



INFECTIOUS DISEASE ALERT®

A twice-monthly update of developments in infectious disease, hospital epidemiology, microbiology, infection control, emporiatrics, and HIV treatment

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Hand Hygiene in Hospitals: Not Enough Time

A B S T R A C T S & C O M M E N T A R Y

Sources: Pittet D, et al. *Ann Intern Med* 1999;130:126-130; Boyce JM. Editorial. *Ann Intern Med* 1999;130:153-155.

Pittet and associates set out to identify predictors of noncompliance with hand-washing during routine patient care in a 1300 bed teaching hospital in Geneva, Switzerland, by examining the activities of 520 nurses, 158 physicians, 166 nursing assistants, and 199 other types of healthcare workers caring for 964 (70%) of the beds in December 1994. Five trained observers noted the number of opportunities for hand-washing that presented themselves after each patient contact; between care of a dirty and a clean body site; after contact with body fluid; before and after care of an intravenous site, a wound, the respiratory and urinary tract, as well as after glove removal; and after any activity involving indirect patient contact or hospital maintenance. They also noted how often hands were actually cleansed. The hospital guidelines recommended that hands be washed with soap and water or be disinfected before and after patient contact, after contact with a potential reservoir of microorganisms such as body fluids and substances, mucous membranes, broken skin, or inanimate objects that are likely to be contaminated, and after removing gloves that were required for contact with mucous membranes, broken skin, or any moist body substance.

Average compliance was only 48% of the 2834 observed opportunities for hand-washing, with physicians being least compliant (30%) and nurses being most compliant (52%). Compliance was better on weekends (59%) than during weekdays (46%) and worst in intensive care units (36%), with medical and surgical wards being 47-52% compliant. Similarly, hands were least likely to be cleansed after procedures involving a high risk of contamination (38%) than after other procedures (49-52%) and when the intensity of patient care was high (37% for more than 60 opportunities for hand-washing compared with 58% for less than 20 opportunities). Pittet et al concluded that the moderate compliance with hand-washing might be explained by the intensity of care, suggesting that

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understaffing may lower the quality of patient care.

■ COMMENT BY J. PETER DONNELLY, PhD

With nosocomial infections complicating as many as one in 10 hospital admissions, the problem is not negligible. Since the days of Ignaz Semmelweis, the medical community has been confronted with the simple truth “clean hands—fewer infections.” Why then did only half of the healthcare workers follow this simple rule? The answer may well lie in the fact that they are all too busy after all. This is almost certainly true for those nurses who have to care for patients’ clean and dirty body sites and are most likely to wash hands once they have finished rather than in between each and every step in the patient’s care. Pittet et al point out that it takes 8-10 seconds to wash the hands and might take 1 minute to go from the patient to the sink, wash their hands, and return to their patient. Nearly half of the observed opportunities to wash the hands occurred at a rate of 21-40 per hour of care, occupying a prohibitively large amount of the working hour. This is reinforced by the better compliance observed on weekends when hospitals run a less intensive service and the extremely poor compliance seen during the care of critically ill patients, confirming the perception of healthcare workers that they are often too busy to wash their hands as recommended.

There is a relationship between the intensity of patient care and noncompliance with hand hygiene recommendations, meaning that hand-washing is not only a matter for the individual but also for the organization. Reducing workloads would, therefore, seem a necessary part of the solution to the problem of failure to wash the hands. In an accompanying editorial, Boyce emphasized that hospital administrators should “strive to create an organizational atmosphere in which adherence to recommended hand hygiene practices is considered an integral part of providing high-quality care.” Strangely, Boyce did not mention improving staff/patient ratios at all, not even for nurses who are perceived to be the most likely to cross-infect patients because of the nature of their contact with patients. Rather, he suggested that a record of adherence to hand hygiene recommendations should form a part of the annual personnel evaluation. Clearly, it is intolerable that hand washing is still neglected to almost the same extent as it was in Semmelweis’s day and it is time for hospitals to get serious about improving hand hygiene in hospitals. But if there really is not enough time to comply with hand hygiene, it is hard to see a solution while there continues to be a drive toward maximizing “productivity” by employing fewer people to care for more patients in a shorter period of time. ❖

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Highlights from the ASTMH Meeting in Puerto Rico: Cancelled, but Not Forgotten

SPECIAL COVERAGE

The clinical sessions that had been a planned part of the American Society of Tropical Medicine and Hygiene meetings had been replete with abstracts of potential interest to our readers. When those meetings were cancelled due to hurricane damage in Puerto Rico, we attempted to retrieve and highlight clinical information that would have been presented at those annual meetings. This issue continues our reviews and highlighting of several additional clinical abstracts by the associate editors. For those who wish to obtain copies of the abstract book, it is officially designated as the Program and Abstracts of the 47th Annual Meeting of the American Society of Tropical Medicine and Hygiene (a supplement to *Am J Trop Med Hyg* 1998;59:3 for September). Additional copies of the abstract book can be obtained from the Society (telephone: 847-480-9592). (Dr. Frank J. Bia is Professor of Medicine and Laboratory Medicine; Co-Director, Tropical Medicine and International

Loiasis

Administration of diethylcarbamazine (DEC) is the current pharmacological standard of care for treatment of *Loa loa* infections. It is curative for approximately 60% of non-endemic patients with loiasis, yet some individuals continue to have signs and symptoms of infection despite multiple courses of DEC. In this abstract, Klion AD and Nutman TB report successful treatment of loiasis with albendazole. Three patients with refractory loiasis, defined as persistent symptoms of monthly Calabar swellings (2 patients) or malaise, myalgias, and arthralgias (1 patient) were given albendazole 200 mg by mouth, twice a day, for 21 days. Following therapy, symptoms resolved in all three patients, and, in two of them with Calabar swellings, symptoms have not recurred in seven years.

Loa loa is a filarial parasite commonly found in West and Central Africa. It is commonly known as the "eye worm" since adult worms are occasionally seen moving across the eyes of patients. It does not result in disfiguring lymphatic filariasis, yet it may cause serious complications when the organism invades the central nervous system or other vital organs. An epidemiological correlation has been observed between loiasis and the occurrence of endomyocardial fibrosis, suggesting that the hypereosinophilia induced by loiasis may lead to cardiac damage. Nephropathy and encephalopathy are far less common. Nodules in the conjunctiva, swelling of the eyelids, and proptosis have each been reported from Uganda as ocular complications of loiasis. Adult worms may be obvious when they pass under the conjunctiva of the eye or under the skin. They usually appear, but then disappear without a trace. Hypereosinophilia, especially in expatriates from nonendemic regions, is common. Clinical manifestations of loiasis include Calabar swellings that are most often observed on the wrists and ankles but can appear anywhere on the body. They are usually painless, nonpitting swellings, 5-20 cm in diameter, and last hours to days. One swelling occurs at a time, and it may recur at irregular intervals for years after the patient has left an endemic area. Other common symptoms include fatigue, generalized malaise, pruritus, and arthralgias. The death of an adult worm may cause a localized abscess, or to their calcification, making them radiographically detectable.

Albendazole has been used more broadly since its introduction—for more than just FDA-approved indications of neurocysticercosis and hydatid disease. It has had a good track record in terms of safety, and adverse events were described generally as mild, resolving without treatment. Abnormal liver function tests, abdominal pain, nausea, vomiting, headache, dizziness, meningeal

signs, reversible alopecia, and fever have all been reported, but at a low incidence rate. Fewer than 1% of patients may develop leukopenia. Albendazole has been shown to be teratogenic in pregnant rats and rabbits and should be avoided in pregnant women at this time.

Although this report describes a small number of cases, each had a remarkable response with prolonged follow-up. Albendazole shows promise as an alternative agent for the treatment of loiasis. It may be an important macrofilaricidal drug addition for treatment of this disease, as well as for the treatment of strongyloidiasis. (*Abstract 77.*)

Strongyloidiasis

A retrospective analysis of patients attending the Tropical Disease Unit at the University of Toronto between 1990 and 1996 assessed those who received *strongyloides* serological evaluation by enzyme-linked immunosorbent assay (EIA). Fifty-six of 94 subjects demonstrated *strongyloides* on stool examinations or culture. *Strongyloides* serology was positive in 95% of those with documented infections. In 46 treated cases, the mean time for 50% reduction of antibody titer was six months. Within that time period, 34% of those with documented infections and 45% of those without documented infections detected developed a negative serological test. Eosinophilia was present in 70% of those with documented infection and in 81% of those who only showed a positive *strongyloides* seropositivity. Return to normal occurred in 66% of those with documented strongyloidiasis and in 45% of those without documented parasites. *Strongyloides* serology appeared to be a sensitive test in this group for predicting successful treatment, with more specificity than following eosinophilia alone.

Unpublished data from our own hospital in Rhode Island support the use of serum antibodies against *Strongyloides stercoralis* to follow patients treated for strongyloidiasis. One family practice physician, who has become popular with the Cambodian community in Rhode Island, has followed approximately 40 asymptomatic patients who had eosinophilia and positive *strongyloides* antibody titers and treated them with thiabendazole. Nearly all tended toward lower antibody titers, although not all were done by the same lab using the same methods. Reference labs had changed hands and altered methodologies, but his findings support the data reported in this abstract from another "real-life" clinical care setting. (*Abstract 78.*) (*Dr. Maria D. Mileno is Director, Travel Medicine, The Miriam Hospital; Assistant Professor, Brown University, Providence, RI.*)

Leptospirosis

Following a 1996 hurricane, the incidence of lep-

tospirosis rose in Puerto Rico and Nicaragua (*TMA Update* 1998;8:2). Now, following Hurricane Mitch, leptospirosis is being increasingly identified in Central America. In addition to prompting cancellation of the 1998 ASTMH meeting, a hurricane can also increase flooding and stimulate increased contact between humans and spirochete-contaminated fresh water.

Had the 1998 ASTMH meeting taken place, DA Person from the Tripler Army Medical Center in Hawaii would have presented a report of nine children from Kosrae State, Federated States of Micronesia, who were diagnosed with severe leptospirosis. Infection is usually acquired through contact of mucus membranes or broken skin with contaminated fresh water, soil, vegetation, or infected animals. Each of these nine children had a history of exposure to a potential source of leptospirosis, and the majority were boys. Pancreatitis and acute renal failure, with anuria lasting 3-6 days, were common; pulmonary findings and a large pleural effusion were noted in one child. In the more recently treated patients, a "pulse" dose of corticosteroids was associated with reversal of renal failure and avoidance of dialysis. (There have been other anecdotal reports of the usefulness of steroids in leptospirosis, but controlled studies are lacking.) Leptospirosis is a common zoonosis. The diagnosis should be considered in individuals with febrile illnesses after potential spirochete exposure. Severe disease with liver and kidney involvement is still treatable. Antibiotic and, perhaps, corticosteroid therapy should be initiated for potentially affected individuals. For a review of the leptospirosis symposium presented at the 1997 ASTMH meetings, see *TMA Update* 1998;8:1-3. (*Abstract 404.*)

Praziquantel Chemotherapy

For years, praziquantel has been a mainstay of therapy for schistosomiasis. In 1995, reduced schistosomiasis cure rates were noted in Senegal, and decreased effectiveness of praziquantel was confirmed in the laboratory (*Am J Trop Med Hyg* 1995;53:61-62). Then, in 1996, a report from the Nile delta region of Egypt noted tolerance of some schistosome strains to repeated treatments with praziquantel (*Am J Trop Med Hyg* 1996;55:214-218).

Morshedy and colleagues from Alexandria University were slated to discuss an area of reduced praziquantel susceptibility in the Nile delta that is hyperendemic for schistosomiasis. In the studied village, 58% of people were infected. Eight weeks following treatment with praziquantel (40 mg/kg), only 53% of previously infected individuals showed parasitologic cure; in children, only about one-third were cured with treatment. Morshedy et al question whether this village is a site of a tolerant or resistant schistosome strain.

Further studies of praziquantel susceptibility in different areas will help confirm if, indeed, this agent is losing effectiveness. In the meantime, further antischistosomal drug development efforts must continue. Practitioners of travel medicine might consider follow-up parasitological testing after praziquantel therapy to confirm cure, especially in travelers who have been to Senegal or Egypt. (*Abstract 81.*)

Malaria

The combination of atovaquone and proguanil (Malarone) has been demonstrated to be effective in the prophylaxis and treatment of malaria. (See *TMA Update* 1998;8:35-36.) Is it safe in subjects who are glucose-6-phosphate dehydrogenase (G6PD) deficient?

Researchers evaluated the use of atovaquone-proguanil in 31 G6PD deficient individuals with uncomplicated falciparum malaria who were enrolled in clinical trials at several sites, and they compared the safety and efficacy of treatment between these patients and "normal" subjects. Similar adverse effects occurred in the two groups, and no G6PD deficient subject was withdrawn due to side effects. Measures of hemolysis were not different when compared in the two groups. Each G6PD deficient patient achieved clinical and parasitologic cure with a three-day course of treatment.

Atovaquone-proguanil appears to be safe in G6PD deficient subjects. It also provides effective cure of falciparum malaria. As resistance to antimalarials increases around the world, this combination therapy holds great potential for increasing usefulness. (*Abstract 75.*) (*Dr. Philip R. Fischer is Associate Professor of Pediatrics, Department of Pediatric & Adolescent Medicine, Mayo Clinic, Rochester, MN.*) ❖

Which of the following is *not* true about leptospirosis?

- Leptospirosis is more common following hurricane-induced flooding.
- Leptospirosis is often contracted from animal urine-contaminated fresh water.
- Antibiotic therapy is helpful for individuals with acute leptospirosis.
- Corticosteroids are the mainstay of therapy for severe, life-threatening leptospirosis.
- Leptospirosis is not associated with severe renal insufficiency unless treated with corticosteroids during the acute phase of the disease.

Neuromuscular Manifestations of HIV in the Antiretroviral Era

Synopsis: *Distal sensory neuropathy and myopathy may occur in patients receiving current dosing regimens of combination antiretroviral therapy.*

Source: Simpson DM, et al. *AIDS* 1998;12:2425-2432.

Among 2467 largely asymptomatic HIV patients followed for more than three years in a multi-center randomized, double-blind, placebo-controlled trial (ACTG175) studying the effects of single vs. combination antiretroviral agents (including zidovudine [ZDV], didanosine [ddI], and zalcitabine [ddC]) for HIV, 9% (225) developed peripheral neuropathy. Of these, 22% (n = 49) were felt to result from protocol treatment or a combination of protocol treatment and HIV and, in the majority, were distal symmetrical polyneuropathy (DSP) in type (73%; n = 36), characterized by symptoms of burning, lancinating pain, pins and needles paresthesiae, and aching in the calves and feet. Among 34 polyneuropathy cases felt to be due to HIV or neither HIV or protocol treatment, only 15% (n = 5) were DSP. Risk factors for DSP development included older age and lower Karnofsky score (a disability scale reflecting patient's ability to perform life's activities), whereas gender, race, previous antiretroviral treatment, CD4 cell count, and body weight were not predictive.

Among 1067 antiretroviral-naïve HIV patients from the same cohort, only six developed myopathy while on the study drug, four with ddI and one each on combined ZDV-ddI and ZDV-ddC. Myalgia and muscle weakness were seen equally in all four treatment arms comprising ZDV alone, ddI alone, ZDV plus ddI, or ZDV plus ddC, and did not correlate with creatine kinase (CK) levels, although the latter were significantly higher in the ZDV-ddC group than in the other treatment groups. DSP and myopathy may occur with combination antiretroviral treatment and may require dose modification.

■ **COMMENT BY MICHAEL RUBIN, MD**

Since there was no control arm which did not receive therapy with a nucleoside analog reverse transcriptase inhibitor, and since there was no difference in frequency of neuropathy or myositis among the treatment arms, the question of the contribution of these drugs to the development of these complications cannot be answered by this study.

While neuropathy is a continuing problem in the management of HIV-infected individuals, the development of clinically significant myopathy appears to have diminished remarkably in frequency.

Polymyositis, necrotizing myopathy, and nemaline myopathy are well characterized forms of HIV-associated myopathy.¹⁻³ AZT (ZDV) myopathy, defined by the presence of ragged red fibers on muscle biopsy, is seen particularly among HIV-treated patients who have a total lifetime intake of more than 200 g of ZDV, and has been reported in 66% of this group. Apoptosis of CD4- and CD8-positive T cells, though present to a significant degree in lymph nodes of HIV patients,⁴ is not involved in clearing T-cell inflammation in HIV associated polymyositis and inflammatory neuropathy,⁶ nor has it been demonstrated in idiopathic polymyositis, dermatomyositis, or inclusion body myositis.⁷

Prior studies have demonstrated the efficacy of AZT in reducing the incidence of HIV-associated dementia. Highly active antiretroviral therapy (HAART) connotes a drug cocktail in which a new generation of anti-HIV drugs, protease inhibitors, including ritonavir (Norvir), saquinavir (Invirase), indinavir (Crixivan), or nelfinavir (Viracept), are added. Protease, essential for the final stage of the HIV life cycle, cleaves large polypeptide chains into functional proteins, allowing the HIV virion to mature. When protease is inhibited, structurally disorganized, noninfectious, and harmless viral particles are released from the cell. More powerful than previous antiretroviral agents in battling HIV, the effect of protease inhibitors on the central nervous system is unknown. Although ZDV penetrates the brain and improves cognition in HIV,⁸ the brain may remain unprotected from HIV dementia with other drug regimens. Total elimination of HIV from the host, the end goal of HIV therapy, may, thus, prove impossible if the brain remains a relatively protected sanctuary for HIV and a source of continued virus replication and dissemination.

Protease inhibitors, metabolized by the hepatic microsomal P450 system including cytochrome P450, 2D6, 3A4, and 2C9, share this pathway with the new generation of selective serotonin reuptake inhibitor antidepressants (SSRIs). The treatment of depression, common in the HIV population, engenders the potential for metabolic competition between these agents, with resultant toxicity of both groups of medication, a situation complicated by the 5-8% incidence of 2D6 deficiency in the caucasian population. The ability of some SSRIs and protease inhibitors to inhibit the P450 system befuddles the situation even further. Fundamental knowledge of the neuropharmacology and psychiatric potential of HAART agents will be critical in the neurologic management of HIV. (*Dr. Rubin is Associate Professor of Clinical Neurology, New York Presbyterian Hospital-Cornell Campus.*) ♦

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Risk factors for distal sensory polyneuropathy development in HIV include:

- a. race.
- b. older age and lower Karnofsky score.
- c. gender.
- d. CD4 cell count.
- e. body weight.

Special Feature

Lyme Disease Vaccine—LYMERix (SmithKline Beecham)

By William T. Elliott, MD, FACP,
and James Chan, PharmD, PhD

Lyme disease is the most common vector-borne infection in the United States and the incidence is increasing, with more than 16,000 cases annually.¹ The disease, caused by the tick-borne spirochete *Borrelia burgdorferi*, can be found throughout the nation but is particularly concentrated in rural and wooded areas in the Northeast, upper Midwest, and Pacific Northwest.

Work has been ongoing for years to develop a vaccine for this potentially debilitating, multisystem disease and, in December 1998, SmithKline Beecham received approval from the FDA to market the first Lyme disease vaccine (LYMERix). The vaccine contains an immunodominant outer surface protein (OspA) of *B. burgdorferi* produced by recombinant DNA technology and expressed by *E. coli*.

Indications

LYMERix is indicated for active immunization against Lyme disease in individuals 15-70 years of age. Safety and efficacy in children has not been established.

Dosage

Primary vaccination consist of 30 mcg/0.5 mL dose given intramuscularly at 0, 1, and 12 months. LYMERix

is supplied as single-dose vials and prefilled syringes.

The efficacy for this vaccine is based on administration of the second and third doses several weeks prior to the onset of the *Borrelia* transmission season in the local geographic area.²

Patients previously infected may also benefit from the vaccine, as such infection may not confer protective immunity.^{2,3} However, LYMERix should not be administered to patients with treatment-resistant Lyme arthritis, since these patients are immune reactive to OspA.²

Potential Advantages

LYMERix is the first vaccine found to be safe and effective for the prevention of Lyme disease. Efficacy has been shown to be 50% in the first year (after 2 doses) and 78% in the second year (after 3 doses) as defined by clinical and serologic evidence of Lyme disease.^{2,4} The incidence of disease was reduced from 0.77% to 0.39% the first year and from 1.27% to 0.27% the second year. The efficacy of preventing asymptomatic disease (defined as seroconversion with no clinical symptoms) was 83% the first year and 100% the second year. The incidence of asymptomatic seroconversion was reduced from 0.23% to 0.04% the first year and 0.27% to 0% the second year.²

Potential Disadvantages

The currently approved regimen requires one year to complete. After two doses, the vaccine provides modest protection of 50% (CI, 14-71%). The second year protection after the third dose increased to 78% (59-88%). SmithKline Beecham is studying several shortened regimens, including 0, 1, and 2 months, which may provide optimal protection,⁵ but the FDA has not approved these regimens. The vaccine has not been approved by the FDA for use in ages younger than 15 years. The percent of reported cases of Lyme disease in this population is 23%.¹

The most commonly reported side effects of LYMERix were injection site pain (22% vs 7% for placebo). Others included chills/rigors (2% vs 0.7%), fever (2.6% vs 1.6%), myalgia (4.8% vs 2.9%), and flu-like symptoms (2.5% vs 1.7%).²

The duration of immunity has not been established,² and longer-term studies will be needed to determine whether boosters are necessary and at what interval.

The vaccine may induce a false-positive serologic test for Lyme disease. If Lyme disease is suspected in a vaccinated patient due to a positive ELISA assay, a Western blot test must be performed.²

Comments

LYMERix is the first vaccine marketed against Lyme disease. The vaccine stimulates the production of antibodies against the OspA. *B. burgdorferi* express OspA while in the midgut of the tick but is no longer detectable once the spirochete is injected into the human host. The vaccine-induced human antibodies must be taken up by the tick during its blood meal and interact with the *B. burgdorferi* in the midgut of the tick to prevent transmission of the spirochete to the human host.

The efficacy of the vaccine was determined in a multicenter, double-blind, randomized, 20-month trial involving more than 10,000 subjects who lived in endemic areas in the United States.⁴ Study sites were in Connecticut, Maine, Massachusetts, Rhode Island, Delaware, Maryland, New Jersey, New York, Pennsylvania, and Wisconsin. Since the vaccine does not prevent all cases of Lyme disease, individuals at risk of exposure must be encouraged to take standard preventive measures such as wearing long-sleeved shirts, pants, treating clothing with tick repellent, and checking for and removing ticks. In addition, the vaccine does not prevent other tick-borne infections such as babesiosis or ehrlichiosis. LYMERix costs approximately \$50 per injection or about \$150 per course.

Clinical Implications

Lyme disease is a multisystem inflammatory disease. It usually, but not always, begins with erythema migrans (including the “bull’s-eye rash) and may be accompanied by flu-like symptoms. Weeks later, characteristics of early dissemination includes secondary skin lesions, neurologic involvement (e.g., meningitis, facial palsy), cardiac involvement (e.g., atrioventricular block), or migratory musculoskeletal pain may develop. Late dissemination includes episodes of arthritis and neurologic or psychiatric symptoms.^{1,6,7} The disease is frequently misdiagnosed, overdiagnosed, and overtreated, but it is also under reported and is a public health concern in endemic area.^{8,9} Lyme disease prevention, detection, and treatment are associated with substantial health care resources, and the disease can result in long-term morbidity.^{6,8,10}

In the Northeast and Midwest the main vector is the deer tick (*Ixodes scapularis*) while in the west the vector is the western black-legged tick (*Ixodes pacificus*). Most cases result from bites by the nymphs which most commonly occur in late spring-summer, although infection is possible at any time of the year.

The high-risk season may vary annually according to local weather conditions. The incidence varies from state to state but most cases are reported in the Northeast and upper Midwest. The highest reported case rates (per 100,000 population) in 1996 occurred in Connecticut (94.8), Rhode Island (53.9), New York (29.2), Pennsylvania (23.3), Delaware (23.9), and New Jersey (27.4). Moderate incidences of infection are reported by states such as Oklahoma, Kansas, Missouri, and Oregon (0.52-1.40 cases per 100,000) and the case rate in California in 1996 was only 0.3 cases per 100,000.^{1,2} The vaccine offers another strategy to prevent Lyme disease along with personal protection, insecticides, and wildlife management. Individuals most likely to benefit from vaccination are those who live, work, or spend their leisure time in endemic areas with frequent and prolonged exposure to wooded or grassy areas infested with Ixodes ticks. Widespread and routine use of the vaccine is not indicated. (Dr. Elliott is Chair, Pharmacy Education, California Division of Kaiser Permanente and Assistant Clinical Professor of Medicine, University of California San Francisco; Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.) ❖

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Which of the following is true about LYMERix?

- a. The duration of immunity has not been established.
- b. It is approved for use in adults and children.
- c. The vaccine is 95% effective after the third dose.
- d. The vaccine prevents tick bites.

Maybe Hotel Food is Better

Source: Kemmerer TP, et al. *Travel Med* 1998;5:184-187.

Corporate travel is a burgeoning part of today's global economy. Kemmerer and associates examined several health-risk behaviors of 226 Coca-Cola employees who traveled to international destinations during a six-month period in 1994. Prior to departure, all employees were referred to a nearby university-based travel medicine clinic where they received counseling, written information, and vaccines. Despite these precautionary measures, nearly one-half of those traveling to malarious countries were noncompliant with their chemoprophylaxis, although none developed malaria. Nearly one-half drank tap water, 14% ate raw meat, and 17% ate raw or poorly cooked seafood while abroad. Although most of the travelers ate the majority of their meals at their hotel, and usually ate hot cooked food, more than one-half ate food from cold salad bars or food that had been at room temperature for a prolonged period. Nineteen percent ate food purchased from street vendors.

Not surprisingly, traveler's diarrhea occurred in 35%. Risk analysis showed that eating in a fast-food establishment and, eating raw fish, raw meat, and foods at room temperature were all highly predictive of the occurrence of diarrheal illness, whereas eating hotel food was strongly protective. Eating food in a local home or purchased from a street vendor, or drinking tap water were not associated with illness in this study. An additional 29% of the travelers developed respiratory infection and 12% required medical attention.

Like others before them, Kemmerer et al discovered that adherence to medication and travel advice is unrelated to

the education level of the individual. Coca-Cola is now exploring ways to improve employee compliance with travel recommendations, including the use of a travel kit with analgesics, antispasmodics, sinus medications, and other helpful aids. ■

Sexual Activity While Traveling

Source: Gehring TM, et al. *J Travel Med* 1998;5:205-209.

Sex tourism—or just plain casual sex while traveling—remains a significant risk factor for STDs and HIV transmission. Up to one-third of new HIV infections in European travelers are believed to be acquired while traveling abroad. Gehring and associates queried departing travelers at the Zurich airport about their planned behavior and, upon return, their actual behavior. All departing travelers (n = 1689) received written information and brochures on health and sex-related issues and condom use, and an additional 418 (41%) agreed to participate in a brief educational intervention, which included a conversation about casual sex and condom use.

Although 93% of passengers knew condoms were the cornerstone of safe sex and virtually everyone who thought they might have sex planned to use condoms, only one-half of the approximate 7% of travelers reporting casual sex actually used them. The brief educational intervention appeared to have no effect on actual behavior. Although alcohol appeared to be the most significant risk factor for unsafe sex, "confidence" and "love" for the sex partner were also frequently referred to by returning travelers as a motivating factor in the decision to proceed without protection. Both this study and the previous one indicate the problem is not knowledge but behavior. Future interventions should be

directed at modifying behavior, not just providing education. ■

Weekly Antifungal Prophylaxis in AIDS

Source: Havlir DV, et al. *Clin Infect Dis* 1998;27:1369-1375.

Because of concerns over the cost-benefits of primary antifungal prophylaxis and the emergence of azole-resistant fungi, the use of prophylactic antifungal agents in patients with AIDS is generally limited to those with severe or frequent recurrences of thrush, or as secondary prophylaxis for esophagitis or other invasive fungal disease. Havlir and associates (including myself) explored whether fluconazole administered once weekly was as effective and less likely to lead to azole resistance when compared with daily dosing. A total of 636 HIV-infected subjects with CD4 counts less than 100/mm³ were randomized to receive fluconazole 400 mg weekly or 200 mg daily.

Deep fungal infection infrequently occurred, although the study was completed in 1995 (before the availability of more highly active antiretroviral therapy). Only 17 (5.5%) of those randomly assigned to daily and 24 (7.7%) of those given weekly fluconazole developed serious fungal infection (P = NS), most of which were esophageal infections, although a few cases of cryptococcal disease occurred. Thrush occurred almost twice as often in patients receiving weekly (19.9%) compared with daily (12.3%) fluconazole. Significant fluconazole resistance was not demonstrated in either treatment group, although only a minority of the isolates were tested.

Weekly fluconazole is an acceptable alternative to daily dosing for prevention of fungal infection in patients at significant risk, although its routine use does not appear warranted in most patients. ■