[1]

Age group	Men B (Bexsero)	MenACWY (Menveo)	MenACWY (Nimenrix)	MenACWY (Menactra)
2-<9 months (from 6 wks) 3 dose Total	2 doses >8 weeks apart 3rd dose @ 12m	2 doses >8 weeks apart 3rd dose @ 12m	2 doses >8 weeks apart 3rd dose @ 12m	No data
9 - <12 months 2 dose Total	1 dose now 2nd dose @ 12m or > 8 weeks	1 dose now 2nd dose @ 12m or > 8 weeks	1 dose now 2nd dose @ 12m or > 8 weeks	
12 -23 months 1/2 doses	2 doses >8 weeks apart	2 doses >8 weeks apart	Single dose	2 doses >8 wks apart
24 months + 1/2 doses	2 doses >8 weeks apart	Single dose	Single dose	Single dose

1 = UK 2+1 schedule – data suggest similar efficacy


FactSheet

Following the Department of Health announcement to include meningococcal ACWY vaccine on the NIP from mid 2018, this fact sheet will be updated as more specific information becomes available.

ncirs NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

Meningococcal disease

MENINGOCOCCAL VACCINES FOR AUSTRALIANS: INFORMATION FOR IMMUNISATION PROVIDERS

This fact sheet provides information for immunisation providers on meningococcal disease and the use of meningococcal vaccines in Australia. It can be used in conjunction with the NCIRS fact sheet Meningococcal vaccines – frequently asked questions to facilitate discussions with parents or other individuals considering receiving meningococcal vaccines.

Vaccines against meningococcal disease – more doses in youngest infants[1]

Age group	Men B (Bexsero)	MenACWY (Menveo)	MenACWY (Nimenrix)	MenACWY (Menactra)
2-<6 months (from 6 wks) 4 dose Total	3 doses >8 weeks apart 4th dose @ 12m	3 doses >8 weeks apart 4th dose @ 12m	3 doses >8 weeks apart 4th dose @ 12m	No data
6 - <12 months 3 dose Total	1 dose now 2nd > 8 weeks 3rd dose @ 12 m	1 dose now 2nd > 8 weeks 3rd @ 12 m	1 dose now 2nd > 8 weeks 3rd dose @ 12m	
12 -23 months 1/2 doses	2 doses >8 weeks apart	2 doses >8 weeks apart	Single dose	2 doses >8 wks apart
24 months + 1/2 doses	2 doses >8 weeks apart	Single dose	Single dose	Single dose

1. Highest achievable antibody responses

Bexsero and Fever

Prophylactic use of paracetamol with Bexsero® vaccination in children aged <2 years

Prophylactic use of paracetamol is recommended with every dose of Bexsero® administered to children <2 years of age. This is an exception to the general recommendation not to routinely give paracetamol with vaccinations unless it is for relief of fever or pain following immunisation – refer to *The Australian Immunisation Handbook*, 10th edition, 2015 update (Chapter 2.3).[20]

SUMMARY: Take home messages -1

1. *At population level*, bacterial meningitis much less common post Hib, Pneumo and Meningo vaccines but *at individual level* devastating disease
2. *Changes @ 6, 12 and 18 months from July 1:*
   - Important that later 3rd dose of PCV13 *AT* 12m
     - 6 month dose continues for high risk
     - ? Purchase for concerned parents
   - Men ACWY replaces combo Hib-Men C

SUMMARY: Take home messages -2

1. Meningococcal disease individual risk is greatest *in first 2 years of life* – rare but devastating
2. Doses of Men B (Bexsero) and ACWY (Nimenrix) can be given *from 6 weeks of age*
   - Protection from one dose uncertain; *biggest increase in protection after 2nd dose*
     - *3rd dose* @ 12 months will likely *increase duration* of protection

Acknowledgements

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40