



# Conjugate Meningococcal Vaccine and Oral Typhoid Vaccine

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# Meningococcal vaccine

- Menactra: New meningococcal vaccine
- Conjugate vaccine
  - Previous (non B) vaccines were polysaccharide
  - Menomune and Mencevax ACWY
- In conjugate vaccines the polysaccharide is conjugated to a protein carrier such as tetanus toxoid or diphtheria toxoid





# How do polysaccharide and conjugate vaccines differ?

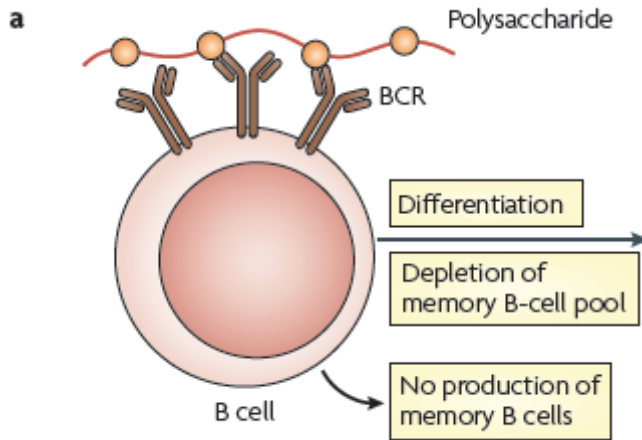


*"You might feel a little prick."*





# How polysaccharide vaccines work

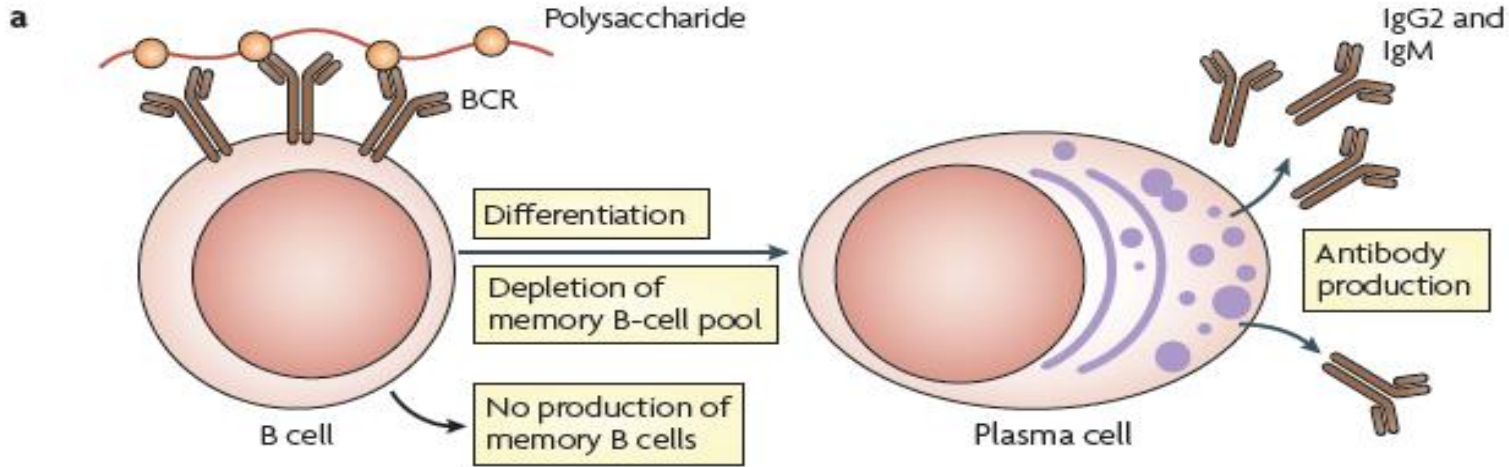


- Polysaccharides stimulate B cells by cross-linking the B-cell receptor (BCR)





# How polysaccharide vaccines work



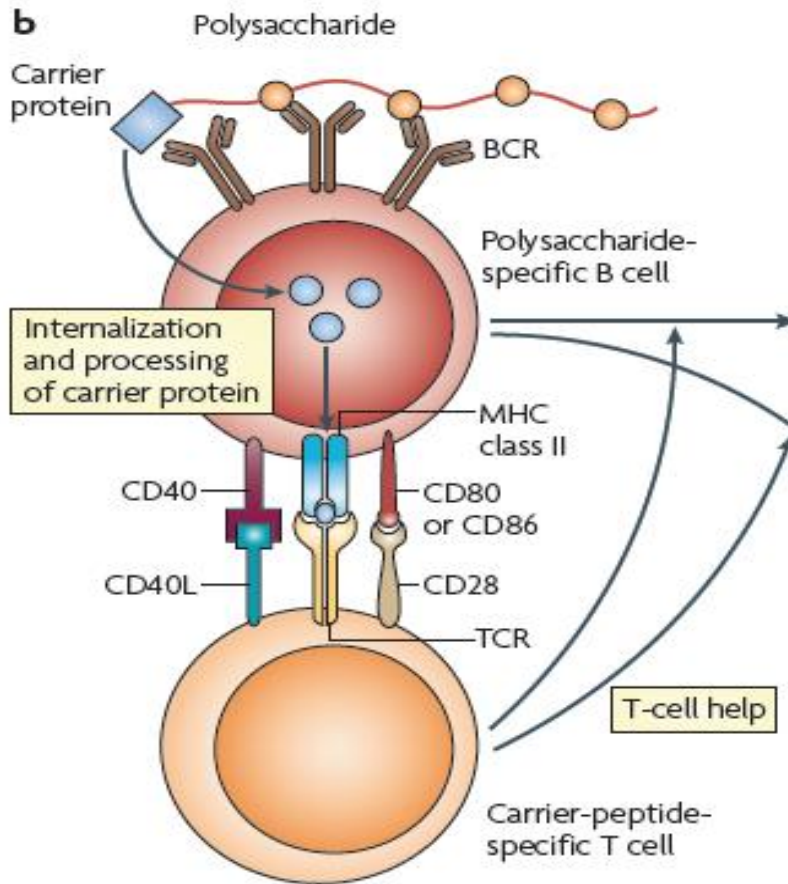
- Drives the production of immunoglobulins
- No production of new memory B cells
- Depletion of the memory B-cell pool so subsequent immune responses are decreased





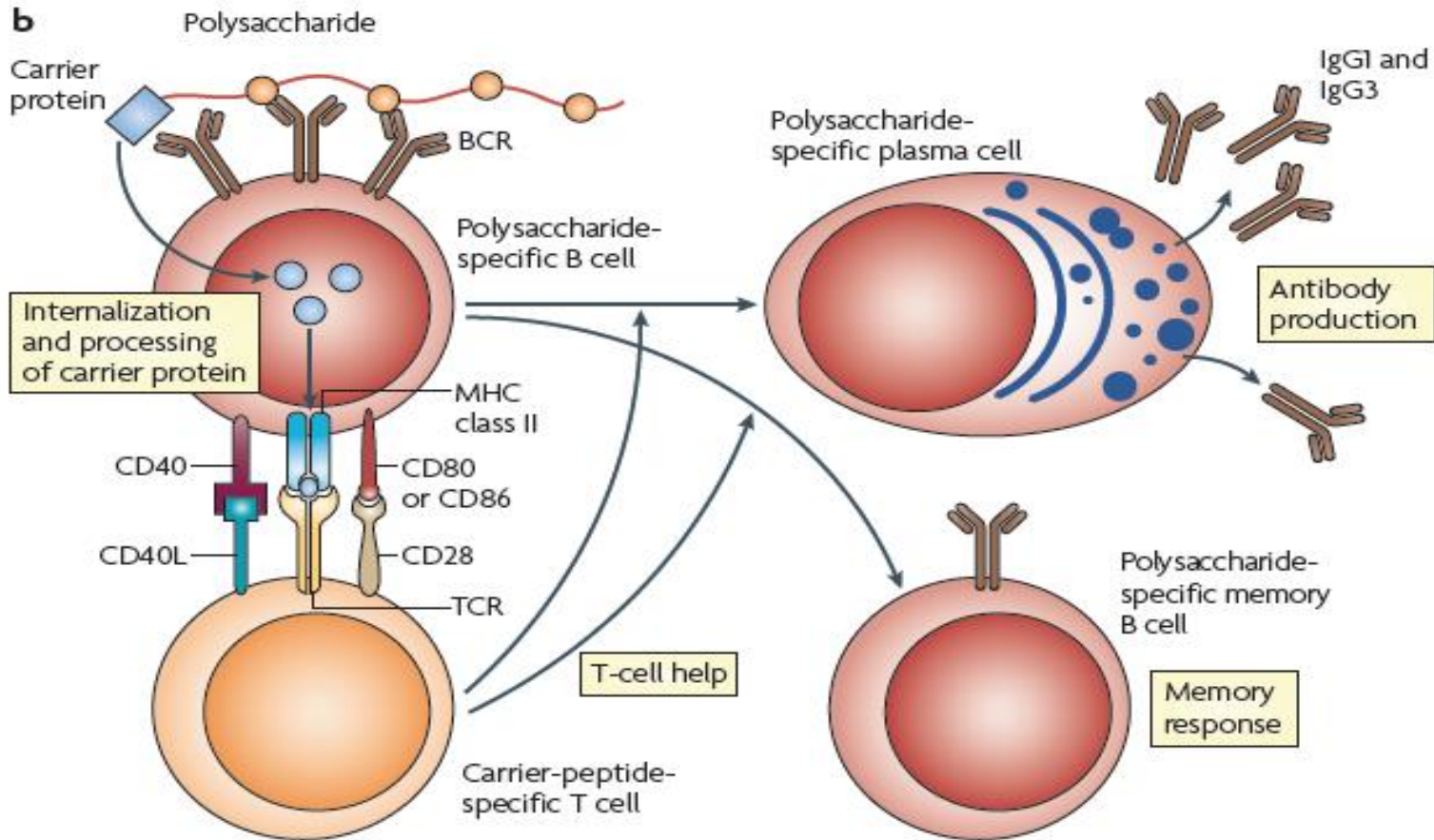
# How conjugate vaccines work

- The carrier protein from protein–polysaccharide conjugate vaccines is processed by the polysaccharide-specific B cell
- Peptides are presented to carrier-peptide-specific T cells, resulting in T-cell help for the production of both plasma cells and memory B cells





# How conjugate vaccines work





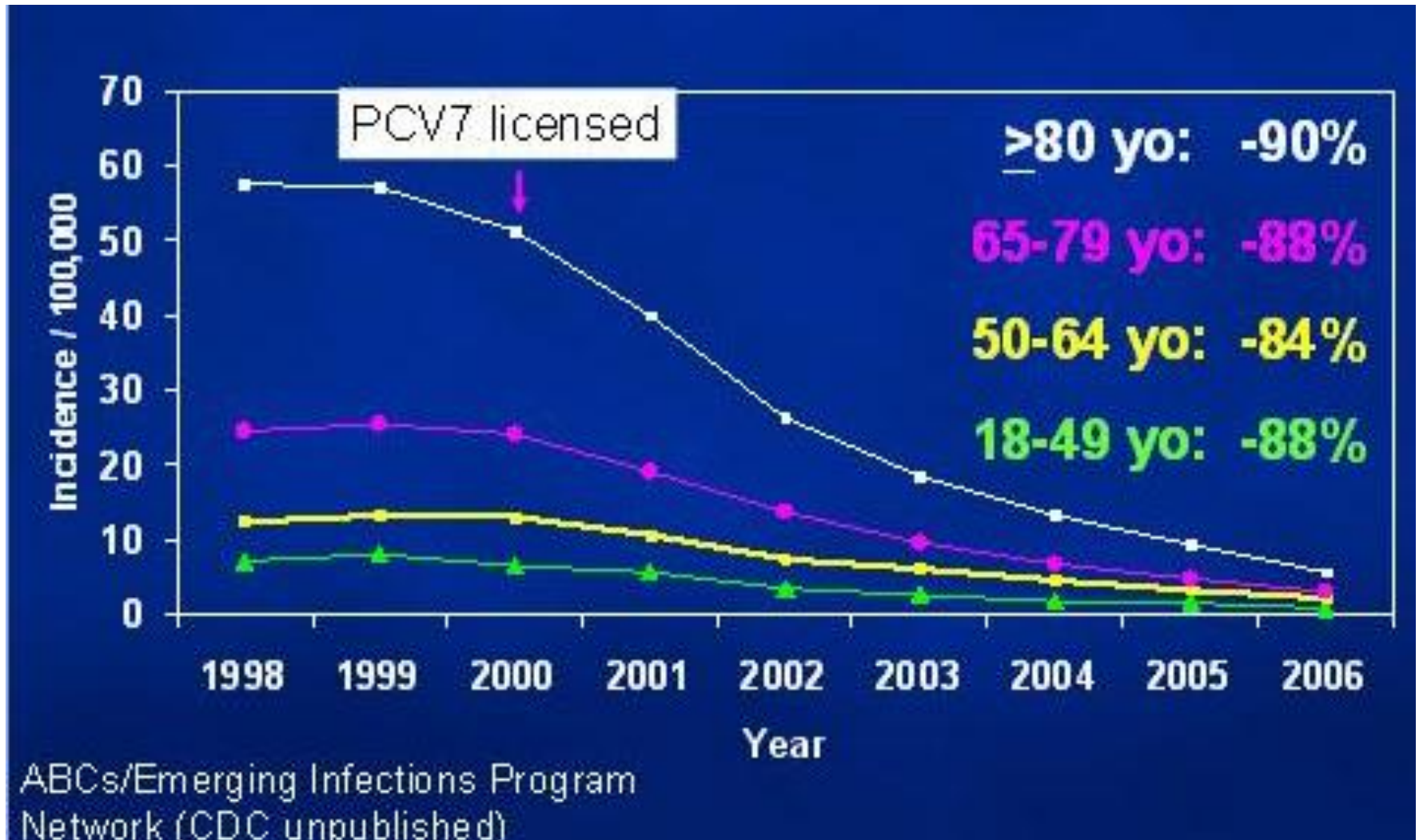
# Conjugate vaccines

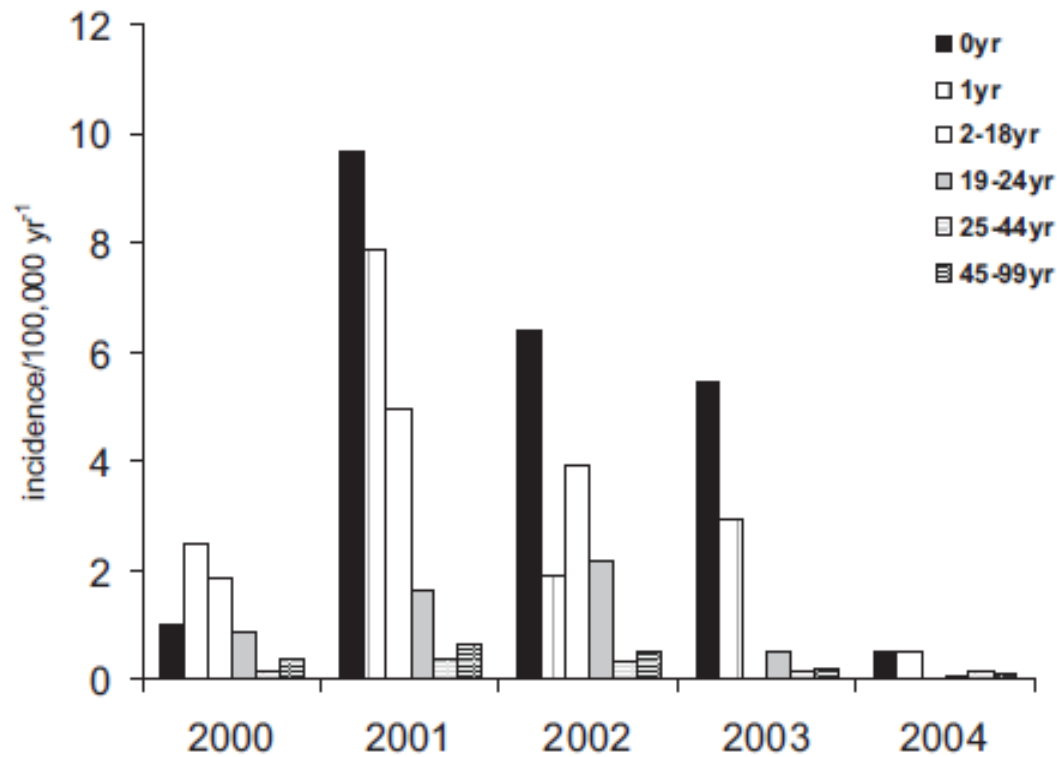
- Induce T cell dependent response
  - Occurs from early infancy
  - More effective in younger infants
  - First dose primes immune system to stronger response to a booster dose
- Reduce nasopharyngeal carriage of *N.meningitidis*
  - reduced community transmission -“herd effect”
  - Seen with introduction of
    - Conjugate *H. influenzae* (Hib)
    - Conjugate pneumococcal vaccines (e.g. Prevenar)
    - Meningococcal serogroup C conjugate vaccine in UK, Netherlands





# Invasive pneumococcal disease (PCV7 serotypes) in non-immunised adults > 18 years





**FIGURE 1.** Incidence of meningococcal C disease in the Netherlands, by age group and year.



# Menactra

- For 2 to 55 years, single dose
- NZ: “need or timing of booster not yet determined”
- US :-If 2-6 when vaccinated boost after 3 years
  - If >7 years boost after 5 years
- Not licensed in NZ for < 2 years of age
- American recommendations:
  - 2- 8 months (off label): 2 doses 1 month apart , booster at 12 months
  - 9- 23 months: 2 doses 3 months apart, boost at 3 years
  - Asplenic, complement deficiencies, HIV: 2 doses 2 months apart





# Responses 28 days after vaccination in 2 to 3 year olds

		Menactra vaccine	Menomune
Serogroup			
A	% titre $\geq$ 1:8	73	64
	GMT	10	10
C	% titre $\geq$ 1:8	63	38
	GMT	27	11
Y	% titre $\geq$ 1:8	88	73
	GMT	51	18
W-135	% titre $\geq$ 1:8	63	33
	GMT	15	5

GMT = Geometric mean titre





## Side effects

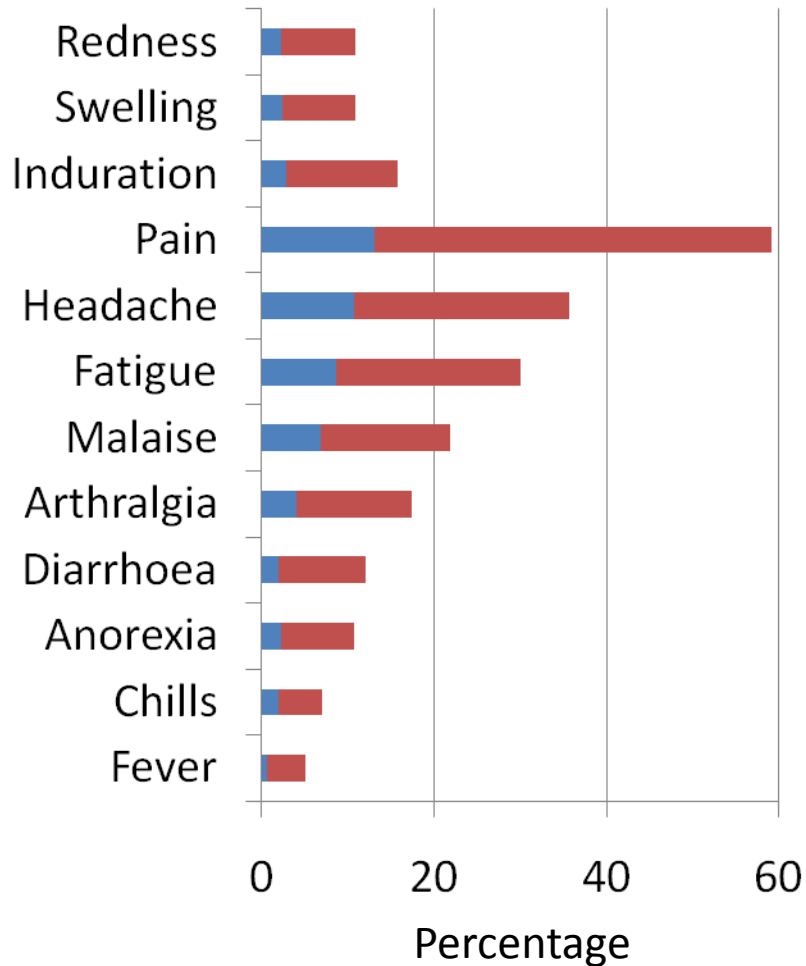
- Serious adverse events in 6 months following Menactra at same rate as after Menomune (1.3%)
- Local reactions more frequent than after Menomune



# Frequency of adverse events in 11 to 18 year olds within 7 days of vaccination

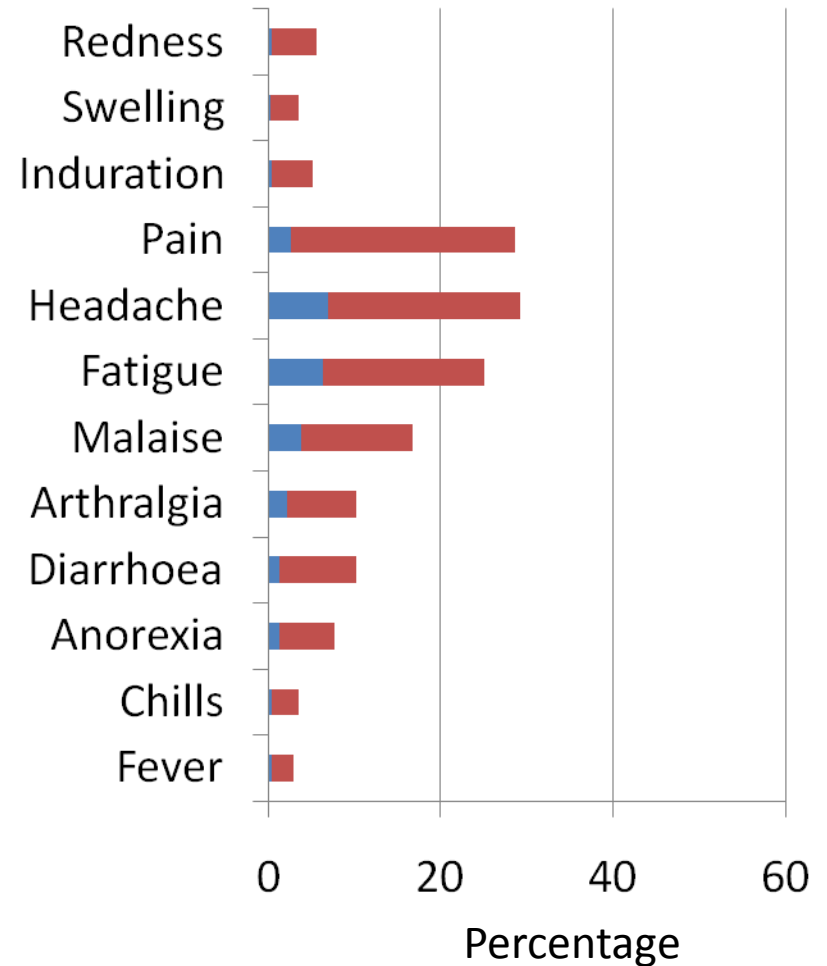
## Menactra vaccine

Moderate or severe Mild



## Menomune vaccine

Moderate or severe Mild





# Guillian –Barre Syndrome (GBS)

- Has been reported following Menactra
- Multi-site retrospective study involving over 12 million adolescents of whom 1.4m received Menactra found no evidence of increased risk
- Previous GBS is a contraindication



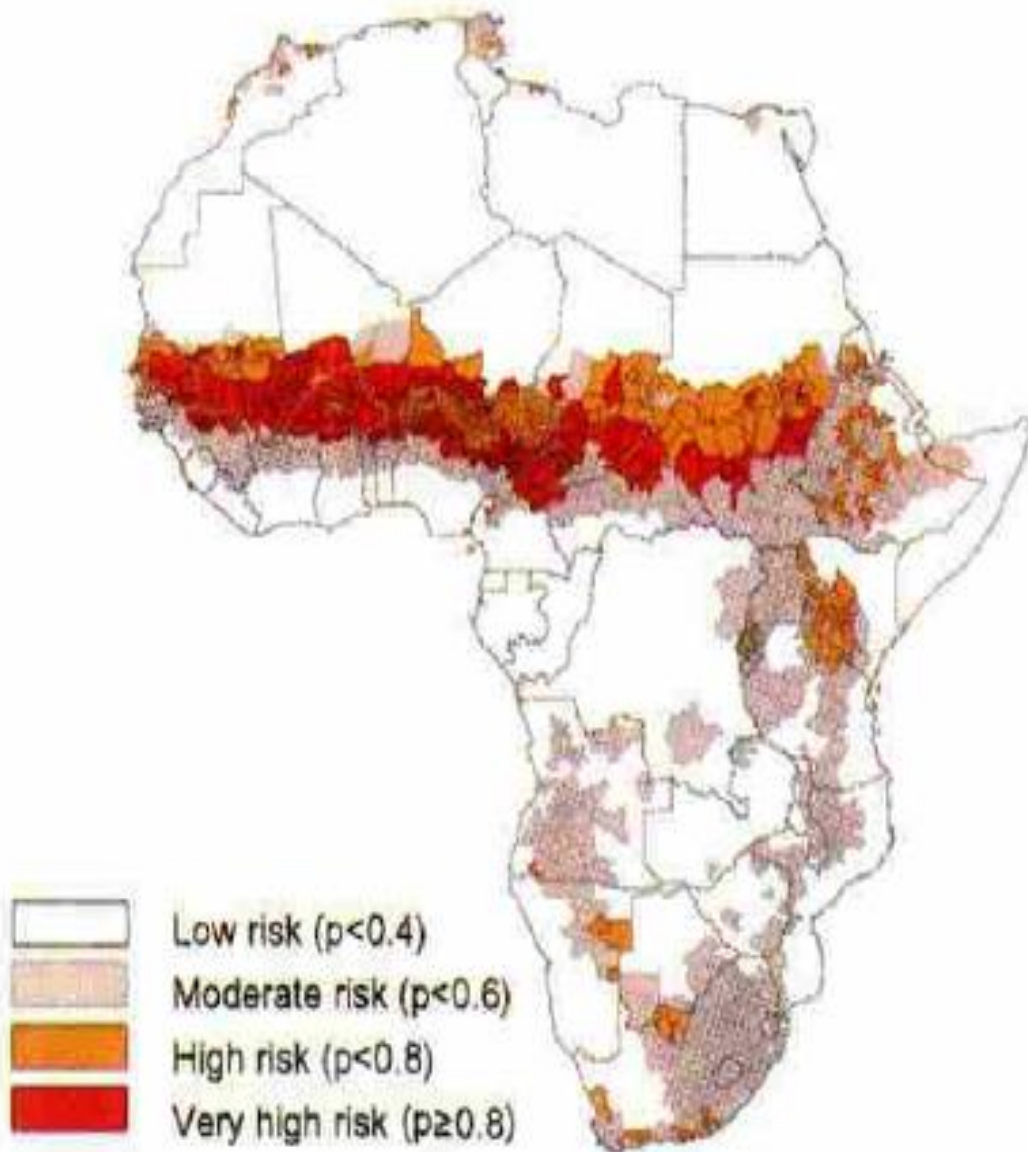


## Who to give it to?

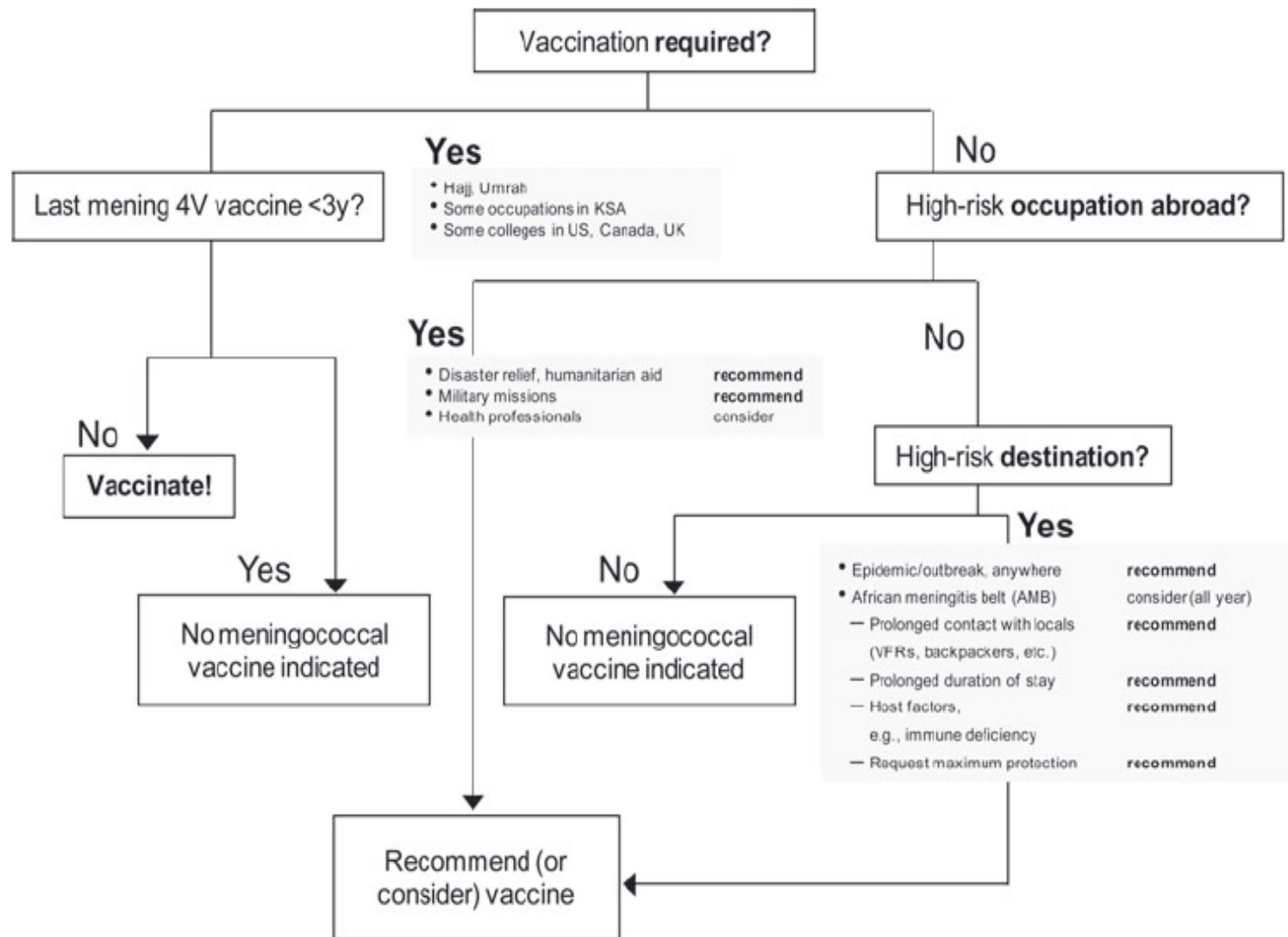
- Travellers to meningitis belt of Africa
  - Particularly if during dry season, health care workers, infants and children
- Those doing the Hajj pilgrimage (meningococcal vaccine in past 3 years is required)
- Consider for adolescents and young adults planning to stay in hostels/ overcrowded conditions
- (Routine vaccine in US for 11-12 year olds with a booster at 16 years)







- **Sahel region** from Senegal and Guinea to Ethiopia
- Northern Uganda
- Eastern DRC
- Rift Valley
- Malawi
- NE Mozambique

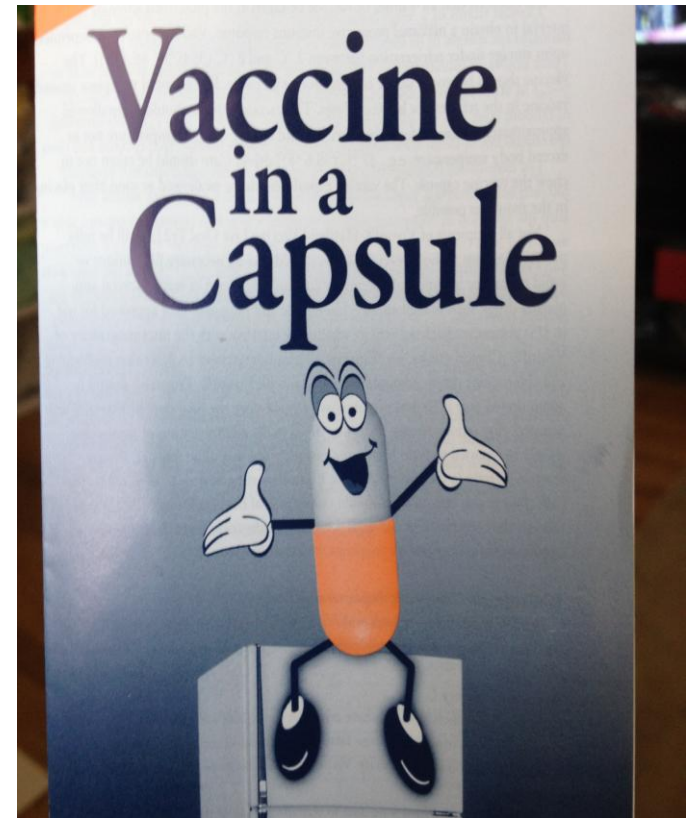


**Figure 4** Meningococcal vaccination decision algorithm for travelers. 4V = quadrivalent; KSA = Kingdom of Saudi Arabia; UK = United Kingdom; US = United States; VFRs = visiting friends and relatives.



# Oral typhoid vaccine

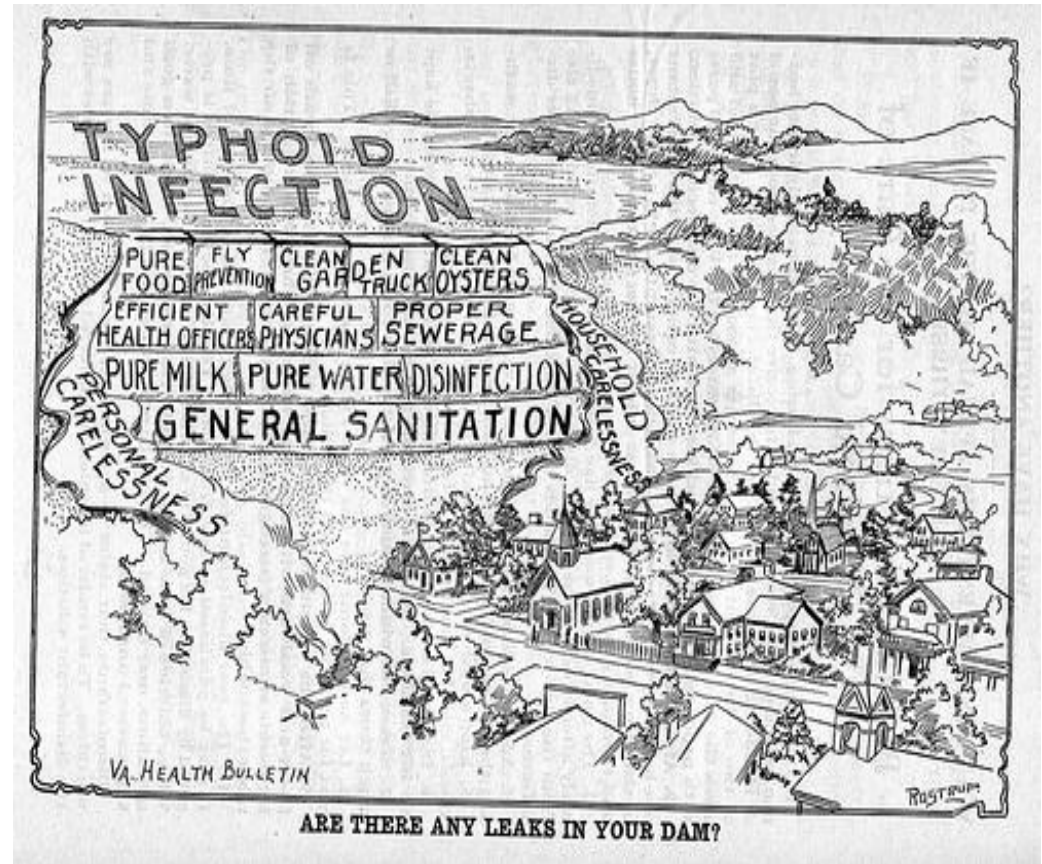
- Vivotif now available again
- Live attenuated vaccine containing Ty21a strain which is deficient in an enzyme so it can't metabolise galactose
- Galactose is present in the gut so vaccine bacteria accumulate galactose and lyse- not detected in stools 3 days after ingestion





# Efficacy

- No studies in travellers
- In endemic areas 50 to 80%
- May provide some protection against paratyphi





## Dosage/ administration

- Keep refrigerated
- 3 doses on alternate days e.g. 1,3 and 5 for those above 6 years of age
- Swallow whole, not chewed
- One hour before a meal with cold or lukewarm drink
- Complete 1 week before potential exposure
- Optimal booster timing unclear: 3 years
- In America they have a 4 dose primary series and boost at 5 years





## Contraindication and precautions

- Immunodeficiency including HIV , drug induced
- Acute febrile illness or GI illness
- Pregnancy
- Concurrent antibiotics (wait > 72 hours after stopping antibiotic)
- Optimally wait 3 days before starting antimalarials but mefloquine, malarone & chloroquine probably Ok





## Adverse effects

- Generally mild- constipation, abdominal cramps, diarrhoea, nausea, vomiting, anorexia, fever, headache, rash



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