Travel Medicine

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Associate Professor of Clinical Medicine,
Microbiology & Immunology

04.9.17
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• Pre-travel consultation
  o Basic elements/topics of discussion
  o Destination based recommendations
    » Vaccines
    » Medications
      ▪ Antimalarials
      ▪ Diarrhea
      ▪ Altitude related illnesses

• Travel related illnesses
  o Common insect borne diseases
Background Information

- Medical history
- Immunocompromised state
  - Medications, HIV, cancer
- Pregnancy/Breastfeeding
- Psychiatric condition/Seizure disorder
- Recent:
  - Surgery
  - Cardiopulmonary/Cerebrovascular events
- Medications
- Allergies
Detailed itinerary: stopovers/side trips

BEST STOPOVERS BETWEEN:
Find the perfect stopover for your flight at: QuestOrganizer.com

USA and Europe

Within Europe

Europe and Asia

Australia and Europe

Brought to you by QuestOrganizer
What is the purpose of the trip?
Will there be any additional activities?
References

Travelers’ Health
http://wwwnc.cdc.gov/travel

• Outbreaks
• Travel issues “in the news”
• “Destinations”

• Malaria map application
  – http://cdc-malaria.ncsa.uiuc.edu/
Keep it simple

Follow the rules

***CDC***
If you can get it here
You can get it there -
and it might be easier
Routine vaccinations
Not just for kids

### Recommended Adult Immunization Schedule—United States - 2016

**Note:** These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

#### Figure 1. Recommended immunization schedule for adults aged 19 years or older, by vaccine and age group

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>AGE GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Influenza</strong></td>
<td>19-21 years</td>
</tr>
<tr>
<td></td>
<td>22-26 years</td>
</tr>
<tr>
<td></td>
<td>27-49 years</td>
</tr>
<tr>
<td></td>
<td>50-59 years</td>
</tr>
<tr>
<td></td>
<td>60-64 years</td>
</tr>
<tr>
<td></td>
<td>≥ 65 years</td>
</tr>
<tr>
<td></td>
<td>1 dose annually</td>
</tr>
<tr>
<td><strong>Tetanus, diphtheria, pertussis (Td/Tdap)</strong></td>
<td>Substitute Tdap for Td</td>
</tr>
<tr>
<td></td>
<td>once, then Td booster</td>
</tr>
<tr>
<td></td>
<td>every 10 yrs</td>
</tr>
<tr>
<td><strong>Varicella</strong></td>
<td>2 doses</td>
</tr>
<tr>
<td><strong>Human papillomavirus (HPV) Female</strong></td>
<td>3 doses</td>
</tr>
<tr>
<td><strong>Human papillomavirus (HPV) Male</strong></td>
<td>3 doses</td>
</tr>
<tr>
<td><strong>Zoster</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Measles, mumps, rubella (MMR)</strong></td>
<td>1 or 2 doses depending on indication</td>
</tr>
<tr>
<td><strong>Pneumococcal 13-valent conjugate (PCV13)</strong></td>
<td>1 dose</td>
</tr>
<tr>
<td><strong>Pneumococcal 23-valent polysaccharide (PPSV23)</strong></td>
<td>1 dose depending on indication</td>
</tr>
<tr>
<td><strong>Hepatitis A</strong></td>
<td>2 or 3 doses depending on vaccine</td>
</tr>
<tr>
<td><strong>Hepatitis B</strong></td>
<td>3 doses</td>
</tr>
<tr>
<td><strong>Meningococcal 4-valent conjugate (MenACWY) or polysaccharide (MPSV4)</strong></td>
<td>1 or more doses depending on indication</td>
</tr>
<tr>
<td><strong>Meningococcal B (MenB)</strong></td>
<td>2 or 3 doses depending on vaccine</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae type b (Hib)</strong></td>
<td>1 or 3 doses depending on indication</td>
</tr>
</tbody>
</table>

*Covered by the Vaccine Injury Compensation Program

- Recommended for all persons who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection; zoster vaccine is recommended regardless of past episode of zoster
- Recommended for persons with a risk factor (medical, occupational, lifestyle, or other indication)
- No recommendation

Report all clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available at [www.vaers.hhs.gov](http://www.vaers.hhs.gov) or by telephone, 800-822-7967.

Information on how to file a Vaccine Injury Compensation Program claim is available at [www.hrsa.gov/vaccinecompensation](http://www.hrsa.gov/vaccinecompensation) or by telephone, 800-338-2382. To file a claim for vaccine injury, contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, D.C. 20005; telephone, 202-357-6400.

Additional information about the vaccines in this schedule, extent of available data, and contraindications for vaccination is also available at [www.cdc.gov/vaccines](http://www.cdc.gov/vaccines) or from the CDC INFO Contact Center at 800-CDC-INFO (800-232-4636) in English and Spanish, 8:00 a.m. - 8:00 p.m. Eastern Time, Monday - Friday, excluding holidays.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

The recommendations in this schedule were approved by the Centers for Disease Control and Prevention’s (CDC) Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians (AAFP), the America College of Physicians (ACP), the American College of Obstetricians and Gynecologists (ACOG) and the American College of Nurse-Midwives (ACNM).
Routine vaccinations adults

– Td or Tdap
– Influenza
– Pneumococcal
Travel related vaccines

• Required
  – By country of entry
    • May include stop overs

• Recommended
  – CDC
Required vaccinations

• Yellow fever
  – Areas of South America and Africa

• Meningococcal
  – Saudi Arabia
    • religious pilgrims
Meningococcal Meningitis Vaccine

Required
Umrah or Hajj

Recommended

Meningitis Belt

December-June
It’s not required do I need it?

• Absolutely!!!!
• Getting sick...catching a fatal disease will ruin your vacation.
Meningococcal vaccines
Serogroups A, C, W, Y

• Conjugate vaccines (MenACWY)
  o Menactra® or Menveo®
  o Adults <55 years
  o ≥56 years
    ▪ MenACWY preferred if
      □ Previously vaccinated (MenACWY)
      □ Multiple doses anticipated
    ▪ Not licensed for this age group.

• Polysaccharide vaccine (MSP4)
  o Menomune®
  o >55 years vaccine naïve
Geographic areas of Yellow Fever Risk

CDC January 2017
Yellow fever – Brazil

Disease outbreak news
24 February 2017

From 1 December 2016 to 22 February 2017, a total of 1336 cases of yellow fever infection (292 confirmed, 920 suspected, and 124 discarded), including 215 deaths (101 confirmed, 109 suspected, 5 discarded), have been detected in six states (Bahia, Espírito Santo, Minas Gerais, Rio Grande do Norte, São Paulo, and Tocantins). The estimated case fatality rate is 35% for confirmed cases and 12% for suspected cases. To date, the majority (86%) of the confirmed cases are men and of which, approximately 81% are aged between 21 and 60 years.
RIO DE JANEIRO — The governor of the Minas Gerais State in southeastern Brazil declared a public health emergency on Friday over an outbreak of yellow fever that appears to have killed at least 10 people so far and led to reports of more than 100 suspected cases of the disease.
UN Sends 3.5M Emergency Yellow Fever Vaccines to Brazil


LONDON — The World Health Organization said it and partners have shipped 3.5 million doses of yellow fever vaccine to Brazil to help the country stamp out its worst outbreak in years.

WHO helps maintain an emergency stockpile of yellow fever vaccine of about 6 million doses, intended to help poor countries. In a statement on Thursday, WHO said Brazil would reimburse the cost later; one of the five vaccine producers is Brazilian.

To date, more than 490 cases of yellow fever have been reported. Since January, WHO and partners have shipped more than 18 million vaccines to Brazil, although no accountability mechanism exists to verify how the shots are used.
“scheduling public health nurses around the clock at the airport and at the sea port… travellers who will be coming from countries where yellow fever is endemic…should be able to produce their yellow fever vaccination certificate”. 
A single dose of yellow fever is adequate for most travelers

- Exceptions:
  - Women who were pregnant (regardless of trimester) when they received their initial dose
  - Hematopoietic stem cell transplant after vaccination if sufficiently immunocompetent to be safely vaccinated
  - HIV infected when vaccinated - booster every 10 years
  - Vaccinated >10 years ago and will be in high risk settings due to season, location, activities, and duration of their travel [Category B].
    - Prolonged period in endemic areas
    - Highly endemic areas (e.g. rural West Africa peak season
    - ongoing outbreak.

- Laboratory workers check titers every 10 years or boost
Yellow fever vaccine
single dose for life

• World Health Organization adopted single dose valid life (beginning 2016)

• Uncertain when and if all countries with yellow fever vaccination requirements will adopt this change
  – Need to check individual country requirements
Yellow fever vaccine in adults

Contraindications
• Allergy to a vaccine component
• Symptomatic HIV infection or CD4 <200/mm3
• Neoplasm, transplant, immunosuppression/immunomodulatory rx

Precautions
• Age ≥60 years
• Asymptomatic HIV infection and CD4 200 to 499/mm3
• Pregnancy
• Breastfeeding
Yellow fever vaccine reactions

Generally mild

• Headaches,
• Myalgias,
• Low-grade fever

Rare serious events

• Anaphylaxis,
• Yellow fever vaccine-associated viscerotropic disease (YEL-AVD)
• Yellow fever vaccine-associated neurologic disease (YEL-AND)
# THIS WEEK

**Polio this week as of 5 April 2017**

## Case breakdown by country

<table>
<thead>
<tr>
<th>Countries</th>
<th>Year-to-date 2017</th>
<th></th>
<th>Year-to-date 2016</th>
<th></th>
<th>Total in 2016</th>
<th></th>
<th>Onset of paralysis of most recent case</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WPV</td>
<td>cVDPV</td>
<td>WPV</td>
<td>cVDPV</td>
<td>WPV</td>
<td>cVDPV</td>
<td>WPV</td>
<td>cVDPV</td>
</tr>
<tr>
<td>Afghanistan</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>13</td>
<td>0</td>
<td>21-Feb-2017</td>
<td>NA</td>
</tr>
<tr>
<td>Lao People’s Democratic Republic</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>NA</td>
<td>11-Jan-2016</td>
</tr>
<tr>
<td>Nigeria</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>21-Aug-2016</td>
<td>28-Oct-2016</td>
</tr>
<tr>
<td>Pakistan</td>
<td>2</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>20</td>
<td>1</td>
<td>13-Feb-2017</td>
<td>17-Dec-2016</td>
</tr>
</tbody>
</table>

NA: onset of paralysis in most recent case is prior to 2015. Figures exclude non-AFP sources. Lao PDR cVDPV1, all others cVDPV2. cVDPV definition: see document “Reporting and classification of vaccine-derived polioviruses” at [pdf]
2017 Polio Vaccine Recommendations

- Has completed a routine series of polio vaccine
  - adult IPV booster dose

- Unvaccinated, incompletely vaccinated, or unknown vaccination status
  - 3 doses of IPV

- >4 week stay and last dose >12 months before exit
  - additional dose of IPV or OPV in country.
    - 4 weeks – 12 months before leaving

★★ Proof of vaccination may be required
Geographical distribution of typhoid fever

https://www.cdc.gov/globalhealth/immunization/othervpds/typhoid.html
Typhoid Vaccines

• Vaccines
  – Oral: Live attenuated
  – Injectable: Vi polysaccharide antigen
  – 60-70% efficacy against *S. typhi*; not *S. paratyphi*

• Schedules
  – Oral: 4 capsules on alternate days; booster at 5 years
  – Vi antigen: single dose; booster at 2 years
• One of the most common vaccine-preventable travel infections
• Risk related to living conditions, length of stay, area visited
  – Risk is highest: rural areas, poor sanitation (eat/drink)
  – Occur in developing countries with “standard” tourist itineraries, accommodations, and eating behaviors.
Hepatitis A vaccines

• Monovalent
  – Havrix (GlaxoSmithKline) or Vaqta (Merck & Co.)
  – Schedule; 0, 1, 6 months
  – Effective any time before departure most <40 years

• IgG (0.02 mL/kg)
  – Unable to take vaccine
  – With vaccine for optimal protection if departure <2 weeks
    • adults aged >40 years, immunocompromised, chronic liver disease or other chronic medical conditions

• Twinrix (A/B combination)
  – 0, 1, 6 months
    • 2 shots for full hep. A protection
  – Accelerated schedule
    • 0, 7, 21–30 days + 12 months
Prevalence of chronic hepatitis B virus infection among adults

CDC 2016
Risk Factors
Hepatitis B

Vaccine schedule
– 0, 1, 6 months
– Accelerated; 0, 7, and 21–30 days + 12 months

*Start the series even if it cannot be completed before departure
Meeting Coverage

ACIP: Cholera Vax Recommended for Travelers

by Molly Walker
Staff Writer, MedPage Today

June 22, 2016

ATLANTA -- The CDC's Advisory Committee on Immunization Practices voted unanimously to recommend the newly FDA-approved cholera vaccine for use in adult travelers to areas with active cholera transmission.

This was a grade A recommendation (for all persons in an age or risk-factor based group) of the CVD 103-HgR vaccine (Vaxchora), which the FDA recently approved for preventing cholera serogroup O1 among adults 18-64 years old.
Cholera Vaccine
Vaxhora (lyophilized CVD 103-HgR)

• Adults 18 - 64 years
• Areas of active cholera transmission
  • Endemic/epidemic and includes cholera activity within the past year
• Reduce chance severe diarrhea
  – 90% at 10 days
  – 80% at 3 months
  – Duration of effect not known beyond 3-6 months
• Side Effects – uncommon
  – Tiredness, headache, abd. Pain, N/V, lack of appetite, diarrhea
Geographic distribution of Japanese encephalitis

[Map showing the geographic distribution of Japanese encephalitis risk areas in Asia, including China, Japan, South Korea, and other countries.]
Japanese Encephalitis Vaccine Recommendations

Endemic areas during the transmission season
- >1 month endemic areas.
  - long-term/recurrent travelers, expatriates in urban areas with visits to rural or agricultural areas
- <1 month outside an urban with increased risk
  - substantial time outdoors rural or agricultural areas, especially during the evening or night
  - camping, hiking, trekking, biking, fishing, hunting, or farming
  - without air conditioning, screens, or bed nets.
- Ongoing JE outbreak
- Uncertain: specific destinations, activities, duration of travel

*JE vaccine is not recommended for short-term travel to urban areas or times outside of transmission season.*
Japanese Encephalitis Vaccine (IXIARO)

Vaccine series
- two-dose series spaced 28 days apart
- booster dose if primary series > one year previously with continued risk or potential reexposure.
- last dose should be given at least 1 week before travel.

Allergic reactions
- Previous reaction = contraindication to further doses.
- Protamine sulfate, a compound known to cause allergic reactions in some people.

You may be at risk of Japanese Encephalitis.
A proven method of protection is vaccination.
Before you travel, ask your healthcare professional if IXIARO® is right for you.
RABIES

Zero deaths by 2030

99% human cases result from dog bites

One death every 15 minutes worldwide

4 out of 10 deaths are in children

2030

VACCINATE TO STOP TRANSMISSION

VACCINATE TO SAVE LIVES

100% vaccine preventable

TODAY

no bite no rabies

#rabies

28 September

World Rabies Day

www.who.int/rabies/en

World Health Organization
Table 3-16. Preexposure immunization for rabies\(^1\)

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>DOSE (mL)</th>
<th>NUMBER OF DOSES</th>
<th>SCHEDULE (DAYS)</th>
<th>ROUTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDCV, Imovax (Sanofi)</td>
<td>1.0</td>
<td>3</td>
<td>0, 7, and 21 or 28</td>
<td>IM</td>
</tr>
<tr>
<td>PCEC, RabAvert (Novartis)</td>
<td>1.0</td>
<td>3</td>
<td>0, 7, and 21 or 28</td>
<td>IM</td>
</tr>
</tbody>
</table>

Abbreviations: HDCV, human diploid cell vaccine; IM, intramuscular; PCEC, purified chick embryo cell.

\(^1\) Patients who are immunosuppressed by disease or medications should postpone preexposure vaccinations and consider avoiding activities for which rabies preexposure prophylaxis is indicated. If this is not possible, immunosuppressed people who are at risk for rabies should have their antibody titers checked after vaccination.
<table>
<thead>
<tr>
<th>Immunization Status</th>
<th>Vaccine/Product</th>
<th>Dose</th>
<th>Number of Doses</th>
<th>Schedule (Days)</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not previously immunized</td>
<td>RIG plus</td>
<td>20 IU/kg body weight</td>
<td>1</td>
<td>0</td>
<td>Infiltrated at bite site (if possible); remainder IM</td>
</tr>
<tr>
<td></td>
<td>HDCV or PCEC</td>
<td>1.0 mL</td>
<td>4²</td>
<td>0, 3, 7, 14</td>
<td>IM (28 if immuno-compromised³)</td>
</tr>
<tr>
<td>Previously immunized⁴,⁵</td>
<td>HDCV or PCEC</td>
<td>1.0 mL</td>
<td>2</td>
<td>0, 3</td>
<td>IM</td>
</tr>
</tbody>
</table>

Abbreviations: RIG, rabies immune globulin; IM, intramuscular; HDCV, human diploid cell vaccine; PCEC, purified chick embryo cell.
Ancient Disease

~ 2700 BC Chinese medical writings
  • The *Nei Ching* - The Canon of Medicine
    • several characteristic symptoms malaria described

*The New York Times*

**Malaria Is a Likely Killer in King Tut's Post-Mortem**

By JOHN NOBLE WILFORD
Published: February 16, 2010

(Z. Hawass et al. JAMA. 2010;303(7):638-647)
George Clooney Answers Your Questions About Malaria
By NICHOLAS KRISTOF

“fever, the chills, and exciting adventures in the toilet..weak..really just very bad flu conditions with a little food poisoning thrown in to make you the perfect party guest”
Symptoms of malaria in 24 civilians

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever and chills</td>
<td>24</td>
</tr>
<tr>
<td>“Classical” malaria fever</td>
<td>7</td>
</tr>
<tr>
<td>Headache</td>
<td>23</td>
</tr>
<tr>
<td>Myalgias</td>
<td>11</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>11</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>7</td>
</tr>
<tr>
<td>Weight loss</td>
<td>7</td>
</tr>
<tr>
<td>Lethargy and confusion</td>
<td>6</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>4</td>
</tr>
</tbody>
</table>
Fever + travel = malaria until proven otherwise

“Since untreated malaria can progress to severe forms that can be rapidly (< 24 hours) fatal, malaria should always be considered in patients that have a history of exposure”*

CDC

*past travel or residence in disease endemic area
Malaria
A preventable and treatable mosquito-borne illness that killed an estimated 584,000 people in 2013, mostly African children.

Global risk
WHO Malaria Report 2014

- Estimated 3.2 billion people at risk,
- 1.2 billion at high risk

- Area of malaria transmission
- Area of limited risk

International funding for malaria control
$2.7 billion in 2013
Target: $5.1 billion

198 million cases in 2013

97 countries with ongoing transmission
13 of the countries reported no new cases in 2013

90 percent of all malaria deaths occur in sub-Saharan Africa

In 2013 an estimated 453,000 children under five killed

Source: WHO

AFP
• *P. falciparum*
  – Africa, Guinea, Haiti, S. America, S.E. Asia, Oceana

• *P. vivax* (Duffy binding protein)
  – Central America, India subcontinent, S. America, S.E. Asia

• *P. malariae*
  – most endemic areas

• *P. ovale*
  – rare outside of Africa

• *P. knowlesi*
  – Southeast Asian country or region in Malaysia
  – Long-tailed and rhesus macaques
  – Initial description in 1930’s

Malaria in “safe” destinations
In summer 2015, a number of cases of malaria were reported in travelers returning to the United States from the Dominican Republic (Figure).
Cases of malaria have been reported in parts of three provinces in South Africa where transmission of the disease does not usually occur. As of March 12, 2017, 53 cases have been reported, most of them in the cities of Thabazimbi and Lephalale in Limpopo Province. Two of the cases were reported in Swartruggens, North West Province, and two more cases in the Doornpoort neighborhood north of Pretoria in Gauteng Province.

The South African National Institute for Communicable Diseases is investigating the cases and working to control mosquitos that spread malaria. Health care providers and the public are being informed about the symptoms, as well as treatment of the disease.

CDC now recommends that travelers to the western Waterberg district of Limpopo Province take prescription medicine to help prevent malaria. CDC previously recommended these medicines only for people traveling to Vembe or Mopane cities in Limpopo province. Medicine to help prevent malaria is not recommended for travelers to North West and Gauteng provinces; however, these travelers should continue to take normal precautions to avoid mosquito bites, including covering exposed skin, using insect repellent, and sleeping in accommodations that are not exposed to the outdoors.

53 cases of malaria where transmission does not usually occur:
- Limpopo Province- cities of Thabazimbi and Lephalale
- North West Province- Swartruggens
- Gauteng Province- Doornpoort neighborhood N. of Pretoria

CDC recommends prophylaxis:
- western Waterberg district of Limpopo Province
- Other areas normal mosquito precautions
Malaria prophylaxis

**Chloroquine** (if sensitive)
Weekly, start 1 week prior to travel

**Atovaquone/proguanil** (Malarone)
Daily dosing
Nausea/vomiting, headache

**Doxycycline**
Daily dosing, photosensitivity, Yeast infections

**Mefloquine** (Larium)
Weekly, start **2 weeks** prior to travel
Contraindicated with
seizures
arrythmias
serious psychiatric illness
Mefloquine (Lariam)
Weekly administration
Contraindicated with
  seizures
  arrhythmias
  ➢ serious psychiatric illness

“The neurologic side effects can include dizziness, loss of balance, or ringing in the ears. The psychiatric side effects can include feeling anxious, mistrustful, depressed, or having hallucinations. Neurologic side effects can occur at any time during drug use, and can last for months to years after the drug is stopped or can be permanent.”
P. falciparum drug resistance
**CDC - Malaria map application**

You searched for country named **Thailand**

<table>
<thead>
<tr>
<th>Country Name</th>
<th>Malaria in Country</th>
<th>Drug Resistance</th>
<th>Malaria Type</th>
<th>Prophylaxis for Areas with Malaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand</td>
<td>Rural, forested areas that border Cambodia, Laos, Burma (Myanmar). Rural, forested areas in districts of Phang Nga and Phuket. None in cities of Bangkok, Chang Mai, Chang Rai, Pattaya, Koh Samui, Koh Phangan, Phang Nga, and Phuket.</td>
<td>Chloroquine Methohexital</td>
<td>P. falciparum 50% (up to 75% some areas), P. vivax 50% (up to 60% some areas), P. ovale remainder</td>
<td>Atovaquone/proguanil or doxycycline.</td>
</tr>
</tbody>
</table>
Nobel Prize in Medicine Awarded to 3 Scientists for Parasite-Fighting Therapies

By LAWRENCE K. ALTMAN  OCT. 5, 2015

Anti-parasite drugs sweep Nobel prize in medicine 2015

Chinese pharmacologist Youyou Tu developed key antimalarial drug artemisinin.

Ewen Callaway & David Cyranoski

05 October 2015 | Updated: 05 October 2015  Nature News

Artemisinin

Satoshi Omura

Youyou Tu
• Artemisinin derivatives (artemether, artesunate)
  – Onset of action may be more rapid than with quinine
    • Coma, high parasitemia
  – Suppositories
  – Late recrudescence (3-4 weeks post rx)
    • Treat with additional agents (MFQ, tetracycline, pyr/sufa)
  – Artemisinin-based combination treatment (ACT)

The leaves of *Artemisia annua*,
the sweet wormwood tree, are the source of artemisinin.

Spread of Malaria Feared as Drug Loses Potency

By THOMAS FULLER
Published: January 26, 2009

TASANH, Cambodia — The afflictions of this impoverished nation

Malaria patients in the intensive care ward of the provincial hospital in Battambang, Cambodia.
2018 travelers vaccine

Dr. Stephen Hoffman
Getting the Jump on Mosquitoes

- Insect repellents
  - Conventional
    - DEET
    - Picaridin
  - Biopesticide
    - Oil of Lemon Eucalyptus (OLE or PMD)
    - IR3535

- Screened/air conditioned accommodations

- Clothing/bed nets
  - Permethrin
Dengue
Chikungunya

Makonde "that which bends up"
Swahili "the illness of the bended walker"
-joint pain/arthritis & fever
-headache, myalgias, rash

Dec. 2013 first reported in Americas

http://link.springer.com/article/10.1007%2Fs13337-010-0012-1/fulltext.html#Fig4
Zika Virus Infection

Many people no or mild symptoms

Most common:
- Fever
- Rash
- Headache
- Joint pain
- Conjunctivitis
- Muscle pain

Guillain-Barre syndrome
Congenital Zika Virus Syndrome Major Findings

- severe microcephaly
- thin cerebral cortices with subcortical calcifications;
- macular scarring and focal pigmentary retinal mottling
- congenital contractures
  - clubfoot or arthrogryposis
  - hypertonia restricting body movement soon after birth.
Countries and Territories with Zika Virus

First discovered 1947 in the Zika Forest in Uganda
Travel to Zika virus endemic area and pregnancy advice

• If without symptoms of infection wait at least 8 weeks post travel before attempting pregnancy to minimize risk.

• Men with a pregnant wife should for the duration of the pregnancy:
  o Use condoms every time they have sex or
  o Not have sex

• Men who have confirmed Zika or symptoms of Zika should for at least 6 months after symptoms begin
  o Use condoms or
  o Not have sex
Fresh fruits and vegetables?
What can you drink?
Fecal – Oral

• Brush teeth with bottled water
• Shower
  – Don’t drink the water
• Airplane food
  --Take care - where was the last port?
• “The best” resorts/hotels
  – Not safe- field sanitation is the issue
Diarrhea

- Bacteria most common cause
  - Enterotoxigenic Escherichia coli
  - Campylobacter jejuni,
  - Shigella spp., and
  - Salmonella spp.
  - other E. coli species

- Imodium (Loperamid)

- Empiric treatment
  - Fluoroquinolone (ciprofloxacin or levofloxacin)
    - Single dose - 3 days
    - Tendon rupture
    - SE Asia resistant Campylobacter isolates
  - Azithromycin
  - Rifaximin
    - noninvasive strains of E. coli
    - No fever or blood in the stools
Parasites

The exotics

Giardia = #1

E. histolytica

Cryptosporidium

Cyclospora

http://en.wikipedia.org/wiki/Cyclospora_cayetanensis
Giardia lamblia

Fecal contamination
- Cysts in food or water
- Streams
  - beavers
- Day care centers

Symptoms
- Diarrhea with foul smelling stools
- Flatulence
Giardia lamblia

The trophozoite stage, attached to the mucous epithelium of the small intestine
Cyst and trophozoite forms

LIFE CYCLE of *GIARDIA INTESTINALIS*

Adapted and redrawn from NCDC
50. *G. lamblia* cysts
49. *Giardia lamblia* trophozoite
Entamoeba histolytica
Endoscopic and Pathological Features of Intestinal Amebiasis

Panel A Intestinal amebiasis on colonoscopy. Panel B shows colonic ulcers averaging 1 to 2 mm in diameter on gross pathological examination. Panel C shows a cross-section of a flanked-shaped colonic ulcer (hematoxylin and eosin, x20). Panel D shows an inflammatory response to intestinal invasion by *Entamoeba histolytica* (hematoxylin and eosin, x100). Arrows indicate *E. histolytica* trophozoites.

NEJM 2003;348:1565-73
Extraintestinal Amebiasis

Panel A Posteroanterior (left-hand side) and lateral (right-hand side) chest radiograph in a patient with amebic liver abscess: elevated right hemidiaphragm and evidence of atelectasis. Panel B shows luminal narrowing (arrow) on a barium-enema examination in a patient with ameboma. Panel C shows two abscesses in the right lobe and one abscess in the left lobe in a patient with amebic liver abscess. In Panel D, abdominal computed tomography amebic liver abscesses: one in the right lobe and one in the left lobe.
Viral diarrhea on cruise ships but......

10-20% cases of traveler’s diarrhea

- Rotoviruses
- Noroviruses
Ebola 2014

Ebola cases and deaths by year, and countries affected.

- **1976**: Sudan, Democratic Republic of Congo
  - 602 cases, 431 deaths
  - Source: World Health Organization

- **1995**: Democratic Republic of Congo
  - 315 cases, 254 deaths

- **2000**: Uganda
  - 425 cases, 224 deaths

- **2007**: Uganda, Democratic Republic of Congo
  - 413 cases, 224 deaths

- **2014**: Guinea, Liberia, Nigeria, Senegal and Sierra Leone
  - 6,553 cases, 3,083 deaths as of Sept. 26

The New York Times
### Countries with Former Widespread Transmission and Current, Established Control Measures

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Cases (Suspected, Probable, and Confirmed)</th>
<th>Laboratory-Confirmed Cases</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guinea</td>
<td>3814</td>
<td>3358</td>
<td>2544</td>
</tr>
<tr>
<td>Sierra Leone</td>
<td>14124</td>
<td>8706</td>
<td>3956</td>
</tr>
<tr>
<td>Liberia</td>
<td>10678</td>
<td>3163</td>
<td>4810</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>28616</strong></td>
<td><strong>15227</strong></td>
<td><strong>11310</strong></td>
</tr>
</tbody>
</table>


Ebola Virus Ecology and Transmission

Ebola virus disease is a zoonotic disease. Zoonotic diseases involve animals and humans.

**Animal-to-Animal Transmission**
Evidence suggests that bats are the reservoir hosts for the Ebola virus. Bats carrying the virus can transmit it to other animals, like apes, monkeys, and duikers (antelopes), as well as to humans.

**Spillover Event**
A "spillover event" occurs when an animal (bat, ape, monkey, duiker) or human becomes infected with Ebola virus through contact with the reservoir host. This contact could occur through hunting or preparing the animal’s meat for eating.

**Human-to-Human Transmission**
Once the Ebola virus has infected the first human, transmission of the virus from one human to another can occur through contact with the blood and body fluids of sick people or with the bodies of those who have died of Ebola.

**Survivor**
Ebola survivors face new challenges after recovery. Some survivors report effects such as tiredness and muscle aches, and can face stigma as they re-enter their communities.

[CDC website link]
Guinea: Government Bans Bat Soup to Halt Ebola Outbreak
By DONALD G. McNEIL     MARCH 26, 2014

To help quell its first Ebola outbreak, the West African nation of Guinea has banned bat soup. Bats are believed to be the natural reservoirs of the filovirus that causes Ebola, and fruit bats are a popular food in West Africa, usually cooked in a peppery soup or smoked over a fire. While boiled bat meat is presumably safe, smoked meat could be dangerous, and butchering bats for the table certainly is. The current outbreak in Guinea has killed 63 people, but the appearance of new cases has slowed significantly, the country’s health ministry said. Most outbreaks are thought to start when jungle hunters eat the flesh of apes that died of Ebola, presumably after eating fruit contaminated by bat feces or saliva. But where bats are in the diet — as they are in parts of Africa, Asia and the Pacific — no intermediary host is needed.
2016 Ebola Travel Recommendations

- No travel notices: Guinea, Liberia, and Sierra Leone
  - No longer widespread transmission
    - Small numbers of cases may continue to occur.
  - Virus can remain in certain body fluids of people who have recovered
    - Semen, fluids: eyes, around brain and spine.
    - No risk of Ebola to most travelers,
  - Avoid contact with:
    - Sick people, dead bodies, or blood and body fluids
    - Animals (such as bats or monkeys)
    - Raw or undercooked meat
      » Do not eat or handle bushmeat (wild animals hunted for food).
21 day monitoring
post possible Ebola exposure

– health care workers who cared for patients with Ebola while the patients were infectious.
  • **Direct active monitoring twice daily** reporting of measured temperatures and symptoms
  • direct observation during at least one of those encounters).

– Anyone who entered an Ebola patient care area & Laboratory workers who handled specimens before inactivated
  • **Active monitoring daily** reporting for 21 days after the last potential exposure
African trypanosomiasis
Sleeping sickness
Stage 2 disease - invasion of internal organs

- *T. brucei rhodesiense*
  - Few weeks
- *T. brucei gambiense*
  - Several months to years
Leishmaniasis

promastigote

www.sbri.org/mission/disease/leishmania.asp
Distribution of Leishmaniasis

Visceral

Cutaneous
Leishmaniasis

Cutaneous

Mucocutaneous

Visceral
Beware fresh water
Altitude

- How high are you going?
- How quickly will you reach high altitude?
- How long is the ascent?

- Degree of hypoxic stress depends upon
  - Altitude
  - Rate of ascent
  - Duration of exposure
Box 2-02. Tips for acclimatization

- Ascend gradually, if possible. Avoid going directly from low altitude to more than 9,000 ft (2,750 m) sleeping altitude in 1 day. Once above 9,000 ft (2,750 m), move sleeping altitude no higher than 1,600 ft (500 m) per day, and plan an extra day for acclimatization every 3,300 ft (1,000 m).

- Consider using acetazolamide to speed acclimatization, if abrupt ascent is unavoidable.

- Avoid alcohol for the first 48 hours.

- Participate in only mild exercise for the first 48 hours.

- Having a high-altitude exposure at more than 9,000 ft (2,750 m) for 2 nights or more, within 30 days before the trip, is useful.
<table>
<thead>
<tr>
<th>RISK CATEGORY</th>
<th>DESCRIPTION</th>
<th>PROPHYLAXIS RECOMMENDATIONS</th>
</tr>
</thead>
</table>
| Low           | • People with no prior history of altitude illness and ascending to less than 9,000 ft (2,750 m)  
                • People taking more than 2 days to arrive at 8,200–9,800 ft (2,500–3,000 m), with subsequent increases in sleeping elevation less than 1,600 ft (500 m) per day, and an extra day for acclimatization every 3,300 ft (1,000 m) | Acetazolamide prophylaxis generally not indicated. |
| Moderate      | • People with prior history of AMS and ascending to 8,200–9,100 ft (2,500–2,800 m) or higher in 1 day  
                • No history of AMS and ascending to more than 9,100 ft (2,800 m) in 1 day  
                • All people ascending more than 1,600 ft (500 m) per day (increase in sleeping elevation) at altitudes above 9,900 ft (3,000 m), but with an extra day for acclimatization every 3,300 ft (1,000 m) | Acetazolamide prophylaxis would be beneficial and should be considered. |
<table>
<thead>
<tr>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>• History of AMS and ascending to more than 9,100 ft (2,800 m) in 1 day</td>
</tr>
<tr>
<td>• All people with a prior history of HACE or HAPE</td>
</tr>
<tr>
<td>• All people ascending to more than 11,400 ft (3,500 m) in 1 day</td>
</tr>
<tr>
<td>• All people ascending more than 1,600 ft (500 m) per day (increase in sleeping elevation) above 9,800 ft (3,000 m), without extra days for acclimatization</td>
</tr>
<tr>
<td>• Very rapid ascents (such as less than 7-day ascents of Mount Kilimanjaro)</td>
</tr>
</tbody>
</table>

Abbreviations: AMS, acute mountain sickness; HACE, high-altitude cerebral edema; HAPE, high-altitude pulmonary edema.
CLINICAL PRESENTATION

Altitude illness is divided into 3 syndromes: acute mountain sickness (AMS), high-altitude cerebral edema (HACE), and high-altitude pulmonary edema (HAPE).

Acute Mountain Sickness

AMS is the most common form of altitude illness, affecting, for example, 25% of all visitors sleeping above 8,000 ft (2,500 m) in Colorado. Symptoms are those of an alcohol hangover: headache is the cardinal symptom, sometimes accompanied by fatigue, loss of appetite, nausea, and occasionally vomiting. Headache onset is usually 2–12 hours after arrival at a higher altitude and often during or after the first night. Preverbal children may develop loss of appetite, irritability, and pallor. AMS generally resolves with 24–72 hours of acclimatization.

High-Altitude Cerebral Edema

HACE is a severe progression of AMS and is rare; it is most often associated with HAPE. In addition to AMS symptoms, lethargy becomes profound, with drowsiness, confusion, and ataxia on tandem gait test. A person with HACE requires immediate descent; death from HACE can ensue within 24 hours of developing ataxia, if the person fails to descend.

High-Altitude Pulmonary Edema

HAPE can occur by itself or in conjunction with AMS and HACE; incidence is 1 per 10,000 skiers in Colorado and up to 1 per 100 climbers at more than 14,000 ft (4,270 m). Initial symptoms are increased breathlessness with exertion, and eventually increased breathlessness at rest, associated with weakness and cough. Oxygen or descent is life-saving. HAPE can be more rapidly fatal than HACE.
Acetazolamide

Acetazolamide prevents AMS when taken before ascent and can speed recovery if taken after symptoms have developed. The drug works by acidifying the blood, which causes an increase in respiration and arterial oxygenation and thus aids acclimatization. An effective dose that minimizes the common side effects of increased urination and paresthesias of the fingers and toes is 125 mg every 12 hours, beginning the day before ascent and continuing the first 2 days at altitude, or longer if ascent continues. Allergic reactions to acetazolamide are uncommon. As a nonantimicrobial sulfonamide, it does not cross-react with antimicrobial sulfonamides. However, it is best avoided by people with history of anaphylaxis to any sulfa. People with history of severe penicillin allergy have occasionally had allergic reactions to acetazolamide. The pediatric dose is 5 mg/kg/day in divided doses, up to 125 mg twice a day.

Dexamethasone

Dexamethasone is effective for preventing and treating AMS and HACE, and perhaps HAPE as well. Unlike acetazolamide, if the drug is discontinued at altitude before acclimatization, rebound can occur. Acetazolamide is preferable to prevent AMS while ascending, with dexamethasone reserved for treatment, as an adjunct to descent. The adult dose is 4 mg every 6 hours. An increasing trend is to use dexamethasone for “summit day” on high peaks such as Kilimanjaro and Aconcagua, in order to prevent abrupt altitude illness.

Nifedipine

Nifedipine prevents HAPE and ameliorates it as well. For prevention, it is generally reserved for people who are particularly susceptible to the condition. The adult dose for prevention or treatment is 30 mg of extended release every 12 hours, or 20 mg every 8 hours.
References

Travelers’ Health
http://wwwnc.cdc.gov/travel

- Outbreaks
- Travel issues “in the news”
- “Destinations”

- Malaria map application
  - http://cdc-malaria.ncsa.uiuc.edu/
Meningitis B: Britain to offer a nationwide vaccination programme against disease

Britain will become the first country in the world to offer a nationwide vaccination programme against meningitis B, the most common cause of bacterial meningitis that kills one in ten infected babies and leaves many more maimed for life.

The illness is the most common cause of bacterial meningitis that kills one in ten infected babies and leaves many more maimed for life.
Keep Records - bring the slides

Babesiosis

Filariasis

Trypanosomiasis

Loiasis
The prophylaxis should begin with immediate, thorough cleansing of all wounds with soap and water.

For postexposure prophylaxis, the first doses for the immunosuppressed patient. The first 4 vaccine doses are given on the same schedule as for an immunocompetent patient, and the fifth dose is given 28 days later. Patient follow-up should include monitoring antibody response. See http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5902a1.htm for more information.

The World Health Organization recommends this fifth dose for all patients, not just those who are immunocompromised.

The U.S. Public Health Service recommends 4 postexposure vaccine doses, on days 0, 3, 7, and 14, unless the patient is immunocompromised in some way, in which case a fifth dose is given.

Immunization with HDCV or PCEC, prior postexposure prophylaxis with HDCV or PCEC, or people previously immunized with any other type of rabies vaccine should be administered.

CDC 2012 guidelines
Zika virus disease (Zika) is a disease caused by the Zika virus, which is spread to people primarily through the bite of an infected Aedes species mosquito. The most common symptoms of Zika are fever, rash, joint pain, and conjunctivitis (red eyes). The illness is usually mild with symptoms lasting for several days to a week after being bitten by an infected mosquito. People usually don't get sick enough to go to the hospital, and they very rarely die of Zika. For this reason, many people might not realize they have been infected. However, Zika virus infection during pregnancy can cause a serious birth defect called microcephaly, as well as other severe fetal brain defects. Once a person has been infected, he or she is likely to be protected from future infections.

Zika virus was first discovered in 1947 and is named after the Zika Forest in Uganda. In 1952, the first human cases of Zika were detected and since then, outbreaks of Zika have been reported in tropical Africa, Southeast Asia, and the Pacific Islands. Zika outbreaks have probably occurred in many locations. Before 2007, at least 14 cases of Zika had been documented, although other cases were likely to have occurred and were not reported. Because the symptoms of Zika are similar to those of many other diseases, many cases may not have been recognized.

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## Travel and Zika

### Suggested timeframe to wait before trying to get pregnant

<table>
<thead>
<tr>
<th>Possible exposure via recent travel or sex without a condom with a man infected with Zika</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zika symptoms</td>
<td>Wait at least 8 weeks after symptoms start</td>
<td>Wait at least 6 months after symptoms start</td>
</tr>
<tr>
<td>No Zika symptoms</td>
<td>Wait at least 8 weeks after exposure</td>
<td>Wait at least 8 weeks after exposure. Talk with your healthcare provider</td>
</tr>
</tbody>
</table>

### People living in areas with Zika

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zika symptoms</td>
<td>Wait at least 8 weeks after symptoms start</td>
</tr>
<tr>
<td>No Zika symptoms</td>
<td>Talk with doctor or healthcare provider</td>
</tr>
</tbody>
</table>

Decisions about pregnancy planning are personal and complex, and the circumstances for women and their partners will vary. Women and their partners should discuss pregnancy planning with a trusted doctor or healthcare provider. As part of counseling with healthcare providers, some women and their partners living in areas with active Zika virus transmission might decide to delay pregnancy.

Women who do not want to get pregnant should talk with their doctor or healthcare provider about ways to prevent unintended pregnancy, including how to use birth control the right way every time. Women should consider safety, effectiveness, availability, and acceptability when choosing a birth control method.
Middle East Respiratory Syndrome (MERS)

- Coronavirus
- First reported in Saudi Arabia in 2012

Severe acute respiratory illness
- Fever, cough, SOB, multiple organ dysfunction

High mortality
- 3-4/10 patients have died.

US cases of MERS
- May 2014
- Indiana and Florida

Health care workers
- Traveled to US from Saudi Arabia

Distribution of confirmed cases of Middle East Respiratory Syndrome
Researchers Say Malaria Deaths Are Twice The Official Count

WHO estimates that 655,000 people died of malaria in 2010. But a new report says no, the real total is twice as high — 1.24 million people

Lancet 2012, 379: 413–3141