Wilbur H. Chen, MD, MS
Travel Vaccines
15 June 2017
Disclosures

- Wilbur Chen received research grants from PaxVax, Inc. as the Principal Investigator for the pivotal licensure studies of Vaxchora
- PaxVax, Inc. is the manufacturer of Vivotif and Vaxchora
Webinar Objectives

• Highlight 6 common travel vaccines
• Understand the geographic locations or epidemiology of the 6 vaccine preventable diseases
• Become familiar with the current vaccine recommendations for these travel vaccines
  - Unable to review all possible travel vaccines
  - Unable to review issues in preventing travel-related illnesses (i.e., traveler’s diarrhea, malaria, mosquito prevention, altitude sickness, etc.)
  - Unable to discuss medical evacuation, travel insurance, or other possible travel medicine matters
Protection during travel
High-Risk Activity...High-Risk for Infection!
Licensed Travel Vaccines in U.S.

- Yellow Fever
- Typhoid
- Hepatitis A
- Japanese Encephalitis
- Cholera
- Meningococcal
- Rabies
- Poliovirus
- Influenza
- Tetanus
- Measles, Mumps, Rubella
- Hepatitis B
- Pneumococcal
- Varicella
- Tick-borne encephalitis
- Anthrax
- Smallpox
- Tularemia
Organization of Lecture

• Pathogen
• Epidemiology/Geography
• Clinical Presentation
• Risk Assessment & Preventive Measures
• Vaccine(s) Available
  – Contraindications/Precautions
  – Adverse Effects
  – Efficacy
Beware of insect bites...
Yellow Fever

• Caused by a Flavivirus
• Transmitted by mosquito bite (*Ae. aegypti*)
• YF causes 200,000 cases of clinical disease and 30,000 deaths each year\(^1\)
• Substantial underreporting\(^2\), due to rural nature

1. WHO. Yellow Fever fact sheet, no. 100
2. Weekly Epi Rec 1990; 65: 213
YF: Epidemiology

Geography
- **Sub-Saharan Africa**
  - 87% cases and 50% case-fatality ratio
- **Tropical South America**
  - 13% cases and 20% case-fatality ratio

Seasonality
- **All-year but peaks with mosquito breeding**
- **South America**: peak rainfall, humidity, temp = Jan-May
- **West Africa**: late rainy season to early dry season = July-Oct

WHO YF Risk Maps, Feb 2011
YF: Clinical Presentation

- Majority of human infections are asymptomatic
- But, spectrum can be mild to severe
- Incubation 3-6 days
- **Initial stage**: Abrupt Fever and severe Headache; non-specific flu symptoms
- Recovery period or brief **remission** (viremia present): 1 day
- **Toxic phase** (15%): F, N/V, myalgia, arthralgia, jaundice, epigastric pain, renal insufficiency, and cardiovascular instability (viremia often not present)
  - Multi-organ failure with bleeding diathesis.
  - Case-fatality ratio 20-50%; especially with severe yellow fever with hepatorenal dysfunction
YF: Risk to Traveler

2-week stay for unvaccinated traveler:

- West Africa 50 illnesses per 100,000
- South America 5 illnesses per 100,000

YF: Prevention

- Clothing barrier
- Insect repellent (DEET)
- Vaccination

There is no specific treatment, limited to supportive care
## Globally available YF Vaccines

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>WHO pre-qualify</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanofi Pasteur, France</td>
<td>1987</td>
</tr>
<tr>
<td>Institut Pasteur de Dakar, Senegal</td>
<td>1999</td>
</tr>
<tr>
<td>Bio-Manguinhos, Brazil</td>
<td>2001</td>
</tr>
<tr>
<td>FSUE Chumakov, Russia</td>
<td>2009</td>
</tr>
</tbody>
</table>
YF Vaccine available in U.S.

YF-Vax® (sanofi pasteur)

- Live, attenuated 17D-204 strain
- Single parenteral dose, 0.5 mL
- Approved: age ≥9 months
- International Certificate of Vaccination
  - valid beginning 10 days after the date of vaccination

International Health Regulations (IHR), since June 2016
- WHO World Health Assembly in May 2014: lifetime (i.e., no booster doses necessary).

ACIP recommendations (Feb 26, 2015)
- 10 year boosters not required
April 2017

Dear Health Care Professional:

This letter is to provide an update on the status of YF-VAX* (Yellow Fever Vaccine) supply. Sanofi Pasteur is experiencing delays in the production process of YF-VAX vaccine and it is anticipated that the product will be unavailable from mid-2017 to mid-2018 as we transition production to a new state-of-the-art facility. Ordering restrictions have been implemented to responsibly manage the limited remaining supply of YF-VAX vaccine. YF-VAX vaccine will continue to be available while current supplies last.

Once YF-VAX vaccine is no longer available, health care providers and patients will be able to find locations that will administer STAMARIL vaccine by visiting the CDC web page at http://wwwnc.cdc.gov/travel/yellow-fever-vaccination-clinics/search. They may also visit http://wwwnc.cdc.gov/travel/ for information about which countries require yellow fever vaccination for entry and for which countries the CDC recommends yellow fever vaccination.
YF Vaccine: Contraindications

- Hypersensitivity to vaccine components: egg/chicken proteins, gelatin, latex (vial stopper)
- Prior anaphylaxis with vaccination
- Immune deficiencies
  - symptomatic HIV, CD4 <200, malignant neoplasms, transplantation, etc.
- Infants age <6 months

YF Vaccine: Precautions

- Age 6-8 months or Age ≥60 years
- Pregnancy and breastfeeding
- Asymptomatic HIV and CD4 200-499
YF Vaccine: Safety and Adverse Effects

• 10-30% mild systemic reactions
  low-grade fever, headache, myalgia

• Hypersensitivity
  1.8 cases/100,000 doses

• Vaccine-associated **Neurologic** Disease (YEL-AND)
  3-28 d post-vax: Meningoencephalitis, GBS, bulbar/Bell palsy
  Overall: 0.8 cases/100,000 doses
  Age 60-69: 1.6 cases/100,000 doses
  Age ≥70: 2.3 cases/100,000 doses

• Vaccine-associated **Viscerotropic** Disease (YEL-AVD)
  Viremia w/multi-organ involvement (63% case fatality)
  Overall: 0.4 cases/100,000 doses
  Age 60-69: 1.0 cases/100,000 doses
  Age ≥70: 2.3 cases/100,000 doses
YF Vaccine: Protection

In endemic populations (assuming vaccine coverage of 60-80% of population):

- Within 10 d: 80-100% immunity
- After 30 d: ≥99% immunity

Among vaccinated travelers from industrialized countries: One case, non-fatal (Spain to West Africa, 1988)


Fig. WHO 2015
YF Outbreak: Angola

(12/2015-7/2016)

Yellow Fever outbreak in Angola

- 3818 suspected cases
- 879 lab-confirmed infections
- 369 deaths
- Exported cases:
  - Dem Rep Congo, n=74
  - Kenya, n=2
  - China, n=11

- YF mass vaccination campaign (initiated 2/2/16)
  - 18 million doses (by mid-June 2016)

WHO update, 01 July 2016

China:
Of 5 with vaccination status info, all 5 cases did not have YF vaccine
YF Outbreak: Brazil

(12/2016-ongoing)

Yellow Fever outbreak in Brazil

- ~2900 suspected cases
- 681 lab-confirmed infections
- 372 deaths

- YF mass vaccination campaign
  - 67 million doses

Ministry of Health, Brazil
CIDRAP update, 20 Apr 2017
Beware of risk through ingestion...
Typhoid

- Human host-restricted bacterial pathogen

*Salmonella enterica* subspecies *enterica* serovar Typhi (*S.* Typhi)
  - *S.* Typhi: 22M illnesses and 200,000 deaths per year

- serovars Paratyphi A, B, or C (*S.* Paratyphi).
  - *S.* Paratyphi: 6M illnesses

- Nontyphoidal *Salmonella* (NTS) include: *S.* Enteriditis and *S.* Typhimurium

- Transmission: fecal-oral

Bull WHO 2004; 82:346-353
Typhoid: Epidemiology

• Associated with poor sanitation and lack of access to clean water

• World-wide distribution
  - High Incidence: >100 cases / 100,000 person years
  - Medium: 10-100 cases / 100,000 person years

• Highest risk: Southern Asia (6-30x higher than other regions)

• No seasonality

Bull WHO 2004; 82:346-353
Typhoid: Clinical Presentation

• Incubation 6-30 days
• **Insidious Onset:** gradual fatigue and fevers (102-104°F); abdominal pain, headache, malaise, anorexia, chills
• Without therapy: illness duration 3-4 weeks
• **Classic Presentation:**
  1\textsuperscript{st} week - *stepwise* fever w/ bradycardia (pulse-temp dissociation)
  2\textsuperscript{nd} week - abdominal pain and “rose spots”
  3\textsuperscript{rd} week – hepatosplenomegaly, intestinal bleeding, perforation
• 15% serious complications: Intestinal hemorrhage, perforation, peritonitis, septic shock
• **Chronic Carrier State:** 1-6% infections; excrete organisms >1 year

  More common in women and those with cholelithiasis or abnormal biliary tract
Typhoid: Risk to Traveler

CDC data, all travelers during 1994-1999:¹
1027 typhoid cases, 3 deaths
—Risk associated with length of stay
—Risk associated with location
53% Indian subcontinent
17% Mexico/Central America
7% Caribbean
3% Africa
4% other

CDC data, travelers to SE Asia during 2008-2011:²
602 typhoid and 142 paratyphoid A cases
5% typhoid cases and 20% paratyphoid cases were vaccinated

¹. CID 2004; 39: 186-91
². Vaccine 2014; 32: 3577-9
Typhoid: Prevention & Treatment

Prevention:
• Safe food and water
• Vaccination

Treatment:
• Rehydration
• Prompt Antibiotics
  – First Line: Fluoroquinolones, 3rd Gen Cephalosporin, azithromycin
  – Beware: FQ resistance in SE Asia!
• Surgery - ileal perforation
• corticosteroids
Globally Available Typhoid Vaccines

Parenteral vaccine:

• Typhoid Vi capsular polysaccharide
  – Typherix (GSK), Typhim Vi (SP), TypBar (Bharat), Shantyph (Shanta), Typho-Vi (BioMed), Zerotyph (Boryung, S. Korea), Typhevac (Shanghai)

• Typhoid Vi conjugate (TT)
  – Peda-typh (BioMed, India), Typbar-TCV (Bharat)

• Combination: ViCPS+Hepatitis A
  – Hepatyrix (GSK), Vivaxim (SP)

Oral vaccine:

• Live Attenuated
  – Vivotif (PaxVax)
Typhoid Vaccines available in the U.S.

**Typhim Vi®** *(sanofi pasteur)*
- Purified Vi capsular polysaccharide (Vi PS)
- Single parenteral dose, 0.5 mL
- Approved: age ≥2 years
- Booster every 2-3 years

**Vivotif®** *(Crucell-PaxVax)*
- Live, attenuated bacterial strain (Ty21a)
- 4 oral doses, spaced alternating days
- Approved: age ≥6 years
- Booster every 5-6 years
Typhoid Vaccine: Contraindication/Precautions

**Typhim Vi®**

- Hypersensitivity to vaccine components: typhoid polysaccharide, phenol, PBS
- Prior anaphylaxis with vaccination

Delay for concurrent acute febrile illness

**Vivotif®**

- Hypersensitivity to vaccine components:
- Prior anaphylaxis with vaccination
- Immunodeficiencies

Delay for concurrent acute febrile illness

*Efficacy reduced with concurrent antibiotics*
# Typhoid Vaccine: Safety & Adverse Effects

<table>
<thead>
<tr>
<th>Typhim Vi®</th>
<th>Vivotif®</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-77% injection site pain, mild</td>
<td>6% abdominal pain</td>
</tr>
<tr>
<td>42% headache</td>
<td>6% nausea</td>
</tr>
<tr>
<td>35% fatigue</td>
<td>5% headache</td>
</tr>
<tr>
<td>1% fever</td>
<td>3% fever</td>
</tr>
<tr>
<td></td>
<td>3% diarrhea</td>
</tr>
<tr>
<td></td>
<td>&lt;2% vomiting</td>
</tr>
<tr>
<td></td>
<td>1% skin rash</td>
</tr>
</tbody>
</table>

No transmission recorded
No vaccinemia or reversion events reported
Typhoid Vaccine: Protection

Typhim Vi®
- Nepal field trial (1986-88): 75% protection against typhoid fever
- South Africa field trial (1985-88): 55% protection against typhoid fever
- India field trial (2004-6): 61% protection

Meta-Analysis (2007): 55% cumulative efficacy at 3 years

Vivotif®
- Egypt field trial (1978-81): 96% protection
- Chile field trials (1982-87):
  - 59% protection, two-doses
  - 67% protection, three-doses
- Indonesia field trial (1986-89):
  - 79% protection, three-doses

Meta-Analysis (2007): 51% cumulative efficacy at 3 years

Protection in U.S. travelers using either vaccine (2008-11): 80% vaccine efficacy

1. NEJM 1987; 317: 1101-4
3. NEJM 2009; 361: 335-44
5. JID 1982; 145: 292-5
6. Vaccine 1990; 8: 81-4
Typhoid Vaccine covers these agents of “Enteric Fever”

- Typhoid
- Paratyphoid (S. Paratyphi A, B, and C)
- Non-typhoidal Salmonella
  - S. Enteritidis
  - S. Typhimurium
  - S. Dublin
  - S. Choleraesuis
  - S. Heidelberg
  - S. Newport
  - Others...
Beware of additional risk through ingestion...
Hepatitis A

- Positive-stranded RNA virus
  - Picornaviridae family, Heparnavirus genus
- Primarily human host-restricted pathogen
  - Some non-human primate sp. hosts
- Single serotype
  - 4 genotypes, but not important for biology
- Transmission: fecal-oral
HAV: Epidemiology

- Associated with poor sanitation and hygiene
- Decline in U.S. with vaccination
- World-wide distribution
- Highest risk: Sub-Saharan Africa, South Asia
- Intermediate risk: Central & South America
- No seasonality
HAV: Clinical Presentation

• **Incubation period:** average 28 days (range 15-50 days)
• **Age <6 years:** majority asymptomatic, 10% jaundice
• **Older than 6 yrs:** >70% jaundice
• **Abrupt Clinical Illness:**
  – Fever, fatigue, loss of appetite, nausea, vomiting, joint pain, abdominal pain, dark urine, clay-color stools, jaundice
• **Duration:** usually 2 months, 10-15% prolonged/relapsing up to 6 months
• **Case-Fatality:** Overall 0.3% (1.8% for age >50 yrs)
HAV: Risk to Traveler

- **CDC, estimated HAV cases (endemic and travelers):**
  
  2011 - 2700 cases  
  2012 - 3000 cases  
  2013 - 3500 cases  

- **Swedish travelers (1997-2005),**
  
  636 travel-related cases  
  East Africa, 14.1 cases /100,000 person months  
  Middle East, 5.8 cases /100,000 person months  
  Indian subcontinent, 5.6 cases/ 100,000 person months  
  Risk highest among those Visiting Friends & Relatives (VFR)

- **Dutch travelers (2003-2011),**
  
  2094 total cases, 931 (44%) from travel  
  Attack rate during 2003-2005, 7.5 per 100,000 travelers  
  Attack rate during 2009-2011, 3.5 per 100,000 travelers

1. CDC Statistics & Surveillance  
Globally Available HAV Vaccines

Inactivated vaccines:
• Monovalent
  – Avaxim (SP), Havrix (GSK), Vaqta (CSL/Merck)
• Combination: HAV+ViCPS
  – Hepatyrix (GSK), Vivaxim (SP)
• Combination: HAV+HBV
  – Twinrix (GSK)

Live Attenuated vaccine:
– H2 & L-A-1 strains (China)
**HAV Vaccines available in U.S.**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Status</th>
<th>Adults:</th>
<th>Children (1-18 y):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Havrix® (GSK)</td>
<td>inactivated, Approved</td>
<td>1 mL IM at 0 &amp; 6-12 m</td>
<td>0.5 mL IM at 0 &amp; 6-12 m</td>
</tr>
<tr>
<td></td>
<td>since 1995</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaqta® (Merck)</td>
<td>inactivated, Approved</td>
<td>1 mL IM at 0 &amp; 6-18 m</td>
<td>0.5 mL IM at 0 &amp; 6-18 m</td>
</tr>
<tr>
<td></td>
<td>since 1996</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Twinrix® (GSK)</td>
<td>inactivated, Approved</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>since 2001</td>
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</tbody>
</table>

**Dosing Options**

- **Standard Dosing:** 0, 1, 6 m
- **Accelerated:** Dosing: 0, 7, 21-30d; 12 m

*Since 2006, routine vaccination of children age ≥1 year*

* MMWR 2006; 55: RR-7
HAV Vaccines:
Contraindications/Precautions

• Prior anaphylaxis with vaccination
• Hypersensitivity to a vaccine component: viral antigen, aluminum hydroxide adjuvant, neomycin
• Latex, vial stopper and syringe plunger
• No special precautions for the immunocompromised
HAV Vaccines: Safety & Adverse Effects

Adults:
• Injection site soreness (56%)
• Headache (14%)
• Malaise (7%)

Children:
• Injection site soreness (15%)
• Feeding problems (8%)
• Headache (4%)
• Injection site induration (4%)
HAV Vaccines: Protection

• Protective antibodies:¹
  – First dose, ≥94% adults and ≥97% children
  – Second dose, 100% adults and children

• Havrix® Thailand field trial:²
  – Efficacy 94% (CI 79-99%) after 2 doses, 1 m apart

• Vaqta® New York trial:³
  – Efficacy 100% (CI 87-100%) after 1 dose

1. MMWR 2006; 55: RR-7
2. JAMA 1994; 271: 1328-34
3. NEJM 1992; 327: 453-7
HAV Vaccines: “Off Schedule”

Delayed second dose:

- Adults, Two-dose, 18 months apart: 100% protective antibody after second dose
- Children, Two-dose, 4-8 years apart: 100% protective antibody after second dose

2. J Travel Med 2004; 11:120-1
Which of the following is not a Flavivirus?

A. Chikungunya
B. Dengue
C. Tick-borne Encephalitis
D. West Nile
E. Yellow Fever
F. Zika
Japanese Encephalitis

• Caused by a Flavivirus
• Transmitted by mosquito bite (Culex sp.)
• JE is estimated to cause ~68,000 clinical cases each year\(^1\)
• Most important cause of viral encephalitis in Asia and Western Pacific
• Substantial underreporting\(^2\), due to rural nature

JE: Epidemiology

Geography

Asia & Western Pacific

- Rural agricultural areas (e.g., rice farming)
- 20-30% case-fatality ratio

Seasonality

- Temperate: peaks summer and fall
- Tropics: all year with peaks during rainy (monsoon) season
JE: Clinical Presentation

- <1% of JE infection develop clinical illness
- ~1 in 200 infections result in severe disease

- Incubation 5-15 days
- **Initial stage**: Fever, Headache, Vomiting
- Progression to **Severe disease** (days): encephalitis, mental status changes, neurological symptoms, movement disorders, seizures (children especially), or death

- Among those with encephalitis, 20-30% fatality
- Among those recovering from acute illness, 30-50% survivors have residual neurologic, cognitive, or psychiatric symptoms
JE: Risk and Prevention

Risk
• Endemic incidence, 1.8 cases per 100,000 residents
• Estimated incidence among unvaccinated travelers to Asia <1 case per 1 million travelers
• 7 documented US traveler cases (1973-2011)

Prevention
• Clothing barrier
• Insect repellent (DEET)
• Vaccination
  o There is no specific treatment, limited to supportive care

Bull WHO 2011; 89:766-74
CDC Yellow Book 2014
Globally Available JE Vaccines

Inactivated vaccine:
• Vero cell, alum-adjuvanted (Intercell) – N. America, Australia, Europe
• Vero cell (Beijing-1 strain) - Japan

Live Attenuated vaccine (Chengdu Inst. Biol Products):
• SA_{14}-14-2 strain - China, India, Nepal, Korea, Sri Lanka, Thailand

Live Chimeric vaccine (SP):
• YF 17D backbone - Australia & Thailand
JE Vaccine in US

Ixaro® (Intercell)

• Inactivated, whole-virus
• Vero cell culture-derived
• SA_{14}-14-2 attenuated strain

• Approved (2009):
  Age ≥3 years
  Two parenteral doses, 0.5 mL, spaced 28 days
  Age 2 months to <3 years
  Two parenteral doses, 0.25 mL, spaced 28 days
  Booster dose after 1 year

*JE-Vax (inactivated mouse brain-derived vaccine) is no longer produced, expired May 2011*
JE Vaccine

**Contraindications**

- Severe Allergic Reactions to vaccine components: protamine sulfate
- Prior anaphylaxis with vaccination

**Precautions**

- Hypersensitivity to vaccine components
- Immunocompromised may have diminished protection
JE Vaccine: Adverse Effects

Adults:
• Injection site pain (25%)
• Headache (20%)
• Myalgia (10%)

Better tolerated than JE-Vax

Children (1-3 years):
• Fever (20%)

Infants (1-11 months):
• Injection site redness (15%)
• Fever (20%)
• Irritability (15%)
• Diarrhea (10%)
JE Vaccine: Protection

• Thailand field trial of JE-MB$^1$
  – Efficacy 91%

• Taiwan, trial of JE-MB, 30-years experience
  – Efficacy 97%$^2$
  – Incidence 1967 (pre-vaccination), 2.05 cases per 100,000$^3$
  – Incidence 2003, 0.11 cases per 100,000$^4$

• Neutralizing antibody (PRNT$_{50}$) of $\geq 1:10$ is a reasonable surrogate of protection$^5$

1. NEJM 1988; 319: 608-14
2. Vaccine 2006; 24: 2669-73
3. AJTMH 1999; 61: 78-84
5. FDA, 16 May 2013 and Vaccine 2005; 23: 5205-11
“Off Label”

JE Vaccine: Accelerated Schedule

• Vaccination should be completed at least 1 week prior to potential exposure

• JE Accelerated Schedule: phase 3 study of Ixiaro and rabies\(^1\)
  
  – Day 1 (JE/Rab), Day 4 (Rab), Day 8 (JE/Rab)
  
  – Non-inferior, rapid short-term protection for up to 2 months
    
    99% seroprotection in accelerated schedule
    
    100% seroprotection in routine schedule
JE Vaccine: Booster Doses

JE Booster Doses

– Current recommendation: single booster at 12-24 months
– 76 months (6.3 years) after booster dose, 96% (64 of 67) maintained PRNT Ab
Beware of sewage contamination of your water...
Cholera

- *Vibrio cholerae*
- Serogroups O1 (and O139)
  - Serotype Inaba or Ogawa
  - Biotype El Tor or Classical
- Rapidly dehydrating diarrhea
- 1.4-4.3 million cases and 28,000-142,000 deaths annually\(^1\)
- Transmission: fecal-oral

WHO, July 2015
Cholera Epidemiology

• Pandemics
  – Currently 7th (since 1961)

• Epidemics
  – Example: post-earthquake Haiti in 2010

• Endemic
  – Examples: India, Nigeria, DRC, Tanzania, Kenya, Ethiopia, Bangladesh

Ali, Bull WHO 2012; 90:209
Globally Available Cholera Vaccines

- Oral inactivated monovalent
  Dukoral (Crucell)
- Oral inactivated bivalent
  Shanchol (Shantha)
  Euvichol (EuBiologics)
- Oral, live monovalent
  Vaxchora (PaxVax)
Cholera Vaccine in U.S.

Vaxchora \((\text{PaxVax})\)

- Live, attenuated O1 classical Inaba strain (CVD 103-HgR)
- Single-dose
- Approved age 18-64 years
- Licensed June 10, 2016
- ACIP Recommendation (June 22, 2016)\(^1\)

“Cholera vaccine (CVD 103-HgR, Vaxchora™) is recommended for adult (18-64 years old) travelers to an area of active cholera transmission”
Cholera Vaccine: Protection

**Primary Efficacy (Mod-Severe Diarrhea)**

<table>
<thead>
<tr>
<th>Vaccine Efficacy</th>
<th>10-Day Vaccine Efficacy</th>
<th>3-Month Vaccine Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>90.3%</td>
<td>62.7 - 100</td>
<td>49.9 - 100</td>
</tr>
<tr>
<td>95% CI</td>
<td>95% CI</td>
<td></td>
</tr>
</tbody>
</table>

**10 Day Challenge**

- Placebo: 40% Mild Diarrhea, 30% Moderate Diarrhea, 30% Severe Diarrhea
- Vaccine: 20% Mild Diarrhea, 40% Moderate Diarrhea, 40% Severe Diarrhea

**3 Month Challenge**

- Placebo: 40% Mild Diarrhea, 40% Moderate Diarrhea, 20% Severe Diarrhea
- Vaccine: 20% Mild Diarrhea, 60% Moderate Diarrhea, 20% Severe Diarrhea

**Average Volume of Diarrhea**

- Days 1 to 10

**Average No. of Diarrheal Stools**

- Days 1 to 10

Chen, CID 2016
Cholera: High Risk Populations

Risk of Infection:
• Travelers visiting friends and relatives
• Long-term travelers (e.g., expatriates)
• Travelers who do no follow safe food and water precautions and personal hygiene (e.g., adventure backpacking)
• Healthcare, aid, relief, and response workers with direct contact with cholera patients

Risk of Poor Outcome with cholera:
• Travelers without ready access to rehydration therapy and medical care
• Blood type O
• Pregnant
• Immunocompromised
• Chronic cardiovascular or renal disease
Meningococcal Meningitis

- *Neisseria meningitidis*
- 6 major serogroups: A, B, C, W-135, X, and Y
- Incidence: (cases/100,000 population)
  - Americas, Europe, Australia  0.3-3/100K
  - Sub-Saharan Africa  100-1000/100K

“Meningitis Belt”

Dry season (Dec – June)

5-10% of population are carriers

Serogroup A,C,X,W

CDC Yellow Book 2016
Meningococcal Vaccines in the U.S.

Monovalent, group B (Bexsero, Trumenba)
Combination
   – C, Y, Hib-TT (MenHibrix)
Quadrivalent Polysaccharide (Menomune)
Quadrivalent Conjugate (Menactra, Menveo)
Meningococcal Vaccines for Travel

To Saudi Arabia (within 3 yrs of travel)

• Age >2 yr 1 dose, Quadrivalent vaccine
• Age 3 m – 2 yr 2 doses, Men A containing vaccine

To endemic & hyperendemic area, during dry season

• 2 m – 55 yr quadrivalent (MCV)
• >55 yr quadrivalent (MPS)
ACIP References

• Yellow Fever - MMWR 2015; 64: 647-650
• Typhoid - MMWR 2015; 64: 305-308
• Hepatitis A - MMWR 2007; 56: 1080-1084
• Cholera – MMWR 2017; 66: 482-485
• Meningococcal - MMWR 2013; 62: 1-27
Safe Travel!