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TRAVELING IN A NEW ERA: ADDRESSING THE CHALLENGES OF EMERGING INFECTIOUS DISEASES IN INTERNATIONAL JOURNEYS

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Abstract: The increasing number of U.S. citizens traveling abroad, particularly during the summer months, has raised concerns about infectious disease risks. This article examines the growing recognition of "new" infectious diseases and their impact on international travelers. Recent outbreaks of diseases like avian influenza, pandemic influenza, Lassa fever, Ebola, Marburg viruses, Middle East respiratory syndrome coronavirus (MERS-CoV), H7N9, Chikungunya, and Zika have added to the existing infectious disease risks for travelers. Understanding these risks is crucial for both travelers and healthcare professionals to ensure appropriate preventive measures and responses.

Keywords: international travel, infectious diseases, avian influenza, pandemic influenza, Lassa fever, Ebola virus, Marburg virus, MERS-CoV, H7N9, Chikungunya virus, Zika virus

Introduction:

Each year more United States citizens travel abroad; this trend is expected to continue as the population increases, and larger proportions are expatriates. In 2015, U.S. citizens made more than 32,789,000 trips outside of North America, most during May through August.¹ As of November 30, 2016, U.S. citizens completed more than 72,550,000 trips outside the country, an 8.0% increase over 2015, year-to-date; trips outside of North America accounted for approximately 44.0%.²

More “new” infectious diseases are being recognized; recent examples: influenza A (avian) H5N1, first recognized in humans in Viet Nam in 2004, became a widespread zoonotic disease by 2008; influenza A (pandemic) H1N1 was first identified and became a global concern in 2009; Lassa, Ebola, and Marburg viruses „reappeared” as human disease risks in Africa in 2012 through 2015.^{3,4,5,6} Middle East respiratory syndrome corona virus (MERS-CoV) first appeared in 2013 and continues as a regional risk to human health; the ongoing risk of influenza A (avian) H7N9 in the Orient was first recognized in 2013, and, by the end of 2014, the H5N6 strain had appeared in China.^{5,6} Since then, Chikungunya and Zika viruses have become human disease risks in the Western Hemisphere.^{7,8} These agents have only added to, not replaced, already-existing infectious disease risks for international travelers.

As more people travel to areas where more disease risks exist, there is increasing need for pre-travel counseling and preventive interventions prior to departure.⁹ We have witnessed this over the past 20 years and conclude that local family medicine providers are best positioned to provide services to satisfy the increasing demand, especially as more families of two and three generations travel together. Clients should receive pre-travel counseling at least

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four to six weeks prior to departure, as some recommended vaccinations are two or more doses administered over a 30-day period.

TTU Family Medicine Travel Med Clinic operations:

We began our Travel Med Clinic, mid-1996, in response to corporate clients who needed to send employees outside the U.S. but could not obtain adequate preventive services locally. We developed a tri-fold brochure listing the available services, contact information, and location. We mailed the brochure to our city/county health department and local health departments in other counties in our patient catchment area of western Texas and eastern New Mexico. The brochure has been up-dated over the years and is available at our clinic's front desk and on our Department's website. The TravelMed Clinic number is also listed in local phone directories, and we receive referrals from other providers and by "word-of-mouth" from previous clients. To mid-November 2016, we had provided pretravel preventive services to over 3,250 persons, for travel to approximately 173 countries and autonomous or special administrative regions, e.g., Hong Kong, Kurdistan, and Macao.

We typically have TravelMed Clinic appointments available two or three half-days most weeks, for four to six international travelers each half-day. Up to three or four individuals traveling to the same destination(s) with the same itinerary may be seen during a "combined" appointment, as a provider's time is primarily used in counseling and answering destination-specific questions. The frequency of clinics varies as to: availability of nursing staff assigned that half-day; and season of the year, as more than 50% of the demand for our pre-travel preventive services occurs between mid-March and mid-July. We request that clients bring their vaccination record[s] to their appointment; children under 18 years of age usually have such records, but most adults do not.

Before deciding on specific recommendations, we ask each traveler to complete a brief medical history and answer three primary questions: "Where are you traveling to?", listing multiple destinations in order of arrival; "How long will you be in-country?"; and "What will you be doing while there?". For premenopausal women, we ask their pregnancy status and conduct a pregnancy test, because live-virus vaccines should not be administered during pregnancy. We also counsel pregnant women, and those who feel they might become pregnant during their trip, that they should postpone elective travel to Zika-endemic areas until after their pregnancy.

Our primary sources for destination-specific recommendations are: the U.S. Centers for Disease Control and Prevention (CDC), especially their Travelers' Health site¹⁰; Health Protection Scotland's Fit for Travel site¹¹, especially their country-specific malaria risk maps; and our subscription to ProMED-mail¹² for late-breaking posts about destination-specific outbreaks. Once a traveler agrees to specific recommended vaccinations, the assigned nurse prepares and administers those. We then discuss other issues with the traveler: prevention of person-to-person (contagious) diseases; necessary precautions for safe food and drinks; protection from arthropod and animal bites; anti-malaria prophylaxis, if necessary; concerns about the environment (e.g., altitude sickness, use of sun screen, etc.); preventing deep-vein thromboses on long airline flights; and any issues related to preexisting medical conditions or treatments. Travelers going on a photo safari to Africa, especially countries in or bordering East Africa's Rift Valley are counseled on how to prevent tsetse flybites. We especially counsel children (and their parents or grandparents) to avoid stray/street dogs and „roadside“ zoos.

Clients who have previously travelled internationally generally need less preventive health counseling. Some clients decline specific recommendations, and some may have additional pre-travel requirements from a sponsoring organization, which we fulfill. Some clients ask if "medical evacuation" insurance is advisable; we generally advise it for those who are going to be out-of-country more than two weeks and/or are going to engage

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in high-risk physical activities, especially in remote destinations. The article by Sanford, McConnell, and Osborn¹³ lists a potentially helpful website, <https://www.squaremouth.com>, for comparing travel insurance options. We remind clients if they have medical questions or problems after arrival at destination, which cannot be addressed by local professionals, the U.S. embassy in that country may be able to assist them.¹⁴ Before a clinic visit is completed, we provide the client with a list of all vaccinations administered during that visit. If they received yellow fever vaccine, we complete that page of their International Certificate of Vaccination (the “yellow card”) and list other vaccinations on the appropriate page. When all electronic notes have been signed by nursing staff, other providers, and the attending physician, the interventions are coded appropriately: each specific vaccine; any prescriptions; and preventive counseling for international travel.

If the client has health insurance, then the visit is billed to the insurer. However, since most plans only cover one “wellness” visit annually, the company may deny the claim if the patient has already had an annual exam or physical. The patient is then billed \$25-50, depending on the complexity of the visit (same as the self-pay cost for those without insurance). This is a competitive price based on a comparison with other in-network clinics (flat fee of \$35, no insurance billed). For students covered by the Academic Health Plan insurance, reimbursement is typically \$20-45.

Our current marketing approach involves posting fees and services on our website, with recommendation that a flat fee is probably best for capturing revenue without tying up additional resources to attempt collection (from a variety of insurance carriers with different policies). Any vaccines received by the client are billed at current rates, which are competitive with local commercial pharmacies.

Who we serve, and where they travel:

The clients we serve travel for many reasons; most trips, however, are elective and of one- to two-weeks duration. We provide a one-stop opportunity for two or three generations of the same family; these clients have ranged in age from three months to 80+ years. Our catchment-area includes large and small universities, and junior colleges, so we serve faculty and students for: academic field trips; return-home trips to visit family; or study-abroad programs of a semester or longer. People on business trips, off-shore oil workers, U.S. Peace Corps volunteers, military reservists, long-term missionaries, and eco-tourists also request our services. Country-specific destinations of our clients have varied from 55 to 85 each year, but the “Top 20” have been, in descending order of frequency: Kenya, India, Brazil, China, Peru, South Africa, Uganda, Costa Rica, Thailand, Viet Nam, Mexico, Tanzania, Zambia, Honduras, Guatemala, Belize, Panama, Ecuador[including the Galapagos Islands], Malawi, and Haiti. Although the year-to-year list varies, the “top 15” have been very consistent. We saw very few clients traveling to Haiti prior to the 2010 earthquake there; since then, we have seen many going to Haiti as members of various medical and non-medical mission teams. Because many international trips are elective, our clinic volume has been negatively impacted by events such as the “9/11” terrorist attacks, the U.S. economic downturn of 2008-2010, and the recent Zika epidemic in the Western Hemisphere.

Clients served from July 2015 - September 2016, and average revenues collected 2010 – 2014.

We selected a random sample of 165 clients’ records from among the 221 seen during July 2015 through September 2016. Fourteen of the 165 were excluded from the sample: eight (seen previously for vaccinations) only needed refills for anti-malaria medications, and six were returning for their 2nd or 3rd pre-exposure dose of rabies vaccine. Demographics of the remaining 151 clients are presented in the Table (below), and we feel this is an

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accurate representation of our TravelMed Clinic practice by: gender; age of client; time outside the U.S.; and reason for travel.

Table: Demographics of random sample of clients seen for pre-travel preventive services at Texas Tech Physicians Family Medicine Clinic; Lubbock, Texas during July 2015 – September 2016.

	Female (n = 84)	Male (n = 67)
Age [in years], mean	33.4	33.7
median	28.0	32
range	5 - 73	1 - 70
Weeks outside the U.S., mean	6.8	7.5
median	2.0	2.0
range	1 - 65	1 - 65
Reason for travel[median time]		
non-medical mission	31.0%; [1.75 wks]	31.3% ; [1.5 wks]
medical mission	10.7% ; [1.5 wks]	11.9% ; [5.0 wks]
vacation/tourism	21.4% ; [1.5 wks]	11.9% ; [1.5 wks]
academic activity	19.0% ; [3.5 wks]	14.9% ; [2.75 wks]
visit family	9.5% ; [2.0 wks]	10.5% ; [2.0 wks]
eco-tourism	3.6% ; [4.0 wks]	3.0% ; [15.0 wks]
business trip	2.4% ; [2.25 wks]	10.5% ; [2.0 wks]
other: adoption; military service; wedding; or religious pilgrimage	2.4%	6.0%

There were very few differences between the female and male clients in this sample; however, females were more likely to have traveled for academic reasons, while males were more likely to have traveled for business. Males also tended to be outside of the U.S. longer if on medical mission trips or eco-tours. We also looked back (2010 – 2014) at revenues collected for our TravelMed Clinic services, before we experienced a significant increase in the cost of yellow fever vaccine.

During those years we had an increase of clients each year (from 154 in 2010, to 252 in 2014) and maintained a stable revenue collection of \$190 - \$205per patient visit, in addition to insurance reimbursements. These data do not include collections for booster vaccine doses, following the initial TravelMed Clinic visit.

Types of services provided prior to international travel:

Vaccinations are our most-requested service, and the most-frequently administered are: tetanus, usually adult Tdap, for which most adults are not “current”; hepatitis A; and typhoid. Yellow fever vaccine is administered to approximately one-third of our clients, as we see many traveling to sub-Saharan Africa and tropical South America. Japanese encephalitis vaccine is often recommended for those traveling to endemic areas in East and Southeast Asia, especially if they will be visiting rural areas, or in-country more than 30 days. Hepatitis B vaccination is

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recommended for those going on medical mission trips; however, most medical professionals are already adequately vaccinated. Meningococcal vaccine and inactivated polio vaccine (one-time adult IPV, as a booster) are recommended for those traveling to destinations where CDC currently recommends such. Seasonal influenza vaccination is always recommended for those traveling during September through March, unless the client has a current vaccination history. Those traveling to the Southern Hemisphere or the equatorial tropics are reminded that “flu season” there is usually not September through March, but if the Northern Hemisphere vaccine formulation is available, we usually recommend it. Vaccine information factsheets¹⁵ are provided to the client, by the nursing staff, for each vaccine administered. Prescriptions for oral anti-malaria medications are the second most-frequent service our clinic provides. We also provide prescriptions for acetazolamide (Diamox®) for those who travel to altitudes above 8,000-9,000 ft. and feel they may need it during acclimatization. We rarely provide prescriptions for “rescue” antibiotics to treat generic travelers’ diarrhea; if a client insists on such a prescription, we usually refer them to their primary care physician.

Counseling about primary prevention:

The vast majority of clients do not „question“ the vaccines we recommend. Some arrive with a “list” and insist those vaccines are what they want, even though some may not be recommended for their destination[s]; yellow fever vaccine is often in this category. We provide each client with a destination-specific printout from CDC’s website¹⁰ and discuss that with them, beginning with the recommended vaccines. We explain why each vaccine is important and why one, or some, on their “list” may not be necessary. Cost is the usual reason a client doesn’t elect one or more vaccines; some insurance plans will not cover all, or part, of vaccine costs for pre-travel prevention. At the conclusion of our discussion, the client decides which vaccine[s] they want, and we honor their decision. This, and further discussion of the risks and benefits of each preventive measure, is shared decision making, and we feel strongly that this is the best approach for our clients.

Probably the most important service we offer clients is counseling to prevent diseases for which there are no available vaccines. Many first-time international travelers think that there is a vaccine to protect against malaria, or they are unaware of the areas where malaria is truly a risk. As we continue through the CDC printout, we discuss primary preventions (correct personal hygiene and behavioral responses) for diseases that are transmitted by: i.) close personal contact; ii.) unsafe foods and non-potable water; iii.) animal contact; iv.) contaminated environments; and v.) various arthropods, primarily mosquitoes and ticks.

The most frequent unsolicited request we receive is for a broad-spectrum antibiotic prescription to either prevent or treat generic travelers’ diarrhea (TD). In response, we remind clients that if they receive destination-specific vaccines, practice good personal hygiene, and are careful about what they eat and drink, they are much less-likely to suffer from generic TD. Even then, some travelers may experience a “change in bowel habits” because they are eating and drinking items with which their gastrointestinal (GI) flora may be unfamiliar.

As long as the GI upset doesn’t last more than 24 -36 hours and they are: i.) not experiencing a fever; ii.) Not becoming dehydrated; and iii.) not seeing blood or mucous in their stool, they should take bismuth subsalicylate (PeptoBismol®), two tablets by mouth after each meal, not to exceed eight tablets/day. Bismuth subsalicylate is contraindicated for those taking salicylates for other medical reasons; in such cases, we recommend loperamide (Imodium®) 4mg by mouth, then 2mg after each loose stool, as needed to relieve TD, not to exceed 8mg/day.¹⁶ If they have a more serious case of TD, we advise them to seek a medical diagnosis from a local professional.

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We don't feel comfortable providing clients with prescriptions for broad spectrum antibiotics, and then advising them to self-medicate when they do not have a diagnosis of bacterial disease[s]. Many cases of generic TD are not infectious, but, if so, are often of viral or protozoal etiology.¹⁷

We feel this counsel is equally as important as the list of recommended vaccines. In one large survey (16 large airports; four continents) of international travelers¹⁸, 52% to 56% of respondents did not perceive hepatitis A to be a risk, likewise 69% to 87% for hepatitis B, and 63% to 90% for typhoid fever. Among European travelers to areas of high malaria risk, 25% did not perceive this disease to be a risk. In a more recent study of pre-travel advice recall¹⁹, 95% of travelers remembered discussing the use of insect repellents to prevent arthropod-borne disease[s], 99% recalled the admonition to drink only bottled or boiled water to help prevent TD, but 13% did not remember to avoid eating raw or unpeeled fruits and vegetables. There is often much information to discuss in a limited amount of time, and some clients will retain more information than others. For that very reason, we provide the destination-specific CDC printout for the client to take with them, after we've highlighted pertinent risks, vaccines, and primary preventive strategies during face-to-face discussions. We also remind clients to call us as soon as possible before departure, should they have additional questions.

Conclusions

Every year more people are traveling to destinations beyond their national borders, and every year this leads to more instances of disease imported back to their country, as well as more cases of illness among those who are traveling.²⁰ Clearly more destination-specific disease prevention counseling should be accomplished, such as that provided in our TravelMed Clinic. We feel strongly that much more pre-travel preventive intervention should begin in local family medicine clinics, where the provider is closest to those who need it, especially multi-generation members of the same family. For readers who want more detailed discussions of specific disease risks faced by international travelers, as well as guidelines for prevention and treatment, we recommend the article by Hill DR, Ericsson CD, Pearson RD, et al.²¹ which also lists many valuable "travel medicine" websites.

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