## When You're on the Visiting Team: Travel Vaccines & Global Health

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### Learning Objectives

- Following this session, participants should be able to
   Apply recommendations and guidelines regarding vaccination for travelers
  - Understand the role of vaccination in travelers with complex co-morbid medical conditions, including contra-indications to certain vaccines
  - Discuss emerging issues in travel vaccination, including uncommonly used vaccines for special categories of travelers at higher risk for certain diseases



#### Three R's of Immunization

- Routine immunizations
  - ► To ensure good health at home and in travel
- Recommended immunizations
  - ▶ To protect traveler from endemic or epidemic diseases present in country of destination
- Required immunizations
  - Required by country of destination
  - Intended to protect host country's population from importation and spread of disease



#### Adult Routine Vaccinations - Through The Lens of Travel Influenza Recommended for all travelers during influenza season The most common travel associated infection Timing of travel and flu season may be relevant ▶ Hepatitis B Body fluid/blood exposure

- Routinely recommended for everyone
- Vaccination not needed for all travelers, risk factor and occupation based
- High risk sexual practices, health care workers, volunteers, medical tourism difficult to assess risk travel
- Adjuvanted vaccine now available (Heplisav-B, 2 doses) as well as Twinrix (HAV/HBV) et al. Immuitations for Travel UpToble. https://www.uptoble.com/content/Immuitations.for -cheplitikt/UbAucore-seart/peutilisticicettifite-1-150kauge\_type-fraitfailidipiig\_rint-infrit701081. Heblished August 2019. Acc

Staff Reports, 366th Public Health Flight. Public health alert: measles and mumps. Mountain Home Air Force Base. Avail https://www.mountainhome.af.mil/News/Article-Display/Article/665711/public-health-alert-measles-and-mumps/. Pub



#### **Routine Vaccines**

- ▶ Measles, Mumps, Rubella
  - Global epidemics of measles associated with vaccine hesitancy
  - Concern in adults who may not have received 2 doses of vaccine, should be considered for all born after 1957
  - Live attenuated vaccines, thus contra-indicated in immunocompromised patients Could also consider serologic testing in high risk patients - cost may be higher than re-vaccination, however
- ► Tetanus, diphtheria, pertussis
  - Ongoing pertussis outbreaks internationally, immunity wanes over time
  - No ACIP recommendation for Tdap booster beyond 1 adult dose ▶ However, could consider Tdap even if recent Td booster for pertussis protection.

Meades, Mamps, Rabella. Shoreland Travas. https://www.travax.com/library/meades-mumps-rubella. Publiched March 14, 2019. Accessed Septemb Tetanus, Diphtheria, Pertussis (? Years and Older). Shoreland Travas. https://www.travas.com/library/tetanus-diphtheria-pertussis. Publiched Found

### **Routine Vaccines**

#### Pneumococcal

Should be given as indicated, not specifically recommended for travels beyond risk factor and age recommendations

#### ► Varicella/Herpes zoster

- Varicella vaccine not generally needed for travel, can consider if no history of disease and not immunocompromised
- Shingles can be problematic if occurring during travel, though no additional risk
- Use of recombinant vaccine (Shingrix) can be considered, occasionally requested in travel consultations
- Side effects of vaccine also to be considered, injection site and systemic symptoms

#### cal-Medical Summary. Shoreland Travax. https://www.travax.com/library/pneumococcal. Published July 10, 2019, Acc ary. Shoreland Travax. https://www.travax.com/library/f d April 9, 2019. A

#### **Travel Vaccines** Recommended Required Yellow fever Influenza ▶ Hepatitis A Meningococcal ▶ Hepatitis B Adult polio booster Typhoid Rabies ► Japanese encephalitis Tick-borne encephalitis Cholera

#### **Recommended Vaccines**

- Vary based on travel itinerary and plans
- Important to obtain full patient medical history to determine risk factors as well as possible contraindications to vaccination

### Hepatitis A

#### Hepatitis A

- Fecal/oral transmission resulting in acute hepatitis, rarely liver failure
   Lower risk in many countries now due to improved sanitation, but also local outbreaks due related to IVDU and homelessness
- Vaccination recommended for travel to countries with intermediate to high endemicity - most developing nations globally
- Counselling regarding food and water safety important
- Vaccine safe in pregnancy, immunocompromised patients
- One dose prior to travel, repeat dose in 6-12 months for long-term protection

reedman et al. Immunizations for Travel. UpToBate. https://www.uptodate.com/contents/immunizations-forrave/fixearch-hepatitiski20A&source-search\_result&selectedTitle-4-150&usage\_type-default&display\_rank-4FH7673081.Pu



## Typhoid

- Systemic bacterial illness, fecal-oral transmission
- South Asia highest risk, also Africa, less in Latin America, increases in MDR strains
- Food safety and hygienic eating habits key
- Vaccines not completely effective 60-70% efficacy
- Available vaccines
  - Live oral vaccine
    - ► Caution in immunocompromised patients
    - Oral capsules on days 1, 3, 5, 7
  - Polysaccharide injectable vaccine
    - Subunit vaccine, safe in immunocompromised patients
  - hold Fever Medical Summary. Shoreland Travax. https://www.travax.com/library/typhold-fever. Published December 15, 2018. A



#### Typhoid - Oral versus IV? Oral vaccine Inactivated Live attenuated Approved for age >6 Approved for age >2 Requires refrigeration Single dose 4 enteric coated tablets - empty Shorter duration of immunity stomach Inactivated by antibiotics - generally within 3 days No issue with antibiotic use GI side effects may occur Injection site side effects Typhold Fever - Medical Summary. Shoreland Travax. https://www.travax.com/library/typhoid-fever. Published December 15, 2018. Acces

#### Rabies

- Virus transmitted by dogs, bats, other animals, resulting in encephalopathy and death
- Endemic to Asia, Africa, Central and South America
   Pre-exposure vaccination based on risk
  - Intra-dermal more immunogenic than IM
  - Exposure to animals
  - Limited immediate medical care
  - Days 0, 7, 21, 28 prior to travel
  - Shorter WHO regimen also now available days 0 and 7 +/- third dose
  - If exposure in unvaccinated, RIG and post-exposure vaccines needed,
  - If previously vaccinated only post-exposure vaccines needed

Hydrophoble ou Morsure de Chien Enragé. Iconographic Collection. Wellcome Collection Gallery. 2018.

#### Case

- 56 year old male travels to Thailand, wakes up in the morning and finds a bat in his room, fairly confident he was not bitten
   No pre-exposure prophylaxis taken
  - What else do we want to know or do?

#### What should we do?

- RIGPost-exposure vaccination
- RIG and post-exposure vaccination

#### Japanese Encephalitis

- Arbovirus endemic in Asia and Western Pacific
  - Useful for travels visiting during periods of transmission
  - Low risk overall for travelers, but severe infection
  - Risk factor based shared decision making
- Inactivated vaccine (IXIARO) available in USA
  - Days 0, 7-28
- Live attenuated vaccine, contraindicated in immunocompromised
- Duration of protection? 3<sup>rd</sup> dose >1 year after primary series

Japanese Encephalitis - Medical Summary. Shoreland Travax. https://www.travax.com/library/japanese-encephalitis. Published December 31, 2018. Accessed Sec



#### Case

- 18 year old male Dartmouth College student planning to backpack across Europe this summer, will be going hiking and camping on several occasions.
- He comes in to travel clinic having read about tick-borne encephalitis online, asks about a vaccine to protect himself against this, as he has had Lyme disease and Babesia previously while at college in New Hampshire
- Can he be vaccinated?

### Tick-borne Encephalitis

Viral CNS infection transmitted by ticks

nalitis - Medical Summary. Shoreland Travax. https://www.trav

- Occurs in Spring/Summer in Northern, Western, and Central Europe, former Soviet Republics
- Travelers to forested areas up to 1500 feet elevation, expats with prolonged stays, extensive outdoor activities
- No vaccine available in the USA
- Can be considered on arrival to Europe for those who will be in high risk areas
  - Adequate immunity takes 4 weeks post-vaccination, however

#### Case

- 27 year old male planning to go to Mozambique to assist in relief efforts following Cyclone Idai with the Red Cross
- Has rheumatoid arthritis on infliximab
- Should he receive cholera vaccine, and if so, which one?

#### Cholera

- Diarrheal illness caused by Gram negative bacterium Vibrio cholerae
- Low risk to travelers in general, vaccination generally not recommended
- Live attenuated oral vaccine (Vaxchora) available against serogroup 01
   New formulation that can be kept refrigerated at 2-8 degrees C
  - 80% efficacy at 3 months post-vaccination, waning protection over 2 years post-immunization
- Not for use in immunocompromised patients
- Other killed bacterial vaccines available globally (Dukoral, Shancol, Euvichol)
- Primarily recommendation to vaccinate aid, refugee, and health care workers traveling to outbreak areas

- Medical Summary. Shoreland Travax. https://www.travax.com/library/cholera. Published October 1, 2018. Acc

#### Cholera Vaccines

Constituent	Killed	Killed	Killed	Vaxenora Live
	whole cell	whole cell	whole cell	attenuated
Route	Oral	Oral	Oral	Oral
Doses	Two	Two	Two	One
Toxin	01, 0139	01	01, 0139	01

Le Petit Journal



### **Required Vaccines**

- Required for travel to specific countries
- Yellow fever is major issue due to availability of vaccine and legal requirements by many nation states for travelers

Yellow Fever - Medical Summary. Shoreland Travax. https://www.travax.com/library/yellow-fever. Published May 23, 2019. Accessed September 23, 2019.

#### Case

- 66W comes to prepare for a "bucket list" trip to Niger to visit her son who is an infectious disease physician at a medical mission hospital in Niamey
- PMH significant for RA on chronic methotrexate and vague history of partial DiGeorge syndrome (hypoplastic thymus)
- She has been to Caribbean before, at which time her routine vaccines were updated and she was provided hep A#1
- Yellow fever vaccine required for travel to Niger

#### Vote

- Give yellow fever vaccine
- Do not give yellow fever vaccine provide medical exemption letter
- Advise against trip, do not provide vaccine or medical exemption

#### Questions

- Does the yellow fever vaccine have to be boosted every 10 years?
- How many lifetime doses are recommended?







#### Yellow Fever Vaccine Availability

- Vaccine Availability
  - > YF-VAX (Sanofi Pasteur) currently unavailable in USA due to production issues - transition to new facility
  - Expected availability in 2020
  - Stamaril (Sanofi Pasteur) similar vaccine used in Europe, currently being used in USA as an investigational new drug in 250 designated centers nationally
  - Significant access issues and strain on travel clinics as a result
  - Fractional dosing not approved by FDA or ACIP, considered an alternative by some given limitations in supply, does not meet entry criteria for countries requiring certificate

ver - Medical Summary. Shoreland Travax. https://www.travax.com/library/yellow-fever. Published May 23, 2019. September 23, 2019.

#### **Vaccine Contraindications**

- Infants < 6 months of age</p>
- Women breastfeeding infants <9 months of age
   Anaphylaxis to previous dose of YF vaccine or constituent such as egg or
  egg proteins
- Skin allergy testing could be done prior to administration if egg sensitivity
- If severe egg allergy, desensitization could be considered if vaccine essential Altered immunity
- Thymus disorders such as thymoma or myasthenia gravis Transplant recipients, other conditions requiring immunosuppressant drugs, active malignancy
- HIV/AIDS with CD4 <200</p>

Yellow Fever - Medical Summary. Shoreland Travax. https://www.travax.com/library/yellow-fever. Published May 23, 2019. Accessed September 23, 2019.



### Meningococcal Vaccine

- Severe bacterial infection causing meningitis due to different strains of *Neisseria* meningitidis
- Epidemics of serogroups C and W in African meningitis belt
- Quadrivalent conjugate vaccines (MCV4, MenACWY) available Vaccination recommended for travelers to meningitis belt dry season (December to June), year round in health care workers
- Required for travelers to Saudi Arabia for
- Hajj certificate of vaccination





#### Adult Polio Booster ▶ Fecal-oral transmission, can result in CNS infection with paralysis Pakistan and Afghanistan remain the only nations with Polio wild-type infection (Nigeria with no infections for 3 years, awaiting WHO certification) Adult polio booster required for travel to Saudi Arabia for Hajj for children up to 15 years of age Several countries also require vaccination of travelers from endemic countries Long stay visitors may also be subject to exit recommendations due to outbreaks Merce for endance The polic endance 1988 1968 2017 Columnia: Countries 125 3 EDAD Tructure Dynamic Polio - Medical Summary. Shoreland Travax. https://w Published May 10, 2019. Accessed September 23, 2019 2017 The Polio Endgame. WHO, Polio Eradication Pro 31, 201



#### **Immunocompromised Patients**

- ► Rise in travelers with complex medical conditions
  - "Bucket list" trips
  - More patients with stable chronic diseases
  - More susceptible to vaccine preventable illnesses which may be endemic at destination
  - Should advise patients to have evacuation insurance and take extra relevant precautions
- Live attenuated vaccines generally contraindicated in these patients
  - MMR, varicella, yellow fever, oral typhoid
  - Other vaccines may result in suboptimal immunity
  - Risk-benefit discussion sometimes relevant if high risk travel planned
  - For stable HIV patients with CD4>200, live vaccines can be given

Immunocompremixed Travelers - Medical Summary. Shoreland Travax. https://www.travax.com/ilbrary. 23, 2019

### **Special Sub-Populations**

- Active malignancy
  - May be on immunosuppressive therapy
  - Influenza, pneumococcal vaccines recommended, as well as other inactivated vaccines
  - Consider serologies for diseases such as measles
  - Delay travel when possible

Immunocompromised Travelers - Medical Summary. Shoreland Travax. https://www.travax.con 23, 2019

- Hematopoietic stem cell transplant recipients
  - Require re-vaccination with all childhood vaccines 6-24 months after transplant, with exception of live vaccines which are contraindication until after 24 months
  - Travel should be avoided during 24 month period post-transplant

#### More Sub-Populations

- Solid organ transplant recipients
   Delay travel until >2 years after transplant when possible
- Immunodeficiencies or use of immunosuppressive drugs
  - Avoid live vaccines

Immunoco 23, 2019

- Consider IVIG to provide passive immunity prior to travel
- Inactivated vaccines recommended
- For immunodeficiencies, asplenic patients pneumococcal, meningococcal, and Hib vaccines to be considered

ed Travelers - Medical Summary. Shoreland Travax. https://

# Chronic Medical Conditions

Chronic renal failure

- Difficult response, high risk of exposure especially in dialysis patientsto induce vaccine
- HBV, influenza, pneumococcal vaccines important
   Chronic liver disease
  - Caution with travel to areas with endemic hepatitis viruses
  - Hepatitis A and B vaccination key

Immunocompromised Travelers - Medical Summary. Shoreland Travax. https://www.travax.com/library/in 23, 2019

- Pneumococcal vaccination
- Diabetes mellitus
  - ► General immune impairment, pre-travel vaccines as for general population, catch up of recommended routine vaccines



### Dengue/Zika Vaccine Efforts

- Dengue

  - No currently available vaccine for travelers
     No currently available vaccine for travelers
     Dengvaxia evidence showing higher risk of severe Dengue infection following vaccination in those not previously infected, should only be used in Dengue sero-positive patients (IgG ELGA)
     Two other promising vaccine candidates in Phase 3 clinical trials
- ▶ Zika
  - Recommendation to men planning to conceive with partners to wait 3 months after last possible Zika exposure such as travel to affected area, 2 months for women who were symptomatic or exposed
     Several vaccines under development currently

  - Challenges in developing neutralizing vaccine safe in pregnancy

Bengue - Medical Rummary Sheveland Traves, https://www.traves.com/litrary/dangue. Fabilited August 1, 2018. Accessed September 22, 2019. National Institute of Allerg and Informational Diseases. ZBa Virus Racches, Available at: https://www.niaid.nih.gov/decases.com/litrary/shevaecha-accessed Recorded September 2, 2019.

#### Case

- 43 year old female nurse who is planning to work in the Democratic Republic of Congo as part of Ebola response efforts by the WHO
- She asks whether there is anything she can do to prevent Ebola infection?



### MERS Coronavirus Vaccine Development

- Middle East Respiratory Syndrome, significant concern globally
- Challenges similar to SARS vaccine development
   Difficult to develop vaccines effective against Coronaviruses
  - Appropriate animal models
  - Several in development, focus on targeting spike glycoprotein on viral surface
     Some promising results in a study on rhesus monkeys with high seroconversion rates using vaccine targeted to MERS spike glycoprotein

Analy M, et al. Special Report: Middle East Respiratory Syndrome. IN Engl J Med 2017. 376.6.534-94. K Multuneni et al. A synthetic common sett-spike protein fOM vaccine Indexce protective Immunity against MEST G-V in morthmany primates. Science Traditional Molicon IV Mol 2017. 101. 7 June 2019. 2019;171. Biolaurat, G., Millel, J., Lictra, B. and Whittaer, G. (2012). Michanism of Commaring Cell Entry Mediated by the Vala Spike Primate. Science Traditional Advance M V Molarity Mediated by the Vala Spike Primate. Science Traditional Advance M V Molarity Mediated by the Vala Spike Primate.



#### The "Holy Grail" A Universal Influenza Vaccine

Wednesday, April 3, 2019

NIH begins first-in-human trial of a universal influenza vaccine candidate

Investigational vaccine designed to provide broad, durable protection from

- flu.
- Major focus of vaccine research on viral proteins less likely to mutate
   Challenge given ability of influenza virus to mutate antigenic drifts and shifts
- Challenge given ability of influenza virus to m
   Vaccine currently in phase 1 clinical trials
- Uses ferritin with part of influenza hemagglutinin protein on its surface (part less likely to mutate)

National institutes of Health (IIIH). (2019). *IIIH begins first-in-human trial of a universal influenza* vaccine candidate. (conline) Available at: https://www.nih.gov/news-events/news-releases/nih-begins-first-human-trial-universal-influenza-vaccine-candidate. Accessed September 23, 2019.

Clinicalitrials gov, (2019). Dose, Safety, Tolerability and Immunogenicity of an Influenza H1 Stabilized Stem Ferritin Vaccine, VRCFLINPF099-00-VP, Adults. [online] Available at: https://clinicalitrials.gov/cl2/show/NCr03814720 Accessed September 23, 2019.

#### Avian Influenza

- Concern regarding H5N1 and H7N9, prior outbreaks related to poultry
- No current significant human-to-human transmission
  - Remains a significant concern however, given antigenic shifts in virus
  - Significant transmissions from birds to humans
  - Several year outbreak, in early 2000s, in Asia and Middle East
  - H5N1 vaccine available, being stockpiled

Centers for Disease Control and Prevention. (2019). Highly Pathagenic Asian Avian Influenza A(HSHT) Virus. [online] Av at: https://www.cdc.gov/flu/avianflu/hSm1-virus.htm. Accessed 23 Sep. 2019.



#### Summary

- Essential to review routine vaccinations with travelers and ensure they are up to date
- Influenza is the most common travel associated infection
- Re-emerging vaccine preventable illnesses such as measles
   Important to consider traveler medical history and risk factors to individualize recommended vaccines
- Consideration of whether to administer or exempt travelers from required vaccines - issues with yellow fever vaccine availability
- Emerging vaccines against global threats, may be relevant for travelers in the future
- An exciting time to be a travel medicine clinician indeed!

### **Resources for Travel Medicine Clinicians**

- CDC Yellow Book
- Shoreland Travax
- IDSA Guidelines for the Practice of Travel Medicine

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Bon Voyage. Pixabay. June 15, 2016.

