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College of Pharmacy and Nutrition
University of Saskatchewan
Saskatoon SK S7N 5C9
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Travel Vaccines

There is a bug going around Canada right now. It's called the 'travel bug', and it gives people the compelling urge to travel far away to exotic locations. While this bug is harmless, there are many other viruses and bugs at these locations that warrant protection for ourselves. Modern day pharmaceuticals have allowed us to prevent many deadly diseases that can be acquired abroad, but they only work when taken appropriately. Therefore, it's important as health care professionals to encourage the correct use of vaccines and antibiotics when patients travel to hazardous locations.

When a patient asks about travel vaccines, the health care professional may want to verify routine vaccinations (tetanus, diphtheria, pertussis, pneumococcus, etc.) are up to date [1]. These immunizations are strongly recommended by the World Health Organization [2] and the Public Health Agency of Canada [1] to prevent unnecessary illness when travelling abroad. The patient should also be aware that it is advisable to visit a travel clinic at least two to three months prior to travel to ensure they can receive their full course of vaccinations before departure [3]. If the patient is inquiring about what vaccinations are needed for a country of interest, visit the International Association for Medical Assistance to Travelers (IAMAT) [4] or Health Canada Travel Guide [5] to find a list of mandatory and recommended vaccines for each country. As a pharmacist, it is also helpful to recommend your patients follow the 5 'I's when traveling [6].

Insects: Use DEET 30% and nets to repel mosquitoes, or go outside when insects are less active

Ingestions: Wash your hands frequently and avoid food and water that may be contaminated

Indiscretions: Use protection in a sexual encounter and use clean needles

Injuries: Wear a seatbelt when travelling, and avoid wild animals or situations that may be dangerous

Insurance: Obtain coverage for when it is needed

Vaccine Pearls:

- Most guidelines for travel are centered on the average healthy adult, yet many do not meet this criteria
- Immunocompromised patients can be characterized by; Active HIV infection, use of immune modulating drugs (infliximab, methotrexate, etc.), ≥20mg/day of prednisone or its equivalent for 14 days or more, cancer patients, transplant patients, etc. [1]
    - If immunocompromised, risks can still be weighed against the benefits if they have not taken a medication that suppresses the immune system for ≥3 months, or are recovering from cancer [1]
    - Even inactive vaccines may not be fully effective in immunocompromised individuals [7]
- Pregnant women, young children, or elderly individuals should be counselled on the limitations of safety and efficacy in each vaccine regarding age and pregnancy concerns on a case by case basis [8]

University of Saskatchewan
Telephone: 1-800-667-3425 (SK); 966-6340 (Saskatoon)
Fax: (306) 966-2286 Text: (306) 260-3554

- While most vaccinations can be given together, some require separate administration:
    - The oral typhoid vaccine may diminish the therapeutic effect of Dukoral, and should be separated by at least 8 hours [9]
    - Administration of Rabies Immune Globulin (RIG) may diminish effect of live vaccines with the exception of the Yellow Fever vaccine. Live organism vaccines should be withheld for up to 6 months following globulin administration. RIG administration after a live vaccine varies in timeframe, but its benefit will usually outweigh risks of a diminished immune response [9]
    - Whenever possible, injected live virus vaccines should be given ≥28 days apart or ≥30 for Yellow Fever vaccine [10]
- Missing a dose does not always give cause to restart a vaccination series:
    - Scheduled doses may be missed due to forgetfulness, inability to get to a clinic, or a drug shortage to name a few. Available data suggests that intervals between doses longer than what's recommended do not affect seroconversion rate or titer volume when the schedule is complete. Therefore it is not necessary to restart a series or add doses if the interval is extended. The only exception to this is the oral typhoid vaccine, which should be restarted if the four dose schedule is not completed within three weeks [10]
- Using different brands of vaccines to complete a series can be possible in some cases:
    - Vaccination schedules should be completed with the same brand if possible. However, a vaccine may be considered interchangeable when:
        - Authorized with the same indications and equal schedules
        - Authorized for the same population
        - Contains comparable antigens
        - Similar in safety, immunogenicity, and efficacy [11]
    - Visit http://www.phac-aspc.gc.ca/publicat/cig-gci/p01-06-eng.php for specific information pertaining to individual vaccines
- Receiving protection against hepatitis A and B after patient has only had one dose of a univalent vaccine:
    - If a patient has already received one dose or multiple doses of a univalent vaccine for hepatitis A or B, they can still receive a combination hepatitis series. Repeating a hepatitis vaccine series is not harmful [12]

Many different vaccines may be required based on which routine vaccinations have been obtained in the past and which diseases are prevalent in the destination country. The following is a discussion of some common vaccinations that may be provided in community pharmacies. A supplemental vaccination table is available at the end of the document.

Cholera & ETEC Travelers' Diarrhea:

These acute intestinal infections are now considered more of a nuisance than a threat for travelers. Cholera is caused by the bacterium *Vibrio cholerae*, and it is spread through contaminated water and food. Symptoms include mild to moderate diarrhea with or without vomiting, potentially leading to leg cramps, severe diarrhea, dehydration, and death. Staying hydrated is the best treatment for this infection, but antibiotics may be warranted in severe cases [2][7]. Enterotoxigenic *Escherichia Coli* (ETEC) accounts for 25 to 50 percent of travelers' diarrhea, and is also transmitted through contaminated food or water. Most episodes are self-limiting and mild in nature with gastrointestinal symptoms. Currently, the oral vaccine Dukoral is not recommended for routine use, and it should therefore be reserved for relief workers and health care professionals in endemic countries [1].

Dukoral, a killed oral vaccine, is about 86 percent effective against epidemic cholera for two years, and roughly 25 percent against ETEC for three months after the second immunization [1]. Two doses are given a minimum of one week apart and a maximum of six weeks apart for adults, while three doses are recommended for children aged two to five with the same dosing interval [2]. Food, drink, and any medication should be avoided one hour before and after each oral dose. The immunogenicity effects of Dukoral differ between cholera and ETEC, but protection is generally seen two weeks after the final dose, and a booster dose is recommended three months after the primary series if the traveler is under ongoing risk [2][13]. If more than 5 years pass since last immunization or booster, the primary series should be repeated [13].

Hepatitis A/B:

Hepatitis A is a viral disease that is largely transmitted via the stool of an infected person through contaminated food and water or close contact. Symptoms can take around a month to appear, and can range from none to severe fever, fatigue, nausea, and vomiting with liver damage and possibly death. Most cases resolve within a few weeks, but some infections can persist for months [1][13].

The Hepatitis B virus is contracted from direct contact with blood or other body fluids, and targets the liver. While 50 percent of adults may develop acute symptoms, roughly 90 to 95 percent will clear the virus and develop lifelong protection. The remaining 5 to 10 percent will develop chronic Hepatitis B [1][13].

Vaccines for Hepatitis A come in a 2 dose regimen with an interval of 6 to 12 months between doses [2][14]. Immunity is seen within two to four weeks, and protection with these vaccines probably lasts 20 years or more. Hepatitis B can be protected against with a 3 dose regimen that is given intramuscularly at 0, 1, and 6 months [13]. An accelerated schedule is available as 0, 7, and 21 days, followed by a booster dose at 1 year for those who need to leave before a standard schedule can be given [14]. Onset of immunity is the same as with Hepatitis A, and protection is thought to last at least 25 years. For patients requiring coverage against both viruses, Twinrix is available in three doses given at 0, 1, and 6 months. The same rapid schedule as Hepatitis B vaccine can be utilized, and immunity also begins to develop 2 to 4 weeks after the first dose [14].

Japanese Encephalitis:

Japanese encephalitis is spread through the bite of a *Culex* mosquito infected with *flavivirus* from a pig or wild bird [2]. Infection can lead to swelling of the brain with consequential nerve and brain damage. The risk is low in urban areas, but increases as travelers visit rural and agriculture locations in Asia. Most cases of infection are asymptomatic, but some individuals will see symptoms begin to emerge within one to two weeks after the initial bite. These symptoms include

fever, headaches, vomiting, neck stiffness, confusion, and mental changes. Untreated cases can progress to paralysis, coma, seizures, and convulsions with 20 to 30 percent mortality [13].

The vaccine for Japanese encephalitis is inactivated and administered intramuscularly in three doses: the first two doses are separated by four weeks and the recommended booster is given at one year. Optimal protection occurs roughly 28 days after the second dose and protection lasts approximately one year. Data on concomitant administration with other vaccines is not currently available, so this vaccine should be administered alone. Pediatric safety studies are underway; however the vaccine is currently only licensed for those aged 18 or older [2][13].

Rabies:

Lyssavirus, the virus that causes rabies, is spread to humans through close contact with the saliva of an infected animal. This could occur as a result of an animal bite, scratch, or lick on open skin [13]. The risks of acquiring rabies after an exposure are not well known, but are most common if an individual is bitten multiple times or if the bites are closer to the head. Post-exposure prophylaxis is strongly encouraged as there is no treatment for the infection. If infected, there is an incubation period of one to three months before two different types of symptoms will develop. 'Furious rabies' (the more common symptom) is characterized by feelings of anxiety, confusion, hyperactivity, hallucinations, fear of water, and seizures. 'Dumb rabies' (the less common symptom) presents more so with weakness and paralysis [2]. If symptoms appear, prognosis is very poor, and death generally follows 7 to 14 days after first presentation as the respiratory system ceases to function [13].

Rabies can be vaccinated against in both a prophylactic and post-exposure fashion. The vaccination used is the same, but the schedule differs. Prophylactic injections require three doses on days 0, 7, and 21 or 28. If the patient is then exposed to rabies while travelling, two additional booster doses should be given on day 0 and 3 after contact with the animal, or as soon as possible [1][2]. Post-bite prophylaxis is suitable for those who are not in constant contact with wild animals while travelling and this includes a four and five-dose regimen. Five doses are currently more common, and consists of injections on days 0, 3, 7, 14, and 28 [1]. If the vaccine cannot be given on the first day after exposure, it should be received as soon as possible to help prevent the risk of infection; however there is no set timeframe for how long an individual can wait before the vaccine is no longer effective [15]. If the bite occurs in someone who has not been previously vaccinated for rabies, a Rabies Immune Globulin (RIG) should be given within 24 hours or up to seven days after the first dose of rabies vaccine [16]. This provides the body with immediate protection until a response to the vaccine has occurred. The rabies vaccine provides immunity 14 to 28 days after the vaccinations are complete, and duration of protection is usually two to three years [1].

Typhoid Fever:

Salmonella typhi is a common bacterium found predominantly in South Asia where standards of hygiene are lower. It is transmitted by consumption of contaminated food or water; *salmonella* infects only humans [6]. The risk of contracting typhoid depends on the destination, duration of travel, and precautions taken. Safe food handling practices are vital, and travelers should avoid non-bottled water, roadside food stands, and eating raw fruits or vegetables among others [17]. If infection occurs, symptoms of *salmonella* emerge one to three weeks post-infection, and present with varying degrees of fever, headache, constipation, diarrhea, and fatigue. Untreated cases can lead to enlargement of the liver and spleen, intestinal bleeding, or pneumonia [13].

While the infection can be treated with antibiotics, there are also two forms of vaccines: oral and intramuscular (IM). The oral vaccine is a live attenuated mutant strain of typhi Ty21a and is administered as one capsule given on days 1,

3, 5, and 7: re-vaccination, if required, is recommended after seven years. The injectable form is an inactive single dose Vi capsular polysaccharide vaccine (ViCPS) that induces protection within a week and lasts for roughly three years. The IM vaccine is licensed for children aged 2 and up while the oral has a minimum age requirement of 5 years [1][3].

Yellow Fever:

The virus responsible for yellow fever is flavivirus, which originates primarily in infected monkeys and is transmitted via mosquitos. The virus is found in urban and rural areas of Africa and central South America. While most infections are asymptomatic, acute illness can occur in two phases beginning after 3 to 6 days. The first phase is characterized by fever, muscular pain, headache, chills, nausea and/or vomiting. Roughly 15% of all individuals will progress to the second phase where severe fever, jaundice, abdominal pain, organ failure and hemorrhagic events may occur. Of those who reach stage two, 50 percent will die within 10 to 14 days of onset. There is no treatment for yellow fever, so prophylactic vaccination is extremely important [1][2][13].

Risk for contracting this virus is highest for those staying an extended period of time in rural or jungle areas at an elevation below 2300 meters [2]. Yellow fever vaccine is a requirement for individuals entering certain high risk countries (proven with an 'International Certificate of Vaccination or Prophylaxis') and is only available through a certified travel clinic. In Saskatchewan, certified clinics are located in Saskatoon, Regina, or Prince Albert. If the patient is not eligible for the vaccine because of a contraindication, a waiver certificate may be granted for travel to high risk countries, but an absence of this certificate may not guarantee entry into the country [13]. An individual benefit-risk assessment is required for patient in whom the vaccine is not recommended. Such patients include pregnant or breastfeeding women, children under nine months of age, adults 60 years or older (primary dose), patients with an egg allergy, or immunocompromised individuals.

Yellow fever vaccine is a single dose, live attenuated virus that is administered subcutaneously (SC) [2]. It takes 10 days for the vaccine to become effective, so the required certificate will only be valid ten days after administration [13]. A booster dose is required after ten years if re-certification is needed [13].

Prepared by: Kalen MacLeod, Pharmacy Intern
Reviewed by: Carmen Bell, BSP; Terry Damm, BSP; Karen Jensen, BSP, MSc

Vaccine	Consider for	Dose schedule	Time to onset & Efficacy	Duration of protection	Contraindications	Adverse reactions	Notes
Cholera/ETEC PO (Killed) DUKORAL	Emergency/ relief workers	2 doses 1-6 wks apart	2 weeks after last dose 25-86%	Cholera – 2 years ETEC – 3 months	Hypersensitivity to previous dose	Mild GI disturbances	Avoid food/ water/ meds 1 hr before & after
Hep A/B IM (Killed) A: (AVAXIM HAVRIX) B: (ENGERIX-B RECOMBIVAX & Infanrix) TWINRIX (A&B) VIVAXIM (A & Typhoid)	Close contact with locals in high risk area	(Hep A only) – 2 doses 0, 6-12 months (Hep B only) – 3 doses 0, 1, 6 months Hep A/Hep B – 3 doses at 0,1,6months or 0,7,21 days + 1year	2-4 weeks after first dose Hep A – 80-90% Hep B – 95-100%	Hep A– 20+ years Hep B – 25+ years	Decreased efficacy with: Smoking, older, obesity, alcoholism, immunocompromised [1], celiac dx, hemodialysis	Local injection site reactions	Junior vaccines of HAVRIX and TWINRIX available for ages 1-18
Japanese Encephalitis IM (Killed) IXIARO	High risk during transmission season (summer and fall)	2 doses 0,28 days	Variable 10-28 days after last dose 95% have antibodies 28 days after 2nd dose	1 year	Hypersensitivity to previous dose. Caution in pregnancy	Local injection site reactions	Not approved for use <18 yrs
Rabies IM (Killed) IMOVAX-Rabies RabAvert Rabies Immune Globulin (RIG)	Close contact with saliva of unknown animal	Prophylactic – 3 doses 0,7,21-28 days Treatment – 5 doses 0,3,7,14,28 days RIG - 24 hours - 7 days after first IM dose	14-28 days IM - 95-98% seroconversion RIG - Immediate protection	2-3 years	Hypersensitivity to previous dose	Malaise, generalized aches, headaches	If contact occurs with previous prophylaxis, give 2 booster doses on 0&3 days
Typhoid PO (Live) VIVOTIF IM (Killed) TYPHERIX TYPHIM Vi	Those visiting poor sanitation areas	Oral - One cap given on days 1,3,5,7 IM- Single dose injection	Typh-O – 7 days Typh-I – 14 days 50%	Oral – 7 years IM – 3 years	Hypersensitivity to previous dose Oral vaccine is contraindicated in pregnancy, IBD, and immunocompromised [1]	Local injection site reactions Oral: Ab pain, N/V/D, Rash, Headache	Oral use only for ≥5yrs of age IM use only for ≥2yrs of age
Yellow Fever SQ (Live) YF-VAX	Extended period in rural/jungle <2300m or high risk country	Single dose	10 days 85% @ 10 days 99% @ 30 days	10 years	Pregnant or breastfeeding, <9 months, >60 yrs (primary dose), Immunocompromised [1], Severe egg allergy	Rare neurological encephalitis or multi-organ failure [2]	Also use mosquito protection (nets, spray [3], etc.)

DOSING for ADULTS ONLY

[1] Immunocompromised: Active HIV infection, immune modulators (Remicade, etc), Steroids (≥20mg/day prednisone for 14 days or more), cancer, etc

[2] Viscerotropic disease (multi organ failure) with fatality rate in excess of 60% - 2.4/100,000 vaccine doses [18]
Neurotropic disease seen in patients under 6 months or over 60 years – 0.13-0.8/100,000 vaccines doses [18]

[3] Insect repellents: Adults 12 & up: 20-30% DEET (lasts 6.5-8 hours) or 20% icaridin (lasts 8 hours) / Kids 6 months-12 years: 20% icaridin or 10% DEET TID [19]

PO = Oral; IM = Intramuscular; SQ = Subcutaneous

Extra:

Combination Typhoid & Hep A vaccine available under ViVAXIM as IM injection for persons >15 years of age

Visit http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-eng.php for complete information on each vaccine

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