AHC Media

Vol. 33, Issue 4, January 2014
www.ahcmedia.com

Infectious Disease [ALERT]

Incisive Commentary and Clinical Abstracts on Current Issues in Infectious Diseases

ABSTRACT & COMMENTARY

Sudden Unexpected Cardiac Death from Lyme Disease

Many more cases of Lyme carditis may go unrecognized

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University, Hospital Epidemiologist, Sequoia Hospital, Redwood City, CA, Editor of Infectious Disease Alert

SOURCE: Centers for Disease and Control and Prevention. Three sudden cardiac deaths associated with Lyme carditis – United States, November 2012-July 2013. *MMWR* 2013;62:993-6.

CDC has reported 3 patients with sudden unexpected death in whom myocardial infection due to *Borrelia burgdorferii* was first detected post-mortem.

• The first case, a Massachusetts resident, was found unresponsive in his automobile and was subsequently pronounced dead. Relatives reported that he had complained of myalgias and arthralgias in the previous 2 weeks. As a potential organ donor, his organs were sent to a tissue bank were examination of his heart revealed evidence of myocarditis. Further examination at CDC identified the presence of spirochetes by immunohistochemistry and Warthin-Starry silver stain while PCR detected *B. burgdorferii*. Serological studies were consistent with early Lyme disease.

• A man with a history of Wolff-Parkinson-White syndrome collapsed at his home in New York state after complaining of chest pain and attempts at resuscitation were unsuccessful. His organs were sent to the same tissue bank that

Financial Disclosure: *Infectious Disease Alert*'s editor, Stan Deresinski, MD, FACP, FIDSA, does research for the National Institutes of Health, and is an advisory board member and consultant for Merck; Updates author, Carol A. Kemper, MD, FACP, does research for Abbott Laboratories and Merck. Peer reviewer Timothy Jenkins, MD, and executive editor Gary Evans report no financial relationships to this field of study.

Infectious Disease [ALERT]

Infectious Disease Alert,
ISSN 0739-7348, is published monthly by
AHC Media, LLC
One Atlanta Plaza
950 East Paces Ferry NE, Suite 2850
Atlanta, GA 30326.
www.ahcmedia.com

Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to *Infectious Disease Alert*, P.O. Box 550669, Atlanta, GA 30355.

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Print: 1 year with *free* *AMA PRA Category 1 Credits™*: $349
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This CME activity is intended for critical care physicians and nurses. It is in effect for 36 months from the date of the publication.

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received those of the first case and, once again, histological examination revealed evidence of panmyocarditis with perivascular lymphoplasmacytic infiltrates. As in the first case, spirochetes were detected by both Warthin-Starry silver stain and immunohistochemistry, with *B. burgdorferii* detected by PCR. There was also serological evidence of acute infection.

• After complaining of episodic shortness of breath and anxiety for 7-10 days, a Connecticut resident collapsed and died while visiting in New Hampshire. When the medical examiner found evidence of myocarditis, cardiac tissue was sent to CDC where diffuse mixed perivascular lymphoplasmacytic pancarditis, spirochetes were identified, and PCR detected nucleic acid of *B. burgdorferii*. Serological studies were consistent with acute infection.

Corneas from cases 2 and 3 were transplanted into 2 recipients prior to knowledge of evidence of Lyme infection of the donors. One received doxycycline and had no evidence of transmission and the second died from unrelated causes before antibiotics could be administered.

COMMENTARY

These 3 patients presumably died an arrhythmic death resulting from their Lyme myocarditis that was undiagnosed during life. Two had underlying cardiac disease — one had Wolff-Parkinson-White syndrome and two had atherosclerosis detected post-mortem. One patient had 7-10 days of respiratory symptoms and one had chest pain just before collapse. None were known to have had a tick bite and none had usual stigmata of Lyme disease such as erythema migrans.

Myocarditis is a rare complication of acute Lyme disease with objective evidence found in approximately 3% of patients with early infection. Most, but not all patients have other clinical evidence of acute Lyme disease such as erythema migrans. Its most common cardiac manifestation is blockage of atrioventricular conduction, which can be of 1st, 2nd, or 3rd degree and which can rapidly change from one degree of severity to another. Symptoms occur a median of 21 days after infection. More severe levels of block generally improves within a week, but complete resolution of the conduction disturbance may last up to 6 weeks. The usual short duration of high degrees of atrioventricular block is such that it can be managed with temporary pacing. When they occur, myocarditis and/or pericarditis is generally mild. Based on some European reports, it has been suggested that the development of a chronic cardiomyopathy may rarely occur.

While the evidence is anecdotal, it has been suggested that patients with cardiac symptoms and/or a markedly prolong PR interval, 2nd degree or 3rd degree atrioventricular block should be hospitalized and initially treated with ceftriaxone. With resolution of high degree block and significant shortening of the PR interval, antibiotic administration may be changed to the oral route with, e.g., doxycycline.

Published reports of mortality from Lyme carditis are very rare. The occurrence of sudden cardiac death in the 3 patients reported by CDC without a diagnosis of Lyme disease during life suggests the possibility that many more cases of Lyme carditis go unrecognized. While in one of the 3 cases the

diagnosis resulted from a request by the medical examiner for evaluation of cardiac tissue by CDC, in the other 2, the diagnosis was made by the tissue banks to which the explanted hearts were sent for possible use in transplantation. ■

ABSTRACT & COMMENTARY

Great Expectations Dashed: Results of another HIV Vaccine Study Disappoint

By Dean L. Winslow, MD, FACP, FIDSA

Clinical Professor of Medicine and Pediatrics Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Associate Editor of Infectious Disease Alert

Dr. Winslow is a consultant for Siemens Diagnostic.

SYNOPSIS: A promising HIV vaccine trial was halted due to evidence of infection and no differences between vaccine and placebo recipients in viral load set point.

SOURCE: Hammer SM, et al. Efficacy trial of a DNA/rAd5 HIV-1 preventive vaccine. *N Engl J Med* 2013; 369: 2083-92.

In a large multi-site study 2504 men (or transgender women) who have sex with men were randomized to receive DNA/rAd5 vaccine or placebo. HIV acquisition was assessed from week 28 as was the HIV RNA set point at 10-20 weeks after diagnosis of HIV infection. The study was halted by the data and safety monitoring board after interim analysis showed that week 28+ infection had been diagnosed in 27 patients in the vaccine group and 21 in the placebo group. There were no differences between vaccine and placebo recipients in viral load set point.

COMMENTARY

The results of this trial are very disappointing. This particular vaccine was one of the most hopeful candidates that have been developed over the past 20 years and employed a recombinant DNA "prime" (6 closed circular plasmids which individually expressed HIV-1 clade B Gag, Pol, and Nef as well as Env proteins from clades A, B, and C) followed by a "boost" using four recombinant Adenovirus 5 vectors expressing an HIV-1 clade B Gag-Pol fusion protein and Env glycoproteins from clades A, B, and C. In earlier studies this "prime-boost" vaccine elicited extremely robust cellular and humoral immune responses in animals and human subjects. Since these preliminary results were so promising it was anticipated that this new vaccine would have some efficacy despite the largely negative efficacy results seen in clinical trials of recombinant HIV-1 Env or Gag proteins or Adenovirus vector vaccines.

I remember participating in a meeting held in Bethesda in about 1990 at which scientists discussed the future of HIV vaccine development. There was a lot of hope at that time that an effective HIV vaccine could be developed in just a few years and would eventually obviate the need for antiretroviral therapy. However, I also remember at that same meeting Dr. William Haseltine standing up (and to the obvious chagrin of Dr. Fauci) proceeding to tell all of us that, "Development of an HIV vaccine is a pretty big stretch since we don't understand the first thing about immunity to retroviruses or even if immunity is possible!"

As a congenital optimist, I'm still hopeful that we will eventually develop an efficacious HIV vaccine—but enough of a realist to not predict a short timeframe for that to occur. ■

ABSTRACT & COMMENTARY

Schistosomiasis in Returned Travelers

By Philip R Fischer, MD, DTM&H

Professor of Pediatrics, Department of Pediatric and Adolescent, Medicine, Mayo Clinic, Rochester, MN.

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

SYNOPSIS: Ten of 19 members of an Israeli tour group chose to swim in the high-altitude fresh water of a crater lake in western Uganda. All 10 (and none of the 9 non-swimmers in the group) developed acute schistosomiasis with headache (10 of 10), fever (9 of 10), eosinophilia (9 of 10), and cough (8 of 10) three to seven weeks after the exposure.

SOURCE: Lachish T, et al. High rate of schistosomiasis in travelers after a brief exposure to the high-altitude nyinambuga crater lake, Uganda. *Clin Infect Dis* 2013;57:1461-4.

It is estimated that 90% of the world's cases of schistosomiasis occur in Africa. The infection results from exposure of human skin to cercarial forms of Schistosoma in fresh water where snail intermediate hosts live. For travelers, Lake Victoria and Lake Malawi are known to pose particular risk.

An 18-year-old presented for care with three weeks of headache, intermittent fever, and weakness (with a one week history of cough and diarrhea) six weeks after he returned from an organized tour in Uganda. There, he had gone swimming for 15 minutes in Lake Nyinambuga, a volcanic crater lake in Western Uganda. His peripheral blood had 9730 eosinophils per microliter (55% of the total white blood cell count).

All nine of the 18-year-old's companions who swam in the lake (mean exposure time estimated to be 22 minutes) and none of the nine non-swimmers on the tour developed similar symptoms. All had headache, nine had fever, nine had eosinophilia (mean count 2690), nine had weakness, eight had cough, seven had neck pain, and six had pruritus. All affected travelers had positive Schistosoma serology by ELISA testing.

Five of the ten afflicted travelers received steroids for symptomatic relief, and all were treated with praziquantel three months after the exposure.

COMMENTARY

Schistosoma parasites cause three sorts of problems for people. First, schistosomes, especially the avian parasite species, can cause an itchy rash (cercarial dermatitis) immediately following exposure of human skin to infested water. For bird parasites, this is a "dead end" infection that is not established in humans. The itch can be bothersome for two to 10 days. This condition occurs in many areas of the world, and the intensity of symptoms relates to the intensity of exposure and the host's history of previous sensitizing exposures.[1] Second, acute schistosomiasis (sometimes called Katayama fever), as seen in the Israeli travelers reported by Lachish and colleagues, occurs two to eight weeks after exposure to human schistosomes as eggs stimulate an allergic-type response. Third, the life-threatening risk of schistosomiasis comes much later when chronic infection has led to portal hypertension (such as with *S. mansoni*) or urinary disease (with *S. haematobium*). There are often no warning symptoms of these chronic infections.

WHAT SHOULD AN INFECTIOUS DISEASE PHYSICIAN DO?

If someone presents with a past history of cercarial dermatitis, they could be advised to either wear skin-covering swimwear or apply DEET (diethyl-meta-toluamide insecticide) cream prior to subsequent exposure to potentially contaminated fresh water. Neither of these measures is fully protective, but symptoms might be moderated by decreasing the degree of contact between skin and cercariae.

During pre-travel consultations, travelers can be warned of the risk of freshwater exposure in Schistosoma-endemic areas of Africa. As pointed out by the Israeli travelers' experience, infection can occur even with relatively brief exposure and in areas at high altitude (more than 1400 meters above sea level) where infection has not previously been reported.[2] One approach is to prohibit all freshwater contact during the trip, but many travelers would prefer to take the risk of infection as a trade-off for the pleasure of swimming in a volcanic crater or water-skiing in Lake Malawi.[3] Vigorous towel drying after exposure may be helpful. Travelers should at least be warned that if they choose to have skin contact with freshwater in a potentially risky area, they should present for testing three months after the trip (by which time a serologic response to infection would be expected to be present) with treatment given in the event of positive results.

Treatment can, of course, be offered to symptomatic patients. Cercarial dermatitis is usually treated with antihistaminics. Steroids may be given orally for severe symptoms of acute schistosomiasis. Anti-parasitic treatment is ineffective for these early stages of infection.[4,5] For established infection (as seen by positive serology three or more months after exposure), praziquantel is given in multiple doses on a single day (with the dose varying with the weight of the patient and the specific infecting Schistosoma species).[6] The chronic consequences, such as portal hypertension, are incompletely reversible; early treatment after an infection-causing exposure is important.

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ABSTRACT & COMMENTARY

Efficacy of Higher-dose Oseltamivir in Adults with Influenza A and B

By Richard R. Watkins, MD, MS, FACP

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

SYNOPSIS: In a prospective, open-label, intervention study conducted over four influenza seasons, higher dose oseltamivir compared to standard dose produced no additional benefits in patients with influenza A infection. It did lead to improved virologic response in those with influenza B, but this did not reach statistical significance.

SOURCE: Lee N, et al. A Prospective Intervention Study on Higher-Dose Oseltamivir Treatment in Adults Hospitalized with Influenza A and B infections. *Clin Infect Dis* 2013; 57:1511-1519.

A common affliction during the winter months, influenza is most often managed with supportive therapy. However, neuraminidase inhibitors like oseltamivir are frequently prescribed to patients with more serious illness including those who require

hospitalization. The efficacy of the standard regimen of oseltamivir, 75 mg twice a day for 5 days, has been questioned especially for those who are seriously ill. Lee et al. aimed to determine if a higher dose of oseltamivir (150 mg twice a day) would be more effective in adults hospitalized with laboratory-confirmed influenza A or B compared to standard-dose therapy.

The study was a prospective, open-label, interventional trial conducted at two hospitals in Hong Kong during four influenza seasons. Inclusion criteria included age ≥ 18 years, hospitalization for laboratory-confirmed influenza A or B infection, presentation within 96 hours from the onset of symptoms, and provision of informed consent. The two study arms included standard therapy, defined as oseltamivir 75 mg twice daily for 5 days, and the comparator therapy, defined as oseltamivir 150 mg twice daily for 5 days or 75 mg twice daily for 5 days in patients with a creatinine clearance of 40-60 mL/minute. Study arms were allocated by hospital site and not individually. In all, 157 patients were randomized, with 87 in the standard therapy arm and 70 in the comparator therapy arm. There were no significant differences between the arms in demographic characteristics, underlying medical conditions and severity of illness at enrollment. A median of 6 nasopharyngeal swabs were collected from each patient between days 0 to 5 after starting oseltamivir.

The investigators found no significant difference in viral RNA negativity at day 5 between the two treatment arms (44.7 % in the comparator group vs. 40.2% in the standard group; P = .634). They did observe a nonsignificant trend toward more frequent day 5 RNA negativity for the comparator therapy arm vs. the standard therapy arm in influenza B patients (80% vs. 57.1%; P = .214) but not in those with influenza A (32.1% vs. 35.2%). Moreover, another nonsignificant trend was found for the comparator therapy being associated with a faster rate of viral DNA decline for influenza B but not A (P = .051). After univariate and multivariate analysis there were no significant differences in clinical outcomes between the two groups including duration of hospitalization, time to discontinuation of supplemental oxygen and time to fever resolution. More adverse events were noted in patients who received the 150 mg twice daily dose (22.0%) compared to those who received the 75 mg twice daily dose (5.3%; P = .004). All of the events were described as mild to moderate.

COMMENTARY

The main finding of the study, that high-dose oseltamivir did not produce a clear benefit in adults with influenza, is not surprising since it agrees with previously reported data.[1] While a trend toward faster viral clearance in patients with influenza B was observed, it did not reach statistical significance. This latter result is interesting because some data suggest influenza B is less susceptible to standard dose oseltamivir.[2] However, it worth emphasizing that influenza B cannot be differentiated from influenza A infection by presenting clinical signs and symptoms.[3] By day 5 in the present study about half of the cases still had a detectable viral load. This suggests that the standard 5-day course of therapy might not be adequate for all patients such as those with prolonged symptoms or who require intensive care.

There are several limitations to the study that deserve comment. The patients were not randomized individually which may have led to unforeseen confounding. The number of patients in the two arms was relatively small and could have made the study underpowered to detect significant differences in virologic and clinical outcomes. Finally, there were very few patients with severe illness so the results might not be generalizable to this population.

The take-home message from this study is that high-dose oseltamivir did not show any significant benefit on the course of influenza A compared to standard-dose therapy. It is uncertain if high-dose oseltamivir is useful for influenza B and this hypothesis requires further clinical investigation. I suggest that clinicians continue to use standard-dose oseltamivir until data showing clear benefit from higher-dose therapy are available.

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of oseltamivir for the treatment of influenza A and influenza B: A Japanese multicenter study of the 2003-2004 and 2004-2005 influenza seasons. *Clin Infect Dis* 2006;43:439-44.

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ABSTRACT & COMMENTARY

Chikungunya Closer to Home

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University, Hospital Epidemiologist, Sequoia Hospital, Redwood City, CA, Editor of Infectious Disease Alert.

SOURCES: WHO. Chikungunya in the French part of the Caribbean isle of Saint Martin. http://www.who.int/csr/don/2013_12_10a/en/index.html

European Centre for Disease Prevention and Control. Autochthonous cases of chikungunya fever on the Caribbena island, Saint Martin. 11 December 2013. http://www.ecdc.europa.eu/en/publications/Publications/chikungunya-st-martin-rapid-risk-assessment.pdf

During an ongoing outbreak of dengue fever on St Martin/Sint Maarten, (the French and Dutch portions of isle of Saint Martin in the northeastern Caribbean 300 km east of Puerto Rico, active case finding detected 5 patients with suspected dengue who had negative testing for this virus at the Arbovirus National Reference Center in Marseille. All 5 patients, whose symptoms began between 12 October and 15 November 2013, had prominent joint symptoms together with fever. Two had confirmed chikungunya infection. With further surveillance a total of 2 confirmed, 4 probable, and 20 suspected cases were detected as of 12 December.

COMMENTARY

Imported cases of chikungunya have occurred in the Americas in the U.S., as well as in Brazil, Canada, French Guyana, Guadoloupe, and Martinique. All of these countries except Canada have also experienced autochtonously acquired dengue. In the U.S., dengue virus infection has been acquired in Florida in Key West and Martin County, as well as in Hawaii, and in Texas — most recently in Houston. Since *Aedes albopictus* and *Aedes albopictus* are each vectors of both dengue and chikungunya virus, with both present in many areas of the Americas, it seemed only a matter of time that locally acquired chikungunya virus infection was detected — and that time has come.

This beautiful Caribbean island is a major tourist attraction, especially at this time of year. It is inevitable that some tourists will bring home something other than just a sun tan — a mosquito-borne infection. ■

CDC ALERT

CDC issues Health Advisory Alert on Chikungunya Virus Infections

As this issue went to press, the Centers for Disease Control and Prevention issued a health advisory notice to public health officials and clinicians on recognizing, managing, and reporting chikungunya virus infections in travelers returning from the Caribbean.

Summary: On December 7, 2013, the World Health Organization (WHO) reported the first local (autochthonous) transmission of chikungunya virus in the Americas. As of December 12th, 10 cases of chikungunya have been confirmed in patients who reside on the French side of St. Martin in the Caribbean. Laboratory testing is pending on additional

suspected cases. Onset of illness for confirmed cases was between October 15 and December 4. At this time, there are no reports of other suspected chikungunya cases outside St. Martin. However, further spread to other countries in the region is possible.

Chikungunya virus infection should be considered in patients with acute onset of fever and polyarthralgia, especially those who have recently traveled to the Caribbean. Healthcare providers are encouraged to report suspected chikungunya cases to their state or local health department to facilitate diagnosis and to mitigate the risk of local transmission.

Background: Chikungunya virus is a mosquito-borne alphavirus transmitted primarily by *Aedes aegypti* and *Aedes albopictus* mosquitoes. Humans are the primary reservoir during epidemics. Outbreaks have been documented in Africa, Southern Europe, Southeast Asia, the Indian subcontinent, and islands in the Indian and Pacific Oceans. Prior to the cases on St. Martin, the only chikungunya cases identified in the Americas were in travelers returning from endemic areas.

Clinical Disease: A majority of people infected with chikungunya virus become symptomatic. The incubation period is typically 3–7 days (range, 2–12 days). The most common clinical findings are acute onset of fever and polyarthralgia. Joint pains are often severe and debilitating. Other symptoms may include headache, myalgia, arthritis, or rash. Persons at risk for more severe disease include neonates (aged <1 month) exposed intrapartum, older adults (e.g., ≥ 65 years), and persons with underlying medical conditions (e.g., hypertension, diabetes, or cardiovascular disease).

Diagnosis: Chikungunya virus infection should be considered in patients with acute onset of fever and polyarthralgia who recently returned from the Caribbean. Laboratory diagnosis is generally accomplished by testing serum to detect virus, viral nucleic acid, or virus-specific immunoglobulin M (IgM) and neutralizing antibodies. During the first week of illness, chikungunya virus infection can often be diagnosed by using viral culture or nucleic acid amplification on serum. Virus-specific IgM and neutralizing antibodies normally develop toward the end of the first week of illness. To definitively rule out the diagnosis, convalescent-phase samples should be obtained from patients whose acute-phase samples test negative.

Chikungunya virus diagnostic testing is performed at CDC, two state health departments (California and New York), and one commercial laboratory (Focus Diagnostics). Healthcare providers should contact their state or local health department to facilitate testing.

Treatment: No specific antiviral treatment is available for chikungunya fever. Treatment is generally palliative and can include rest, fluids, and use of analgesics and antipyretics. Because of similar geographic distribution and symptoms, patients with suspected chikungunya virus infections also should be evaluated and managed for possible dengue virus infection. People infected with chikungunya or dengue virus should be protected from further mosquito exposure during the first few days of illness to prevent other mosquitoes from becoming infected and reduce the risk of local transmission.

Prevention: No vaccine or preventive drug is available. The best way to prevent chikungunya virus infection is to avoid mosquito bites. Use air conditioning or screens when indoors. Use insect repellents and wear long sleeves and pants when outdoors. People at increased risk for severe disease should consider not traveling to areas with ongoing chikungunya outbreaks.

Recommendations for Health Care Providers and Public Health Practitioners

- Chikungunya virus infection should be considered in patients with acute onset of fever and polyarthralgia, especially those who have recently traveled to the Caribbean.
- Healthcare providers are encouraged to report suspected chikungunya cases to their state or local health department to facilitate diagnosis and to mitigate the risk of local transmission.
- Health departments should perform surveillance for chikungunya cases in returning travelers and be aware of the risk of possible local transmission in areas where Aedes species mosquitoes are currently active.
- State health departments are encouraged to report laboratory-confirmed chikungunya virus infections to ArboNET, the national surveillance system for arthropod-borne viruses. ■

NEWS BRIEF

Stanford offers WEB Course in Antibiotic Stewardship

The division of Infectious Diseases in the Stanford University School of Medicine is offering an online course on one of the hottest topics in health care epidemiology: antibiotic stewardship.

"Antimicrobial Stewardship: Optimization of Antibiotic Practices" offers a practical approach to prescribing antibiotic therapy and development of antimicrobial stewardship to physicians and pharmacists across all specialties and settings.

Available until Nov. 22, 2015, the course offers six hours of CME credit for a processing fee of $20. Otherwise there is no charge.

It is estimated that approximately 50% of antibiotic use, in both the outpatient and inpatient settings, is inappropriate. At the same time, in contrast to any other class of drugs, every antibiotic use has a potential public health consequence. Inappropriate use may not harm only the individual patient, but contributes to societal harm by exerting an unnecessary selective pressure that may lead to antibiotic resistance among bacteria.

Part I of the course focuses on the underlying clinical science of antimicrobial use. Part 2 details the practical aspects of implementing an antimicrobial stewardship program, as well as the application of such programs to special circumstances and populations.

Learning objectives include:

•Develop skills to apply IDSA guidelines in treating common infections such as acute rhinosinusitis.

•Apply evidence based antibiotic management to treat sepsis.

•Implement principles of antimicrobial stewardship when providing care to special populations and in various settings.

•Apply evidence based antibiotic management to surgical patients requiring antibiotic prophylaxis.

•Apply evidence based antibiotic stewardship program in the outpatient setting

For more on information on the course go to:
https://www.coursera.org/course/antimicrobial ■

Infectious Disease [ALERT]

Updates

By Carol A. Kemper, MD, FACP

Travel medicine anxiety:

Fear the needle

Noble LM, et al. The Impact of Injection Anxiety on Education of Travelers About Common Travel Risks. *J Travel Med* 2013 Nov 19, 2013. doi:10.1111/jtm.12081. [Epub ahead of print]

I recall attending the International Society of Travel Medicine conference in Acapulco years ago, when a clever colleague conducted a clinical survey of conference participants regarding their usual advice to travelers to Mexico — and how many of them followed their own advice (very few). Conducting my own personal experiment, I can testify to the fact that eating street food in Mexico does, indeed, result in gastrointestinal illness. Infectious Disease physicians apparently like to take risks when it comes to their own travel advice.

Turns out — our clients are not much better at following our travel medicine recommendations, perhaps for different reasons. These authors examined the extent to which anxiety or fear about immunizations affected the retention of travel medicine consultation. Standardized information was provided to

105 pre-travelers. Clinicians were also asked to gauge the level of anxiety of the pre-traveler.

Each pre-travel client completed a self-reported survey regarding their general anxiety about injections and needle phobia — and then these results were compared with the ability to recall specific information immediately post-consultation and >24 hours later. Unfortunately, immediate recall of 15 different pieces of information varied from only 2% to 70% — and decreased even further by the following day. The inability to retain information appeared unrelated to injection anxiety or fear of needles. More than one-third (39%) expressed varying levels of anxiety of immunization, and clinicians were pretty good at gauging the anxiety level of their clients. (I would think anxiety about the cost of immunization might be more important than fear of needles). ■

Risking exposure to MDR in the U.S.

Moonan PK, et al. Transmission of multidrug-resistant tuberculosis in the USA: A cross-sectional study. *Lancet Infectious Dis* 2013;13:777-784.

In order to assess the risk of transmission of resistant tuberculosis within the U.S. — and contributing factors — Moonan et al analyzed genotypic clustering of MDR-TB isolates. The authors gathered all cases of MDR-TB reported to the US National Tuberculosis Surveillance System (NTSS) and National Tuberculosis Genotyping Service (NTGS) from eight states, including California from 2007 to 2009, Texas from 2007 to 2009, as well as Colorado, Maryland, New York , Massachusetts, Tennessee and Washington. Drug resistance was defined as any resistance reported to the NTSS; and for the purposes of this project, genotypes were defined as a discrete combination of spoligotype and 12-locus variable-number-tandem repeat units. A cluster was defined as at least two cases of MDR TB, including at least one study case and another case in one of the 8 states with a matching genotype between 2005 and 2011. The index case was temporally the first case identified in a cluster. And epidemiological links were the same as those usually used for contact investigation activities, such as family member, close colleague, and other individuals in close, regular contact.

From the database, 268 cases of MDR-TB were identified during the study period. Of these 168 cases were reported from one of the eight states above, 92 (55%) of whom were willing to participate in an interview. A total of 75 (82%) of these 92 people were foreign-born. Based on the in-depth interviews and available health records, the investigators determined that (9%) of these 92 people developed TB as the result of an exposure within the United States to a recognized source, and 12 people (13%) were part of an outbreak resulting from transmission within the U.S. but from an unknown source. Four of these later served as the source for another case.

Therefore 22% of the MDR-TB cases were the result of exposure to a recognized or unknown case of TB within the U.S. Twenty (22%) of the MDR cases were diagnosed within 3 months of entry into the U.S., and therefore probably had active TB on entry to the U.S. And 38 (41%) were diagnosed with reactivation TB that proved to be MDR. A smaller percent of the MDR-TB cases (15%) were considered relapsed TB cases, from a prior recognized episode of TB. There was insufficient information to classify (10%) of the cases based on their presentation. Notably, 3 individuals diagnosed with XDR-TB (from Nepal, Russia and Krygyzstan) were all diagnosed within 3 months of entry into the U.S.

Of these 92 cases, 28% had the same genotype as another individual with MDR-TB in the same state during the surveillance period. Clustered cases were also more likely to be male, Latino, in prison at the time of diagnosis, and have an isolate of Euro-American phylogenetic lineage. Fourteen clusters were identified in total, 13% of which were of Euro-American phylogenetic lineage. Eights clusters had an identifiable source case; two included transmission to a child, and one across state lines. More than half the cases involved excessive use of alcohol or illicit drugs. Overall, people with MDR-

TB attributed to transmission within the U.S. were more likely to be male, have been born in the U.S., be of Hispanic ethnic origin, abuse illicit drugs or alcohol, and have an isolate of Euro-American phylogeny.

During this investigation, the authors identified 1166 people exposed to cases of MDR-TB, 353 of whom (30%) had evidence of latent TB. Assuming a 10% risk of active disease, exposure to these cases might result in approximately 35 future cases of MDR-TB within the U.S.. Data is lacking as to how best to prophylax these exposures.

Unfortunately, most of these cases of newly diagnosed and reactivation TB were not captured on entry to the U.S. Confronting yet again another case of active pulmonary TB in my Silicon Valley-based immigrant population, I am repeatedly asked why individuals with TB are not screened by the public health department. Efforts in immigration clinics are directed at capturing cases of active TB — not latent TB, and the public health department does not have the resources to screen and prophylax cases of latent TB — that is our job. Even persons with active TB can slip by these screening efforts — as illegal immigrants — or by simply arriving on one of the new work VISAs, visiting family for an extended time, or arriving as a refugee or under asylum (where no TB screening is required — only a vague recommendation they see a doctor after arrival in the U.S.). ■

TB screening, therapy in HIV pts in Brazil

Durovni B, et al. Effect of improved tuberculosis screening and isoniazid prevention therapy on incidence of tuberculosis and death in patients with HIV in clinics in Rio de Janeiro, Brazil: A stepped wedge, cluster-randomised trial. *Lancet* 2013; Published on-line August 13, 2013. S1473-3099(13)70187-7.

The authors conducted a large-scale intervention in 29 HIV clinics in Rio de Janeiro to assess whether improved TB screening and INH treatment would result in a lower incidence of TB infection and death in their HIV-infected population. TB remains a significant problem in Brazil, and 10% of the cases of TB in Rio are HIV-co-infected. TB continues to be a significant contributor of death in people with HIV-infection in Brazil.

The intervention was simply to increase screening of individuals attending HIV clinics for TB, to improve the use of PPD and detection of positive skin tests, and to increase the use of INH prevention. Two clinics were randomly selected to begin the intervention in a step-wise fashion every two months from 2005-2009. In addition, a control period for examining rates of TB and death was selected from 2003-2005.

During the intervention period, rates of skin testing increased from 19 person/100 person-years to 59/100 person-years. Isoniazid prevention increased from 36/100 eligible person-years to 144/100 eligible person-years. A total of 221 cases of TB were diagnosed during the control period and 254 cases during the intervention period. A total of 17,413 persons visited the clinic at least once during the study period; 12,816 of these were eligible for the intervention — so this was an enormous interventional study. Of these 472 had a positive TB skin test at study start. Of the remainder, 60% had at least one skin test during the study period, and of those eligible for a second test, 47% received a second test. Twenty percent had a positive result, and 82% started INH treatment. Of these, 85% of those starting INH completed a course of therapy. 1.5 % reported treatment-limiting side effects.

After adjusting for age, CD4 count, and sex, the intervention — although only 4 years in duration — was associated with a 27% reduction in TB cases and a 31% reduction in TB deaths. A secondary analysis examining the effect of TB screening on retention in clinics, and the benefit specifically to those patients retained in care found an even greater benefit to the intervention – with a 58% reduction in the incidence of TB infection and a 55% reduction in TB and death. The authors believe the intervention proved to, as a whole, result in improved care by increasing awareness of TB in the study population, and improved diagnosis of active TB cases. ■

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CME QUESTIONS

1. Which of the following is correct?

A. Myocarditis occurs in approximately 30% of patients with Lyme disease.
B. Congestive heart failure is the most common manifestation of Lyme carditis.
C. Cardiac involvement due to Lyme disease may go unrecognized.
D. Sudden death in patients with Lyme carditis is usually die to acute coronary artery occlusion.

2. Which of the following is correct?

A. Infections due to Schistosoma parasites require exposures in excess of 3 hours.
B. Katayama fever is the chronic form of schistosomiasis.
C. Cercarial dermatitis (swimmers itch) is inevitably followed by chronic schistosomiasis.
D. Eosinophilia is a common finding in acute schistosomiasis.

3. According to the CDC, because of similar geographic distribution and symptoms, patients with suspected chikungunya virus infections also should be evaluated for:

A. malaria
B. Japanese encephalitis
C. West Nile
D. dengue

CME OBJECTIVES

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

- discuss the diagnosis of infectious diseases;
- explain current data regarding the use of new antibiotics for commonly diagnosed diseases and new uses for traditional drugs;
- discuss the latent information regarding risks, benefits, and cost-effectiveness of new and traditional diagnostic tests; and
- discuss new information regarding how infectious diseases are transmitted and how such information can lead to the development of new therapies

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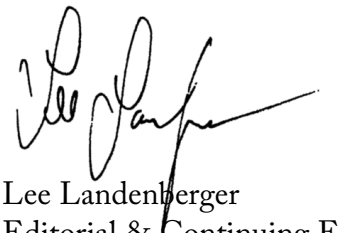

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