VACCINE UPDATE

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“It is better not to fall ill ... than to be cured.”

Giovanni Maria Lancisio  
(1654-1720)
TRACKING PROGRESS AGAINST VACCINE ASSOCIATED DISEASES

Cases in U.S.

<table>
<thead>
<tr>
<th>Disease</th>
<th>1950</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>5796</td>
<td>0</td>
</tr>
<tr>
<td>Tetanus</td>
<td>486</td>
<td>15</td>
</tr>
<tr>
<td>Pertussis</td>
<td>120,718</td>
<td>10,007</td>
</tr>
<tr>
<td>Polio</td>
<td>33,300</td>
<td>0</td>
</tr>
<tr>
<td>Measles</td>
<td>319,124</td>
<td>32</td>
</tr>
</tbody>
</table>

GLOBAL MEASLES DEATHS ↓ FROM 750,000 (2000) TO 200,000 (2007)

Travel Clinic

An opportunity for Sharing vaccine Success stories and Teaching “Vaccine 101” – ?

Variola major (last natural infection acquired Somalia, 1977)
General Rec's for Vaccination and Immunoprophylaxis

Spacing of Immunobiologics
Simultaneous administration
Missed doses and boosters
Antibody containing blood products

Vaccination of Persons with Acute Illness

Altered Immunocompetence

Vaccination for Last-Minute Travelers

Allergy to Vaccine Components

Reporting Adverse Events following immunization

Injection Route and Injection Site
International Certificate of Vaccination or Prophylaxis (ICVP)

- Under the revised IHR (2005), effective Dec 15, 2007, all countries must issue a new ICVP. Persons who receive YF after this date must provide proof of vaccination on an ICVP.
- ICVP must be signed by licensed physician or HCW designated by MD supervising administration of the vaccine
- Exemption from Vaccination and Waiver Letters

October 14, 2009
No Reports yet today.

October 13, 2009

PRO/AH/EDR> Influenza pandemic (H1N1) 2009 (69); case management

PRO/EDR> Meningitis, meningococcal; New Zealand; (North Island)

PRO/EDR> Measles - South Africa (05):
Immunizations for Travel -- I

Routine Childhood and Adult Vaccines
- Tetanus-diphtheria or TDaP
- Polio
- Measles-Mumps-Rubella
- Varicella
- Hepatitis B
- Influenza – seasonal and H1N1
- Pneumococcal

Immunizations for Travel -- II

Vaccines for Special Settings or Risks
- Yellow Fever*
- Hepatitis A / Hepatitis B
- Typhoid
- Meningococcal*
- Rabies
- Japanese encephalitis

Immunizations for Travel -- III

Vaccines rarely if ever used
- Smallpox
- Cholera
- BCG
- Tick-borne encephalitis
- Anthrax
Tetanus–San Lazaro Hospital, Manila, 1987

Pharyngeal membrane of diphtheria

[Image of a patient with tetanus]
FIGURE 2. Number of reported pertussis cases, by year — United States, 1923–2006


FIGURE 3. Frequencies of selected solicited adverse events in adults aged 18–64 years within 16 days after a single dose of ADACEL® tetanus, reduced diphtheria, and acellular pertussis (Tdap) vaccine or tetanus and reduced diphtheria toxoids (Td) vaccine — United States, 2001–2002

Vaccine-associated Paralytic Polio (VAPP)

• 1991- Last wild virus polio case in Americas
• 1999- Change to exclusive IPV use in USA
• 1995- Imported VAPP in unvaccinated US adult who traveled abroad, likely from contact with infant recently vaccinated with OPV
• 1995- Unvaccinated IC infant and 4 children in two other families in same rural community infected with vaccine-derived PV, presumably originating from OPV-using country
**Independent Outbreaks of VAPP**

<table>
<thead>
<tr>
<th>Country</th>
<th>Year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belarus</td>
<td>1965–66</td>
</tr>
<tr>
<td>Canada</td>
<td>1966–68</td>
</tr>
<tr>
<td>Egypt</td>
<td>1983–1993</td>
</tr>
<tr>
<td>Hispaniola</td>
<td>2000–2001</td>
</tr>
<tr>
<td>Philippines</td>
<td>2001</td>
</tr>
<tr>
<td>Madagascar</td>
<td>2001–2002</td>
</tr>
<tr>
<td>Haiti</td>
<td>2002</td>
</tr>
<tr>
<td>China</td>
<td>2006</td>
</tr>
<tr>
<td>Cambodia</td>
<td>2005–2006</td>
</tr>
<tr>
<td>Myanmar</td>
<td>2006–2007</td>
</tr>
<tr>
<td>Syria, Kuwait and Egypt</td>
<td></td>
</tr>
</tbody>
</table>

Since 2005, WHO has been tracking vaccine-caused polio in northern Nigeria caused by a mutation in live oral polio vaccines.
Gamma globulin—instant, short-lived protection against measles, varicella

Food-borne hazards: always a risk

Risk of Hepatitis A: sidewalk crab stand—Taiwan, 1983

**Hepatitis A Vaccine**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dose</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Havrix (GSK)</td>
<td>1 ml (1440 U)</td>
<td>0, 6-12 mo</td>
</tr>
<tr>
<td>Vaqta (Merck)</td>
<td>1 ml (50 U)</td>
<td>0, 6-12 mo</td>
</tr>
<tr>
<td>Twinrix (GSK)</td>
<td>1 ml (720, 20)</td>
<td>0, 1, 6 mo</td>
</tr>
</tbody>
</table>

(Accelerated (4-dose) schedule for Twinrix: 0, 7, 21 days and 12 mo)
Acute hepatitis B -- Bangkok, 1999


Typhoid Vaccine Efficacy

<table>
<thead>
<tr>
<th>Type</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td>42-93%</td>
</tr>
<tr>
<td>Oral Ty21a (US volunteers)</td>
<td>87%</td>
</tr>
<tr>
<td>Oral Ty21a (Egypt)</td>
<td>90%</td>
</tr>
<tr>
<td>Oral Ty21a (Chile)</td>
<td>67%</td>
</tr>
<tr>
<td>Vi capsular polysaccharide</td>
<td>70%</td>
</tr>
</tbody>
</table>

Hemorrhagic skin infarcts of meningococcemia
Kellie Lim, MD (UCLA class of 2007)

Japanese encephalitis – Kaohsiung Med Center, Taiwan, 1983

Yellow Fever in Africa and the Americas
NOTE: NOT ALL RABID ANIMALS LOOK LIKE THIS!

Recovered cholera pt with IV bottles required for re-hydration

FOCUS ON VACCINES

Yellow Fever
Japanese encephalitis
Rabies
Typhoid
Influenza
Yellow Fever: Second look at virus and vaccine

Yellow Fever Disease – I

• YF virus transmitted predominantly by Aedes and Haemogogus mosquitoes in jungle, savannah and urban cycles (in urban settings can be spread human-mosquito-human)

• Endemic in equatorial Africa and South America

• Causes a range of disease from a mild febrile illness to jaundice and hemorrhage

• Estimated 200,000 cases and 30,000 deaths/year

Yellow Fever Disease – II

Pan-organ viral disease with viremia 10^-9 pfu → fever, hepatic, renal, myocardial injury, hemorrhage, shock, 50% mortality.

Rough estimate of risks of illness and death for an unvaccinated traveler traveling for 2 weeks to endemic area

–West Africa: 50 and 10 per 100,000 pop
–South America: 5 and 1 per 100,000 pop
**Yellow Fever Disease – III**

- Asymptomatic / inapparent infection in most
- Incubation 3-6 days
- Initial influenza like onset
- After brief remission, ~ 15% progress
- Overall CFR for cases with jaundice is 20-50%
- Dx by virus-specific IgM / IgG antibodies

1970-2002: 9 cases reported in unvaccinated US/European travelers; 5 traveled to West Africa, 4 traveled to South America; 8 of 9 died

**Yellow Fever Vaccine**

- No antiviral rx; original 17D vaccine developed 1937 following 176 passages of wild-type virus in mouse and chicken tissue
- > 500 million doses given since 1937
- 6 makers produce 30-60 million doses/yr in embryonated chicken eggs
- One dose of vaccine contains 10^4—10^6 pfu of virus

**Host Immune Response following YF vaccination**

- Low viremia (<200 pfu/ml) in approx half of vaccinees
- 17-D mediated immunity in 95% at 10 days
- IgM antibodies 3-7 d post-vaccination; neutralizing antibodies 7 d post-vaccination, persist 45 years
- 17 D strain potent inducer of CD4+ and CD8+ cytotoxic cells
Serious Yellow Fever Vaccine Adverse Events

**Anaphylaxis**
- Egg, chicken proteins, and gelatin
- Rate of 1.8 per 100,000 doses

**Neurotropic disease**
- Two types: direct viral invasion or autoimmune-mediated
- Rate of 0.8 per 100,000 doses

**Viscerotropic disease**
- Vaccine virus causes a disease similar to natural virus
- Rate of 0.4 per 100,000 doses
- Case fatality ratio of 50%

**YF vaccine-assoc. neurotropic disease**

*YEL-AND*
- Primary vaccinees - 2-30 d post-vaccination
- Focal neurologic dysfunction (aphasia, paresis)  
- Mental status change  
- New-onset seizure or recurrence
- CSF pleocytosis (>5 WBC) or ↑ protein
- Recovery in 95%

Overall 0.8 /100,000; 60-69 years 1.6/100,000; >70 years 2.3/100,000
**YF vaccine-assoc. visceral disease (YEL-AVD)**

Primary vaccinees - 2-5 d post vaccination
- Fever, myalgia, arthralgia
- ↑ LFTs, bilirubin, possible liver failure
- Thrombocytopenia, lymphocytopenia
- Rhabdomyolysis - Hypotension
- Renal failure - Respiratory failure
- Recovery in 40%

Overall 0.4 /100,000; 60-69 years 1.0/100,000; > 70 years

**Precautions and Contraindications for Administration of YF Vaccine**

- AGE (<6 MONTHS, > 60 YEARS)
- THYMUS DISEASE
- PREGNANCY
- IMMUNOSUPPRESSION
- HIV-RELATED IMMUNOSUPPRESSION
- HYPERSENSITIVITY (EGG)

**Case Study: “Fatal multi-organ failure due to YF vaccine associated viscerotropic disease “**

(Belsher et al, Vaccine 25 (2007): 8480-85)

Previously healthy 22 yo woman traveling to Bolivia (Td, Hep A, typhoid → (8d later) YF
2 d post-YF: local inflammation at inoculation site
5 d post-YF: T 103.5, axillary LAD
7 d post-YF: pleural fluid, ↓ BP, anuric RF
11 d post-YF: death

Estimated viral titer 61,000 PFU (day 5), 106,500 PFU (day 6) vs 100 PFU in most healthy vaccinees
Japanese encephalitis: Second Look at Virus and Vaccine

JE DISEASE – FACTS and TRENDS

30,000-50,000 cases/yr (underestimate)
Case-infection ratio ~ 1 : 250
30% of symptomatic cases are fatal
50% of survivors have neurologic impairment
JE risk related to:
TIME (season, time outdoors -crepuscular vector)
PLACE (geographical range poorly defined, dynamic)
PERSON (host factors influence risk of severe case)

JE Vaccine

Inactivated Vero cell culture-derived vaccine (IXIARO) approved for > 18 year old travelers on March 30, 2009—2 doses IM.

Vaccine based on attenuated SA14 virus isolated from Culex pipiens mosquito in China; SA14 previously used in highly effective vaccine programs in China and South Asia.

IXIARO formulated without thimerosal, gelatin or other stabilizers.

Angioedema: US marines on Okinawa 13/14,249; Ixiaro 0/4210
Challenges in Recommending JE Vaccine for Travelers

- Balancing low risk of disease and small chance of AE following immunization
- ACIP rec: ≥ 1 month in endemic area OR shorter-term travel with higher risk
- Evaluation of individual travelers: consider itinerary, activities, and best information re current level of JE activity in destination

ADVISE JE VACCINATION

- All expats - Repeat travelers
- Prolonged duration of stay
- Travel itinerary including rural areas
- Travelers wishing maximum protection

CONSIDER JE VACCINATION

- Greater outdoor exposure
- Individuals ≥ 50 yrs; Children < 10 yrs
- Chronic illness, including solid organ transplant, cochlear implants or other CNS devices, HTN, DM, CRF, anti-TNF rx, pregnancy?
- (balancing unknown risks associated with vaccination)

RABIES
To State the Obvious ...

- Traveler knowledge of rabies is low—many travelers unaware of risk in destination
- Many travelers unaware of non-dog vectors (eg cats, foxes, monkeys, bats)
- Only 50% aware of pre-exposure vaccination
- Immediate washing with soap and water
- Post-exposure regimen


- 320 cases, 1998 to 2005
- Mainly tourists from developed countries (median travel 23 days)
- Pre-travel encounter in 45% of the cases
- A greater proportion of patients with animal-related injuries were FEMALE (54.7% vs 47.4% other travel-related dx) and YOUNG (<15 yrs 6.2% vs 2.6%).
- 75 % of cases occurred in countries endemic for rabies
- Animals involved: dogs (51%), monkeys (21%), cats (8%), bats (.7%)
- Males were more likely to be injured by dogs
- Only 66% of all patients reported with animal-related injury received rabies post-exposure prophylaxis.

Typhoid Fever: Have we Forgotten ??
**TYPHOID FEVER: A Look at Recent Trends**

*JAMA “Typhoid Fever in the US,” 1999-2006*

- 1902 patients: median age 22 yrs (1-90), 73% hospitalized, 79% traveled overseas within 30 days of illness
- 13% multi-drug resistant (AMP, CP, TMP-SX)
- 38% decreased susceptibility to Ciprofloxacin, increasing from 19% in 1999 to 54% in 2006
- Patients with resistant infections more likely to report travel to Indian subcontinent

**Typhoid Fever Cases Reports by State, United States 1999-2006**

<table>
<thead>
<tr>
<th>State</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>550 (29%)</td>
</tr>
<tr>
<td>New York</td>
<td>279 (15%)</td>
</tr>
<tr>
<td>New Jersey</td>
<td>133 (7%)</td>
</tr>
<tr>
<td>Texas</td>
<td>96 (5)</td>
</tr>
<tr>
<td>Virginia</td>
<td>78 (4)</td>
</tr>
</tbody>
</table>

**Countries Visited by Typhoid Fever Patients in 30 days before illness**

<table>
<thead>
<tr>
<th>Countries</th>
<th>No. of Travelers</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>606 (47%)</td>
</tr>
<tr>
<td>Pakistan</td>
<td>126 (10%)</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>124 (10%)</td>
</tr>
<tr>
<td>Mexico</td>
<td>90 (7%)</td>
</tr>
<tr>
<td>Philippines</td>
<td>57 (4%)</td>
</tr>
</tbody>
</table>
Renewed attention to old and new respiratory viruses

Can you name the emerging infectious diseases linked to these animal hosts?

Influenza and International Travel

- Risk of exposure depends on time of year and destination
- In the tropics, seasonal influenza can occur throughout the year
- In temperate Southern Hemisphere, most cases occur from April through September
- Risk associated with groups
- Risk associated with avian exposure
- Heightened fear of H1N1 – prophylactic oseltamivir--NOT
Final word on respiratory viruses: WASH HANDS