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ABSTRACT & COMMENTARY

Hepatitis B and C Screening

By Lin H. Chen, MD

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Dr. Chen has received research grants from the Centers for Disease Control and Prevention and Xcellerex.

SYNOPSIS: *Adults with private healthcare insurance in the US have suboptimal testing for chronic HBV and HCV. Clearly, increased awareness is needed regarding HBV and HCV infections, epidemiology, risk, and screening.*

SOURCE: Spradling PR, Rupp L, Moorman AC, et al. Hepatitis B and C virus infection among 1.2 million persons with access to care: Factors associated with testing and infection prevalence. *Clin Infect Dis* 2012;55(8):1047-55.

This observational cohort study was conducted among 1.25 million adults from 4 private US healthcare organizations (HCO): Geisinger Health System, Danville, Pennsylvania; Henry Ford Health System, Detroit, Michigan; Kaiser Permanente-Northwest, Portland, Oregon; Kaiser Permanente, Honolulu, Hawaii. The study included persons who had ≥1 clinical encounter during 2006-2008 and ≥12 months of follow-up before 2009. The data on infections from this cohort was compared with those from the National Health and Nutrition Examination Survey (NHANES).

Hepatitis B virus (HBV) testing was done on 18.8% of 866,886 persons without a previous diagnosis, resulting in a 1.4% positive rate. Hepatitis C virus (HCV) testing was done on 12.7% of 865,659 persons without previous diagnosis, resulting in 5.5% positive. Among persons with at least 2 abnormal serum alanine aminotransferase (ALT), less than half were tested for HBV or HCV. Tests found that Asians were most likely to be infected with HBV (adjusted OR 6.33 compared to whites) whereas persons aged 50-59 years were most likely to be infected with HCV (adjusted OR 6.04 compared to age <30 years). The investigators estimate from NHANES that nearly ½ of HCV and 1/5 of HBV infections still remain unidentified.

■ COMMENTARY

It is estimated that 1-2% of the US population has chronic HBV or HCV infection, about 3.5-5.3 million persons, or 3-5 times more frequent than HIV infection. Among them, about 800,000-1.4 million have chronic HBV while 2.7-3.9 million have chronic HCV.[1] The last few years have brought advances in treatment for both HBV and HCV (for example, tenofovir, entecavir, telaprevir and boceprevir), and early therapy of chronically infected persons may provide sustained virologic response.

Both HBV and HCV are blood-borne infections. HBV can be transmitted vertically from infected mothers to infants during birth, as well as via sexual contact, sharing needles, and needle stick injuries. Foreign-born persons from endemic countries have an increased likelihood of being chronically infected. Asians and Pacific Islanders are the predominant groups of Americans with chronic HBV infection as well as having a disproportionately high incidence of hepatocellular carcinoma (HCC). However, African-American adults have the highest rate of acute infection, particularly in the South.[1]

HCV is usually transmitted via percutaneous blood exposure, including receipt of a blood transfusion before 1992 when testing for HCV became available, injection drug use, tattooing by unregulated shops, needle sticks, invasive procedures prior to universal precautions, and also sexual contact. African Americans and Hispanics have higher HCV infection rates than whites.[1]

Spradling and colleagues have demonstrated the low testing rates for HBV and HCV among large cohorts in the U.S. who have private health insurance. Their data substantiate the increased risk for HBV associated with Asian race. They also illustrate the low rate of HBV and HCV testing (14.9%) following determination of an elevated serum ALT, which only increases to 42-44% following a second elevated ALT.

Because more than half of new HBV infections diagnosed in the US were in foreign-born persons, the Centers for Disease Control and Prevention (CDC) expanded testing recommendations for HBV infection in 2008 to include persons born in countries with HBsAg prevalence of ≥2%. Despite this recommendation, and despite the demonstration of cost-effectiveness using 2% prevalence for screening chronic HBV, testing for HBV in the foreign-born has remained inconsistent. Many health care providers still lack knowledge about HBV infection, available tests, screening, and vaccination in these high-risk populations. The Boston Area Travel Medicine Network (BATMN), a research collaboration of 5 travel clinics in the greater Boston Area, found that only 25% of persons born in countries with HBV prevalence of ≥2% had been tested before their pre-travel consultations. An additional 11% of the at-risk travelers tested at the travel clinic visits led to new diagnosis of chronic HBV infection in 3.3%.[9]

Similarly, the CDC has recommended HCV testing for persons with possible exposures since 1998. However, risk-based testing strategy has yielded suboptimal results in identifying HCV-infected persons; a number of studies have found that providers lacked knowledge about HCV prevalence, natural history, diagnostic tests and treatment, and recommendations for testing. Moreover, only 55% of persons with HCV infection reported known exposure risk, and the remaining 45% reported no recognized exposure risk.[10] In 2012, CDC also expanded routine screening for HCV infection to include persons born between 1945-1965.[10]

The Institute of Medicine has identified deficiencies in knowledge and awareness, surveillance, immunization, and services for viral hepatitis in the US, and recommended strategies to optimize prevention and control of HBV and HCV, policies fully endorsed by the Department of Health and Human

Services and CDC.[1,3,10] Early diagnosis of chronic HBV and HCV infections can lead to improved therapeutic response, lower viral loads, halt progression to cirrhosis, and prevent hepatocellular carcinoma. Immunization should also be recommended for non-immune persons at risk for HBV exposure, household members and sexual contacts of HBV-infected individuals.

Specialists in fields with expertise in hepatitis and who may evaluate patients for reasons such as international travel — including those in travel and tropical medicine, infectious diseases, and gastroenterology — can reach this broader population that needs to be screened. Through the collaboration of specialists with primary care providers, significantly improvement of screening in high-risk populations is achievable. ■

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Human Brucellosis Exposure from a Harbor Porpoise

ABSTRACT & COMMENTARY

By Maria D. Mileno, MD

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Dr. Mileno reports no financial relationships to this field of study.

SYNOPSIS: *A porpoise carcass on the southern coast of Maine was recovered by a rescue team affiliated with a marine mammal facility; a tissue sample sent for culture grew an organism with morphologic and microscopic characteristics of a Brucella species. The Centers for Disease Control and Preventiion confirmed the isolate as* B. ceti *and initiated an investigation to determine whether aerosol exposure occurred among the 4 individuals who performed the necropsy evaluation of the porpoise.*

SOURCE: Sears S., Colby K., Tiller R, et al. Human Exposures to Marine *Brucella* Isolated from a Harbor Porpoise - Maine, 2012. MMWR 2012;61(25):461-463

On January 28th 2012 a porpoise carcass found by a rescue team affiliated with a marine mammal facility underwent a necropsy at a small room in a university facility within 24 hours. It was undertaken by a faculty member, two students and a community volunteer. They each wore gowns and gloves, but they worked without respiratory precautions. Necrotic tissue was removed from the uterine horn. An electric saw with an oscillating blade was used to cut the skull to evaluate the brain. The same individuals who performed the necropsy also cleaned the room after the procedure. Air was exhausted from the room directly outdoors thus persons in adjacent rooms to the necropsy room were felt to have minimal to no risk for exposure to *Brucella* organisms.

A swab sample of uterine horn tissue was sent for culture to a laboratory specializing in veterinary diagnostics, and an isolate was successfully cultured; it was forwarded to another lab for further identification. This event had already triggered high suspicion for a potential *Brucella* species infection and standard biosafety level 3 (BSL-3) precautions were taken at both laboratories, including use of biosafety cabinet for specimen manipulation. CDC received the samples on February 15th for confirmatory testing and the isolate was identified by multilocus sequence typing as sequence type 23 - a known sequence type associated with harbor porpoises. DNA testing for marine species are limited, and given that it was from a cetacean, the isolate was likely *B. ceti*

as opposed to *B. pinnepedialis*.

Since the staff members did not use respiratory protection while handling the porpoise or its specimens the four exposed staff members were advised to immediately begin a 3-week regimen of rifampicin and doxycycline for antimicrobial prophylaxis. They were to also conduct daily fever checks, undergo monitoring for symptoms of acute febrile illness weekly and have their serum tested for *Brucella* antibodies immediately, and at regular intervals for 24 weeks after the last known exposure. None of the four persons were found to have seroconverted nor did they become ill.

■ COMMENTARY

Brucellosis remains a significant worldwide economic and public health problem, especially in Mediterranean countries. Clinical manifestations of this zoonotic disease in humans are often nonspecific and variable making it difficult to recognize. Economically, brucellosis is an important disease of domesticated animals, yet the worldwide incidence of human brucellosis is unknown.

Much has been learned since 1887 when Sir David Bruce isolated *B. melitensis* from a sick patient and eradication programs were implemented in the U.S., however pockets of infection remain. *B. abortus* is a reproductive disease of cattle, bison, buffalo elk and camels, as well as secondary hosts such as goats, horses, dogs and wolves. This persistence of the organism in wildlife is an obstacle to its complete eradication in the U.S.[1,2] Large populations of feral swine in California, Texas, Florida and Hawaii harbor *Brucella* organisms as well. Dogs are a principal reservoir of *B. canis* in the U.S. and disease outbreaks have been reported in kennels and shelters.[3] Cases have also been reported among dog breeders and kennel workers who were exposed during the birthing process when exposed to infected tissues. Routes of transmission include foodborne exposures through ingestion of unpasteurized dairy projects. Direct or indirect exposure to the organism occurs through broken skin or mucous membranes when in contact with the aborted fetuses, placental fluids and tissues or during the slaughtering and butchering process. Aerosol transmission through inhalation or conjunctival inoculation do occur, but person-to-person transmission is very rare. An investigation of brucellosis cases among feral swine hunters led to the publication of an educational brochure for hunters by the USDA.

Among those working with marine mammals a few reports of human cases of neurobrucellosis exist.[4] Populations at risk include American Indian/Alaska natives who hunt marine mammals, wildlife researchers, veterinary staff as well as marine mammal rescue workers, such as those who were those involved in this reported case.

Some of the other systemic consequences of brucellosis can be severe and unexpected. The epidemiologic and clinical characteristics of 44 cases of aortic brucellosis were recently summarized by Cascio et al through a review of the literature and two additional cases of their own. This cardiovascular complication of brucellosis involved the ascending thoracic aorta in 18 patients. In 16 it occurred as a consequence of endocarditis occurring during brucellosis, and the descending thoracic aorta or the abdominal aorta were involved in the remaining 30 cases. In these latter cases it was associated with spondylodiscitis of the lumbar spine in 13 patients. A history of symptoms indicative of brucellosis was not universally present.[5]

Brucellosis is one of the 10 most frequently reported laboratory acquired infections in the U.S. Infections are most often due to direct handling of the organism, or being in close vicinity to its handling. Routine clinical laboratory procedures completed outside of a biological safety cabinet have led to exposures as well as accidents due to equipment malfunctions. There will be newly published guidelines this year for safe work practices in human and animal medical diagnostic laboratories which address how isolates are tracked between labs, risk assessment for potentially exposed workers, and recommendations for post-exposure prophylaxis. ■

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More Than Skin Deep

ABSTRACT & COMMENTARY

By Philip R. Fischer, MD, DTM&H

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Dr. Fischer reports no financial relationships to this field of study.

SYNOPSIS: *Despite advances in travel-related medications and immunizations, skin problems are still common among international travelers. Preventive behaviors, though not always well implemented, could*

be protective. Awareness of common skin problems associated with travel can assist providers in making accurate diagnoses and proposing effective treatments.

SOURCE: Morris-Jones R, Morris-Jones S. Travel-associated skin disease. *Infect Dis Clin N Am* 2012; 26:675-689.

Almost anywhere in the world, insect bites can become uncomfortable entities. In sensitized individuals, allergic reactions can actually cause severe symptoms. The traveler does not usually have a specific recollection of being bitten, and bites usually have a central raised red area with surrounding paler erythema. Wound care is helpful to ensure cleanliness and decrease the risk of secondary infection, and symptomatic relief is available with oral antihistamines and topical corticosteroid creams. Future bites are usually avoidable by using repellents, insecticides, and barriers (clothes, nets).

Larvae can grow in human skin and cause myiasis, usually from Tumbu fly infections occurring in Africa and from botflies in Latin America. Covering the lesion(s) with oil for up to two hours causes the larvae to move out where they may be grabbed and removed with forceps. Tungiasis occurs when fleas develop in the skin; surrounding skin may be gently unroofed and the fleas extracted. Mites, such as scabies, burrow in the skin and can concurrently cause widespread pruritic lesions. Overnight application of topical treatments such as permethrin or malathion can be effective against scabies, but they should be repeated two weeks later since eggs might have survived the first treatment and continued to develop. Oral ivermectin is another treatment option. Cutaneous larva migrans results when animal hookworms happen to enter human skin; itchy serpiginous lesions result, and treatment with oral albendazole or ivermectin usually is effective.

Jellyfish stings are usually minor inconveniences, but stings from some jellyfish species lead to dangerous reactions. Immediate treatment usually involves rinsing the area with saltwater to remove nematocysts. Snake and scorpion bites can be uncomfortable; antivenom is required to treat severe systemic reactions to some species.

Symptomatic dengue fever can include both blanching and petechial rashes; supportive care is essential. Tick-borne illnesses can manifest themselves as peripheral rashes that become petechial; doxycycline is often effective treatment.

■ COMMENTARY

For 21 years, *Travel Medicine Advisor* has been informing travel medicine practitioners about the changing epidemiology of illness and about new advances in diagnostic methods and effective treatment. There has been progress. Some people practicing today barely remember a world without hepatitis A vaccines, mefloquine, and atovaquone-proguanil. Yet, during the past two decades, *TMA* informed readers about each of these then-new products. Compared to the time when *TMA* started, we are much better at preventing and treating many tropical illnesses. Beyond immunization and chemoprophylaxis, however, many other effective illness-preventing strategies require ongoing behavioral changes during trips, and this behavior modification is not easy.

A recent study of 152 traveling Dutch children identified insect bites as their most common travel-related ailment. Interestingly, 11% had bothersome bites prior to traveling, and 40% had bothersome bites during travel. Along with diarrhea (9% pre-travel and 30% during travel) and the common cold (6% pre-travel and 15% during travel), sunburn was another of the common ailments with 3% of Dutch children sunburned prior to travel and 19% having sunburn during travel.[1] Whether at home or traveling, these skin problems could have been prevented with the use of insect repellents and sunscreen.

For years, fever, diarrhea, and skin problems have been major concerns in returned travelers.[2] In a retrospective review of over 34,000 returned travelers who sought care at an outpatient travel clinic in Germany, 12% had skin problems.[3] Specific causes include arthropods in 23%, bacteria in 22%, helminths in 11%, and protozoa in 6%.[3] Similarly, skin problems ranked second only to diarrhea and were responsible for 25% of pediatric post-travel consultations in GeoSentinel-based travel clinics within 19 countries.[4] Skin problems were particularly common in children returning from Latin America.[4]

Astute travel medicine practitioners will be aware of less common causes of dermatitis in travelers such as caterpillar stings[5] and phytophotodermatitis from dribbled lime juice.[6] But, the common travel-related skin problems should be preventable — with careful insect bite avoidance, use of sunscreen, and cleaning of sites of superficial traumatic injury.

The practice of travel medicine is advancing. What will shape travel medicine in the years to come? While continuing to build on successes in the battle against life-threatening illness, we will devote increasing efforts to counter leisure-limiting inconveniences. There will continue to be improvements in pre-travel medical interventions, but we should also pursue evidence-based during-travel behavioral modifications that prevent injuries and avoid inconveniences. Perhaps there will be new injections and prescriptions that somehow prevent insect bites, sunburns, and dermatologic infections and infestations. More likely, however, travel medicine will enter into a new era, an era during which health advice is translated into hour-by-hour and day-by-day implementation of health-promoting behaviors. Environmental enhancements will improve the health not just of travelers but, importantly, of local populations. International travel will increase, and health should improve for all. ■

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Meningococcal Vaccine Recommendations for HIV+ Men Who Have Sex with Men

ABSTRACT & COMMENTARY

By Mary-Louise Scully M.D.

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Dr. Scully reports no financial relationships to this field of study.

SYNOPSIS: *A cluster of cases of invasive meningococcal disease among men who have sex with men (MSM) in New York City since September 1, 2012 prompts expanded recommendations for meningococcal vaccination in HIV-infected MSM patients felt to be at increased risk.*

SOURCE: New York City Department of Health and Hygiene. Alert # 28, 2012. Update: Meningococcal Vaccine Recommendations for HIV infected Men Who Have Sex With Men. https://a816-health29ssl.nyc.gov/sites/NYCHAN/WebPages/home.aspx Accessed Nov. 10, 2012.

Massachusetts Department of Public Health. Health Advisory. Meningococcal Vaccine Recommendations for Men Who have Sex With Men, October 25, 2012. http://www.mass.gov/eohhs/docs/dph/cdc/immunization/alerts-meningococcal-msm.pdf Accessed Nov. 10, 2012

There have been 14 cases of invasive Neisseria meningitidis infection among men who have sex with men (MSM) in the New York City (NYC) area since 2010. There was 1 case in 2010, 4 cases in 2011, and now 9 cases in 2012. Nine of 14 total cases were HIV-infected, and 3 of the 4 deaths that occurred were also in HIV-infected patients. Serogroup C *Neisseria meningitidis* was the predominant serogroup responsible for disease. The median age was 32 with a range from 21-59 years. Six cases lived in Brooklyn, 3 in Manhattan, 2 in the Bronx, 2 in Queens, and one was undomiciled. The estimated annual incidence rate of invasive meningococcal disease (IMD) in MSM is 5.9 per 100,000 compared to a rate in all other New Yorkers of 0.25 per 100,000.

In October, the New York Department of Health and Hygiene issued a recommendation to administer meningococcal vaccination to HIV-infected men who are NYC residents and who had intimate contact with a man met either through an online website, smart phone application, bar, or party since September 1, 2012. On October 25, 2012 the Massachusetts Department of Health followed up with a recommendation to immunize MSM, especially those infected with HIV, if their travel or travel plans included visiting NYC with expected close social interaction with other MSM, or if such social interaction with men from NYC occurs on a regular basis.

■ COMMENTARY

Invasive meningococcal disease (IMD) remains a feared disease both among the lay population and heath care workers, as the disease is known for its rapid progression and high morbidity and mortality if there is a delay in diagnosis and initiation of treatment. IMD can begin with non-specific flu-like symptoms, but can progress quickly to severe headache, stiff neck, photophobia, nausea, vomiting, altered mental status, and sepsis. All ill patients should be closely examined for the presence of a petechial or purpuric rash, which is often present with meningococcemia. However, in the early stages of illness the rash may be maculopapular and blanch. In addition, severe muscle pain, usually in the extremities or back, or severe abdominal pain may be an early clue to the diagnosis.

Three quadrivalent meningococcal vaccines are available in the United States and include protection against the four serogroups of *N. meningitidis* (A, C, W135, and Y). Serogroup B is not included in any of the vaccines. Serogroups B, C, and Y cause the majority of disease in the United States, whereas serogroup A, C, and W-135 are associated with outbreaks within the classic meningitis belt of sub-Saharan Africa.[1] In patients 55 years of age and younger, a meningococcal conjugate vaccine (MCV4) should be used. HIV- infected adolescents and HIV-infected patients under age 55 who meet criteria for immunization should receive two doses of MCV4 separated by 8 weeks. For patients 56 years and older polysaccharide vaccine (MPSV4) is the approved vaccine for use and only one dose is needed. However, health care providers have the option to administer MCV4 off-label

to older patients with the same 2-dose schedule used in younger patients. Influenza vaccine can be administered at the same time as either MCV4 or MPSV4.

At the present time, meningococcal vaccine is not universally recommended for all HIV-infected patients, though the lesson learned from this outbreak is that MSM and in particular HIV-infected MSM are at higher risk for invasive meningococcal disease and death. So in light of this report, in my own practice I plan to discuss and offer meningococcal vaccination to all my HIV-infected MSM patients since as Ben Franklin once said wisely "an ounce of prevention is worth a pound of cure." ■

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Differences in Travel-Associated Diseases between Older and Younger Adults

ABSTRACT & COMMENTARY

By Richard R. Watkins, MD, MS, FACP

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Dr. Watkins reports no financial relationships to this field of study.

SYNOPSIS: *This study analyzed prospective data from 1997 to 2009 on ill international travelers. Compared to younger travelers, those 60 years and older had a higher incidence of lower respiratory infections, high-altitude pulmonary edema, phlebitis and pulmonary embolism, arthropod bites, severe malaria, rickettsiosis, gastritis, peptic ulcers, esophagitis and gastroesophageal reflux disease, trauma and injuries, urinary tract infections, heart disease, and death.*

SOURCE: Gautret P, Gaudart J, Leder K, et al. Travel-Associated Illness in Older Adults (>60 y). *J Travel Med* 2012;19:169-77.

Currently adults aged 60 years and older represent 15%-30% of international travelers. This age group is believed to be at increased risk for travel-related illnesses for several reasons, including their increased probability of underlying medical conditions, waning immunity from previous vaccinations, reduced immune response to vaccines given prior to their trip, and a greater predisposition to acquiring certain diseases. Indeed, this is well known by those in the insurance industry who regularly charge older travelers much higher premiums than their younger counterparts. In this study, investigators sought to determine the range of illnesses among older adult travelers. They utilized prospective data from patients who presented to GeoSentinel sites from March 1997 to August 2009.

The GeoSentinel Surveillance Network is a group of travel medicine clinics on six continents where ill travelers are seen during or after traveling to a range of destinations. Patients were eligible to be included in the database if they crossed an international border and sought medical advice at a GeoSentinel clinic for a presumed travel-related illness, or had been diagnosed with a disease related to travel history by the clinic physician. Data collected included demographic information, travel data, reason for travel, inpatient or outpatient status, history of a pre-travel clinic visit, and travel-related clinical findings. Co-morbid illnesses and chronic conditions were not documented in the database.

A total of 63,076 ill adult travelers were included in the database, of which 7,034 were aged 60 years and older (8.4%). Compared to younger travelers, older patients were more likely to be male, reside in North America, travel for tourism, travel for a shorter duration, and less likely to have sought travel advice before their trip. Acute diarrhea was the most common illness in both groups, although it was comparatively less frequent among the older travelers. Respiratory illness was the second most common condition in the older group, while febrile systemic illness was second in the younger travelers. Illnesses that were significantly more common in the older group included lower respiratory tract infections, high-altitude pulmonary edema, arthropod bites, Plasmodium falciparum severe malaria, rickettsiosis, gastritis, peptic ulcer, gastroesophageal reflux disease, strongyloides, trauma and injuries, altitude sickness, vertigo, cerebrovascular accident, urinary tract infections, heart disease, phlebitis, pulmonary embolism, and death. Subanalysis revealed an inverse relationship between age and *P. falciparum* malaria and dengue among ill travelers ($p < 0.001$).

The main strength of this study was its multicenter design, which allowed for a large number of participants from many countries. It was limited because the data collected may not be representative of the overall population of travelers, and the results may not be generalizable to the illnesses usually seen at non-specialized primary care offices where mild or self-limited conditions present with more frequency. Also, underlying chronic diseases were not documented by GeoSentinel which does not allow evaluation of their impact on travel-associated morbidity. The authors concluded that older travelers have a higher relative proportion of life-threatening illnesses (lower respiratory tract infection [LRTI], high-altitude pulmonary edema, severe *P. falciparum* malaria, cardiovascular disease, and pulmonary embolism) and should be specifically targeted for prevention of such diseases.

■ COMMENTARY

It has become common to see adults aged 60 years and older in travel clinic. Individuals in this age group are believed to be at higher risk for travel-associated illnesses.[1] Hence, it seems prudent that specific travel advice tailored to this age group be established, in addition to other routine precautions and interventions (i.e. vaccines) given to all travelers. The study by Gautret and colleagues provides useful data towards building this base of recommendations. It was a large multicenter study that used data collected from the GeoSentinel Surveillance Network, which is supported by the Centers for Disease Control and Prevention. The authors found that the spectrum of illnesses varied widely depending on the age of travelers after eliminating confounding factors, such as travel destination. Older travelers suffered more morbidity from age-related conditions, such as cardiovascular diseases. Another recent study confirmed this observation, wherein the main cause of death in travelers over age 65 was cardiovascular (70%), followed by infectious disease (12%).[2] It was interesting that acute diarrhea occurred with less frequency in the group of older travelers. The authors speculate this was due to an increased likelihood of past exposure to pathogens or better adherence to reduced risky dietary exposures. Alternatively, the older travelers may have taken antibiotics and/or antimotility agents with more frequency. Given their greater proportionate morbidity from LRTIs, older travelers should take precaution against respiratory illnesses. The authors suggest good hand hygiene, use of disposable handkerchiefs, and face-masks in crowded conditions. Influenza was the most common vaccine-preventable disease in the study, supporting the recommendation that all travelers be given the influenza vaccine. Pneumococcal vaccination is another intervention older travelers can do to lessen their risk for LRTI, as can younger travelers with chronic illnesses. With the higher risk for severe illness from *P. falciparum* malaria in older travelers, malaria chemoprophylaxis along with insect repellant and mosquito nets should be emphasized. ■

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CME Objectives & Instructions

Upon completion of this educational activity, participants should be able to:

- discuss the latest data regarding the diagnosis and treatment of various travel-related diseases;
- explain new data concerning recommended precautions and prophylaxis for patients traveling to specific areas of the world;
- implement strategies in the practice setting to inform patients of disease outbreaks and epidemics relevant to their travel plans.

To earn credit for this activity, please follow these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

CME Questions

1. Chronic hepatitis B and chronic hepatitis C infections:
   A. Can usually be detected by review of exposure risks.
   B. Are uniformly screened for in persons with private health insurance.
   C. Have newer antiviral therapies that can lead to sustained viral response.
   D. Occur rarely in Western developed countries such as the US.

2. Each of the following represents a common or usual scenario for the transmission of brucellosis except one. Which of the following is least likely to result in transmission of brucellosis.
   A. Person-to-person transmission.
   B. Inhalation exposure from infected aerosols.
   C. Transmission through cuts or open lacerations.
   D. Exposure to animal tissues during birthing.

3. Which of the following statements are true about invasive meningococcal disease (IMD) and its prevention?
   A. Serogroup B can be prevented with vaccination
   B. Meningococcal vaccination is contraindicated at ages over 65
   C. The annual incidence rate of IMD in MSM in New York City exceeds that of the general population.
   D. Meningococcal vaccine should not be co-administered with influenza vaccine.

PHARMACOLOGY WATCH

Supplement to *Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Hospital Medicine Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.*

Menopausal Hormone Therapy and the Risk for VTE, AD

In this issue: Menopausal hormone therapy and risk of VTE and AD; patients' understanding of chemotherapy benefits; and FDA actions.

Hormone therapy and VTE risk

The different drug formulations of menopausal hormone therapy (HT) may determine the risk of venous thromboembolism (VTE), according to a new study. It is known that combined estrogen-progesterone therapy has a higher risk of VTE than estrogen-only therapy, and oral therapy has a higher risk than transdermal therapy. Now, a follow-up study from the Million Women Study with more than 3.3 million patient-years of follow-up looks at the varying risks of different HT combinations. The risk of VTE was again found to be significantly higher for combination estrogen-progesterone therapy compared to estrogen-only therapy (relative risks [RR] = 2.07 [95% confidence intervals (CI) 1.86-2.31] vs 1.42 [1.21-1.66]). Transdermal estrogen-only therapy resulted in no excess risk for VTE (RR 0.82 [0.64-1.06]). Among users of combination estrogen-progesterone, the risk of VTE varied by progestin type with significantly greater risk for preparations containing medroxyprogesterone compared to other progestins (2.67 [2.25-3.16] vs 1.91 [1.69-2.17]; *P* heterogeneity = 0.0007). The risk of VTE was significantly higher (2 times the risk) in the first 2 years after starting combination HT than later years. Five-year risks for pulmonary embolism (PE), both fatal and nonfatal, were calculated as: 1 in 664 for never users of hormone therapy, 1 in 475 for current users of oral estrogen-only, 1 in 390 for users of estrogen-progesterone containing norethisterone/norgestrel, and 1 in 250 for users of estrogen-progestin therapy containing medroxyprogesterone. The authors conclude that VTE risk varies considerably by HT formulation and is greatest in users of oral estrogen-progesterone therapy containing medroxyprogesterone. One case of PE could be avoided for every 1295 current users of oral HT if estrogen-only rather than estrogen-progesterone was used. Among combined HT users, one PE in 700 women could be avoided by use of a progestin other than medroxyprogesterone (*J Thromb Haemost* published online Sept. 10, 2012. doi: 10.1111/j.1538-7836.2012.04919.x). These data follow on the Women's Health Initiative, which also showed a higher risk of breast cancer for combination hormone replacement therapy vs estrogen-only therapy, but this risk is offset by the risk of endometrial cancer in women with an intact uterus on unopposed estrogen. ■

Hormone therapy and AD risk

Does the timing of menopausal HT affect the risk of Alzheimer's disease (AD)? Several studies have suggested the timing of postmenopausal HT is critical, especially during the first 5 years after menopause when hormones appear to be somewhat neuroprotective. The Women's Health Initiative (WHI) study clearly showed that starting HT after age 65 had no effect on cognition and in fact may be harmful. Now a new study confirms that starting HT immediately after menopause may have neuroprotective benefits. In a follow-up from the Cache

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County study, 1768 women provided a detailed history on age at menopause and use of HT between 1995 and 2006. During this interval, 176 women developed AD. Women who used any type of HT within 5 years of menopause were at 30% less risk of AD (95% CI, 0.49-0.99), especially if they used it for 10 years or more. By contrast, woman who started HT 5 or more years after menopause did not have a decreased rate of AD. Confirming the WHI findings, rates of dementia were nearly doubled among those who began combination estrogen-progesterone compounds later in life. The authors conclude that the association of HT and the risk of AD may depend on the timing of use. HT appears to be beneficial during the critical window near menopause, but may be associated with an increased risk if initiated later in life. (*Neurology* 2012;79:1846-1852). An accompanying editorial suggests that AD and coronary heart disease share common risk factors. WHI data show that women assigned to HT close to menopause had a reduction in the risk of coronary heart disease, whereas women given HT later in life had increased risk. The same seems to be true for the risk of AD. Two soon-to-be published studies will provide evidence regarding hormone effects on cognition in younger postmenopausal women (*Neurology* 2012;79:1840-1841). The decision to initiate HT in postmenopausal women is generally based on severity of symptoms, risk of breast cancer, risk of venous thromboembolic disease, and other factors. Benefits on cognition and potential protection against AD may now need to be added to the equation. ■

Chemotherapy often misunderstood

Chemotherapy for metastatic lung or colon cancer may provide palliation and prolongation of life by weeks or months, but a new study shows that most patients with these diseases erroneously think that chemotherapy is curative. Researchers studied nearly 2000 patients in the Cancer Care Outcomes Research and Surveillance study who were alive 4 months after diagnosis of stage IV lung cancer or colorectal cancer. All patients received chemotherapy. Overall, 69% of patients with lung cancer and 81% of those with colorectal cancer did not report understanding that chemotherapy "was not at all likely to cure their cancer." This misunderstanding about the benefits of chemotherapy was more prevalent among nonwhite and Hispanic patients as compared to non-Hispanic white patients (odds ratio [OR] for Hispanic patients 2.82, 95% CI, 1.51-5.25; OR black patients 2.93, 95% CI, 1.80-4.78). Patients who rated communication with their physician favorably also had a higher OR (1.90; 95% CI, 1.33-2.72). Educational level, functional status, and the patient's role in decision making were not associated with inaccurate beliefs about chemotherapy. The authors conclude that "many patients receiving chemotherapy for incurable cancers may not understand that chemotherapy is unlikely to be curative." This misunderstanding suggests that patients "have not met the standard for true ongoing informed consent" and may not accept toxic treatment with no reasonable hope of cure. The data also suggest that patients rate their doctors as better communicators if they are more optimistic. The authors suggest that honest communication is "a marker of quality of care" but may cause lower patient ratings (*N Engl J Med* 2012;367:1616-1625). ■

FDA actions

The FDA has approved a new drug for the treatment of chronic myelogenous leukemia (CML). Omacetaxine mepesuccinate is a protein translation inhibitor that was originally identified in the 1970s as a potential treatment for CML as well as other hematologic conditions and even solid tumors. It was eventually dropped from development as the tyrosine kinase inhibitors (TKIs) became the mainstay of therapy. Emerging resistance to imatinib and other TKIs has led to renewed interest in the drug. It was recently approved for chronic, accelerated, or blast-phase Philadelphia-chromosome-positive CML that is resistant or in patients who are intolerant of other therapies including TKIs. Approval was based on a study of patients in chronic or accelerated-phase CML who had been treated with two or more TKIs. Omacetaxine is administered by subcutaneous injection. It is marketed by Teva Pharmaceuticals as Synribo. It joins Pfizer's bosutinib (Bosulif), which also was recently approved for the same indication.

The FDA has approved perampanel as adjunctive treatment for partial onset seizures in patients 12 years of age and older. The drug is the first in its class of noncompetitive AMPA receptor antagonists that are taken orally once daily. Approval was based on data from three Phase 3 studies of nearly 1500 patients with partial-onset seizures which found that perampanel, when used as an adjunctive therapy with other anti-seizure medications, significantly reduced seizure frequency. The drug comes with a boxed warning regarding serious neuropsychiatric events including agitation, aggression, anxiety, paranoia, euphoria, anger, and irritably. Perampanel is marketed by Eisai Inc. as Fycompa. ■