Travel vaccine update

Alex Padiglione
Disclosures

Nil significant to this lecture
Travel – changing face
Meningococcal
Japanese encephalitis
Yellow fever
Ebola
Travel is common
6.7 million short-term departures
Over half – 3rd world  ABS 2010

Yet quality of evidence re travel vaccines mixed
- Better for more common diseases
Steffen et al J Trav Med Online 6 Nov 2014
<table>
<thead>
<tr>
<th>VPD</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travelers' diarrhea</td>
<td>Cohorts ($n = 3$)</td>
<td>Yes for incidence rate</td>
<td>Moderate to high</td>
</tr>
<tr>
<td>ETEC</td>
<td>By-product of intervention studies</td>
<td>Variations depending on destinations</td>
<td>Moderate</td>
</tr>
<tr>
<td>WC/rBS vaccine efficacy against TD</td>
<td>Nonrandomized, nonblinded, &amp; expert opinions</td>
<td>Broad variation</td>
<td>Very low</td>
</tr>
<tr>
<td>Influenza</td>
<td>Cohorts ($n = 3$)</td>
<td>Yes</td>
<td>Moderate to high</td>
</tr>
<tr>
<td>Typhoid</td>
<td>Notification</td>
<td>On order of magnitude</td>
<td>Moderate</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Notification</td>
<td>On order of magnitude</td>
<td>Moderate</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Notification</td>
<td>On order of magnitude</td>
<td>Moderate</td>
</tr>
<tr>
<td>Rabies</td>
<td>Anecdotal collection</td>
<td>Only one review</td>
<td>Very low for rabies infection</td>
</tr>
<tr>
<td>Tick-borne encephalitis</td>
<td>Expert opinion</td>
<td>Only one statement</td>
<td>Very low</td>
</tr>
<tr>
<td>Meningococcal disease</td>
<td>Notification</td>
<td>Only one review</td>
<td>Very low</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>Anecdotal reports</td>
<td>Only one review</td>
<td>Very low</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>Notification (WHO)</td>
<td>Probably reliable</td>
<td>Moderate</td>
</tr>
<tr>
<td>Cholera</td>
<td>Notification (WHO)</td>
<td>Questionable</td>
<td>Very low</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Expert opinion</td>
<td>Repeated one statement</td>
<td>Very low</td>
</tr>
</tbody>
</table>
Meningococcal disease
Meningococcus

13 strains

Most common are A, B, C, W135, Y

Australia: B & C

Africa/Asia: A
Meningococcal vaccines: non travel

Meningococcal C conjugate vaccine
  Funded: All children ≥12 months

Meningococcal B conjugate vaccine “Bexsero”
  Not yet funded: Infants, 15-19 yrs
Meningococcal disease: Travel

Quadrivalent meningococcal vaccine
(A, C, W135 & Y antigens)

Recommended:

• ‘Meningitis belt’ of sub-Saharan Africa
• Pilgrims to Mecca (“Hajj” or “Umra”)
  – evidence of recent vaccination within 3 years
• HCWs/Aid workers
Quadrivalent Meningococcal vaccines

ACW135Y

**Conjugate** (4vMenCV)
Menveo or Menactra
0.5 mL IM Single dose
5 yearly?

preferred over older polysaccharide vaccine

**Polysaccharide** (4vMenPV)
Mencevax or Menomune
0.5 mL SC Single dose
3–5 yearly boosters if at ongoing risk
Japanese encephalitis
Japanese encephalitis

Virus similar to yellow fever

<1% infected develop encephalitis but still 35,000-50,000 cases/yr

Of encephalitis cases -
   20-30% die
   35% permanent brain damage

In endemic areas, almost everyone infected by age 15 yrs
Japanese encephalitis vaccine

Mainly Rural, irrigated paddy & pig-farming areas

Recommended:
1 month in rural areas of high risk in endemic regions

Shorter-term travellers - consider if:
- wet season
- repeated
- outdoor activity
- inadequately screened against mosquitoes

Expats >1 year in Asia, even if mostly urban areas
Japanese encephalitis

387 Australian travellers – none infected

2 previous studies:

1 case per 5 million travellers

Ratnam et al J Trav Med 2013; 20(3) 206–208
Hatz et al. J Travel Med 2009 May-Jun; 16(3) :200-3
Japanese encephalitis vaccines

Jespect 0.5 mL IM
    0, 28 days

Imojev 0.5 mL SC
    Single dose

(No longer manufactured: JE-Vax, Japan, old inactivated mouse brain-derived vaccine)
Imojev

Live attenuated, monovalent viral vaccine

Recombinant:

YF vaccine virus: 2 genes replaced with 2 genes from Japanese encephalitis virus
<table>
<thead>
<tr>
<th></th>
<th>Imojev</th>
<th>JEspect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doses</strong></td>
<td>1</td>
<td>2: days 0, 28</td>
</tr>
<tr>
<td><strong>Type</strong></td>
<td>Live attenuated</td>
<td>Inactivated</td>
</tr>
<tr>
<td><strong>Complete before travel</strong></td>
<td>2 weeks</td>
<td>1 week</td>
</tr>
<tr>
<td><strong>Pregnancy/ breastfeeding</strong></td>
<td>Avoid (inc for 28 days after)</td>
<td>Not routine, probably OK Little data in breastfeeding Give if at significant risk</td>
</tr>
<tr>
<td><strong>Kids</strong></td>
<td>≥12 months</td>
<td>≥18 yrs but seems safe ≥12 months (use half dose under 3) “if alternative not avail or CI”</td>
</tr>
<tr>
<td><strong>Protective Ab</strong></td>
<td>Children (1–2 yrs): 96% Adults: 99%</td>
<td>98%</td>
</tr>
<tr>
<td><strong>Adjuvants/Antibiotics</strong></td>
<td>Nil</td>
<td>Aluminium</td>
</tr>
<tr>
<td><strong>Co-administration</strong></td>
<td>Ok with YF Probably with other live vaccines Simultaneous or separate by 4 weeks (separate sites)</td>
<td>OK with hep A Probably with others Give in separate limbs</td>
</tr>
<tr>
<td><strong>Immunocompromised</strong></td>
<td>Avoid</td>
<td>Safe – but little data on efficacy</td>
</tr>
</tbody>
</table>
Booster doses?

Not well defined for either: Limited data

Imojev: booster not currently recommended

   protective antibody levels 5yrs after single dose

JEspect: readminister after 1 year (ongoing / high risk)

Older mouse brain-derived vaccine- can boost with Imojev or JEspect
"I rather think I am on the track of the real germ"
Jesse Lazear
Cuba, September 8, 1900.

Died 17 days later of fulminating yellow fever, aged 34
YF worldwide

130 000 cases each year
~15% severe
~1/2 of those will die
=30 000 deaths, worldwide each year,

90% in Africa!
Yellow fever

All travellers aged ≥9 months if
   Transmission areas, or
   Required by country for entry

Each country - own legislation (in accordance with WHO)

Age ≥60 years: risk of adverse events vs potential for disease
Low potential for exposure  São Tomé and Príncipe; Tanzania
Low potential for exposure in some areas only  Eritrea; Somalia; Zambia
Not on official WHO list (YF risk)
= Proof of vaccination should not be required if travelling from one of these
CDC YF recommendations

C/I

Allergy
Age <6 months
CD4<200 (<15%)
Thymus disorder
Primary immunodeficiency
Neoplasm
Transplantation
Immunosuppressive or immunomodulatory Px

Precautions

Age 6-8 months
Age >60 yrs
CD4 200-499 (15-24%)
Pregnancy
Breast feeding
## Yellow Fever: Competing Risks

<table>
<thead>
<tr>
<th>Region</th>
<th>Disease</th>
<th>Neurotropic AE</th>
<th>Viscerotropic AE</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Africa</td>
<td>Illness: 500</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Death: 100</td>
<td>Age 60-69: 16</td>
<td>Age 60-69: 10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Age &gt;70: 23</td>
<td>Age &gt;70: 23</td>
</tr>
<tr>
<td>South America</td>
<td>Illness: 50</td>
<td>//</td>
<td>//</td>
</tr>
<tr>
<td></td>
<td>Death: 10</td>
<td>//</td>
<td>//</td>
</tr>
</tbody>
</table>

// / million vaccinees / million vaccinees

2 week stays / 2 week stays
Evidence of good long term immunity!

Eg Since 1930’s
600 million doses dispensed
-only 12 known cases of YF post-vaccination
  (Only 1 in a traveller)

All developed within 5 years of vaccination
= 1º failure, immunity doesn’t decrease with time
WHO

YF does not require boosters
   Infants, Immunocompromised may be exceptions

Countries have until June 2016 to change laws
**No change to practice** until then

32% drop in pts at dedicated Travel clinics (France)?

Wyplosz et al J Trav Med Online 11 Nov 2014
Ebola vaccine

An Urgent International Priority

Rupa Kanapathipillai, et al

NEJM October 7, 2014
WHO meeting Geneva Sept 29/30th

2 main candidates, both Live, express glycoproteins from ebola
   Several others at earlier, preclinical stages

Nonhuman primates: both 100% efficacy

Human studies Phase 1: underway

WHO consultation on ebola vaccines. Geneva, october 1, 2014
HTTP://WHO.INT/MEDIAGENTRE/NEWS/EBOLA/01-OCTOBER-2014/EN/
Another WHO meeting planned later this month
  Preliminary results phase 1 trials available

Even if safe & immunogenic – not available in substantial quantity until early 2015 at the earliest

Needs funding

Unlikely to be 100% effective:
More capacity in affected countries still needed urgently
Travel – common, but dodgy data
Meningococcal – Quadrivalent conjugate vaccine
Japanese encephalitis – rare; 2 options,
  more uptake by those who actually need it
Yellow fever – better risk assessment, no boosters after June 2016
Ebola – coming soon (hopefully)
The End