AHC Media

Vol. 34, Issue 12, September 2015
www.AHCMedia.com

Infectious Disease [ALERT]

Incisive Commentary and Clinical Abstracts on Current Issues in Infectious Diseases

ABSTRACT & COMMENTARY

Borrelia Miyamotoi Disease in the Northeastern United States

By Dean L. Winslow, MD, FACP, FIDSA

Dr. Winslow is Clinical Professor of Medicine, Division of General Medical Disciplines, Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, CA.

Dr. Winslow reports no financial relationships relevant to this field of study.

SYNOPSIS: Of 11,515 patients presenting to primary care clinics, urgent care clinics, or emergency departments during 2013-2014 who underwent testing for evaluation of fever, 97 cases of *Borrelia miyamotoi* disease (BMD) were identified by PCR. Patients with BMD generally presented with high fever, headache, myalgia/arthralgia, and also frequently had elevated liver enzymes, neutropenia, and thrombocytopenia.

SOURCE: Molloy PJ, et al. *Borrelia miyamotoi* disease in the Northeastern United States: A case series. *Ann Intern Med* 2015;163: 91-99.

Patients from Massachusetts, Rhode Island, New Jersey, and New York who presented to primary care or urgent care clinics or emergency departments during 2013 and 2014 with fever and whose physicians had suspicion for tick-borne illness had whole blood samples submitted to IMUGEN laboratories for assessment of infection due to various tick-borne pathogens (*B. burgdorferi*, *B. miyamotoi*, *Babesia microti*, *Anaplasma phagocytophilum*) using real-time PCR. In addition, serologic assessment of antibodies to *B. miyamotoi* and *B. burdorferi* was performed.

Ninety-seven patients (0.8% of total tested) with positive PCR for *B. miyamotoi* DNA were identified. (By comparison, 3.1% contained *B. microti* DNA, 1.4% *A. phagocytophilum* DNA, and 1.7% *B. burgdorferi* DNA.) The majority of cases of *B. miyamotoi* infection occurred in May-September of both years. Of the patients with

Financial Disclosure: *Infectious Disease Alert*'s editor, Stan Deresinski, MD, FACP, FIDSA, reports no financial relationships relevant to this field of study. Peer reviewer Patrick Joseph, MD, is laboratory director for Genomic Health, Siemens Corp., and CareDx; Shelly Morrow Mark reports that her spouse works for a company that has created advertising for Uroplasty. Updates author, Carol A. Kemper, MD, FACP, and continuing education and editorial director Lee Landenberger 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.

GST Registration Number: R128870672.
POSTMASTER: Send address changes to *Infectious Disease Alert*, P.O. Box 550669, Atlanta, GA 30355.

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1-800-688-2421
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Subscription Prices
United States:
Print: 1 year with free *AMA PRA Category 1 Credits™*: $349
Add $19.99 for shipping & handling.
Online only: 1 year (Single user) with ***free*** *AMA PRA Category 1 Credits™*: $299

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positive *B. miyamotoi* PCR results, 51 had sufficient medical records available for review. The mean age of patients was 55 years. Ninety-six percent presented with fever, 96% with severe headache, 84% with myalgia, 76% arthralgia, 82% malaise/fatigue, 8% rash, 6% gastrointestinal symptoms, 6% cardiac/respiratory symptoms, and 8% neurologic symptoms. Approximately one half of the patients had leukopenia, thrombocytopenia, elevated ALT/AST, or various combinations of these abnormalities. Twenty-four percent of patients required hospital admission. All patients responded clinically to empiric treatment with doxycycline.

An EIA to detect antibodies to a *B. miyamotoi* recombinant glycophosphodiester phosphodiesterase (rGlpQ) antigen was developed. At initial presentation, only 16% of patients had IgM or IgG antibodies present, and this increased to 78% of convalescent phase samples. Interestingly, only 20% of patients demonstrated IgG or IgA class antibodies, even in convalescent samples. *B. miyamotoi* patients commonly demonstrated antibody reactivity to *B. burgdorferi* in the EIA test, but only 10% of patients demonstrated diagnostic reactivity in *B. burgdorferi* immunoblot assays (suggesting that some of these patients may have been co-infected with both *B. miyamotoi* and *B. burgdorferi*).

■ COMMENTARY

Since the original description of human cases of *B. miyamotoi* infection in Russia in 2011,[1] sporadic cases have been identified in the Netherlands and Japan, and beginning in 2013, cases have been identified in New England.[2,3] The current study suggests that *B. miyamotoi* not uncommonly causes a febrile illness in the Northeastern United States, with similar clinical features as *A. phagocytophilum* (formerly known as granulocytic Ehrlichiosis) and may be almost as common.

One minor criticism of this study is that it was retrospective and included only symptomatic patients with high pretest probability of having a tick-borne illness. Further studies will be of interest to characterize the prevalence of this disease in the population and to determine the frequency of less severe illness and asymptomatic infection. It is of note that the deer tick (*Ixodes dammini*) and the black-legged tick (*Ixodes scapularis*) are the vectors for *B. burgdorferi*, *B. microti*, and *A. phagocytophilum,* as well as the Powassan deer tick virus. Apparent co-infection with *B. burgdorferi* and *B. miyamotoi* was seen in this study, and it is likely that co-infection with *B. miyamotoi* and these other tick-borne pathogens will likely be increasingly recognized. Since molecular diagnostic tests for most pathogens are not generally available with a short turn-around time, prompt empirical administration of doxycycline remains important in the management of these patients. ■

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Legionella in the Bronx

By Stan Deresinski, MD, FACP, FIDSA

Dr. Deresinski is Clinical Professor of Medicine, Stanford University.

Dr. Deresinski reports no financial relationships relevant to this field of study.

On July 30, 2015, *The New York Times* reported that the New York City Department of Public Health was investigating an outbreak of Legionnaire's disease in the South Bronx. At that time, 31 cases with 2 deaths had been reported

since July 10. The number of cases continued to increase, and by August 10, a total of 113 cases were reported. Of these, 76 had been treated and discharged from care, and 12 patients, all with comorbidities, had died.

Legionella was detected in five of 17 cooling towers tested in the affected areas, including towers at the Opera House Hotel and the Lincoln Medical and Mental Health Center.[1] Each of the five cooling towers was disinfected, with plans for continued monitoring for the presence of the organism. On August 6, New York City buildings with cooling towers were ordered to have their units assessed by an environmental consultant and disinfected within two weeks.

At the time of this writing, the outbreak appears to be burning out, with no newly diagnosed cases in the interval between August 3 and August 10, and no new deaths since August 4. ■

REFERENCE

1. Yee V. Officials seek source of Legionnaires' outbreak in the Bronx. *The New York Times*. Aug. 2, 2015. http://www.nytimes.com/2015/08/03/nyregion/officials-seek-source-of-legionnaires-outbreak-in-the-bronx.html.

ABSTRACT & COMMENTARY

Risk of Herpes Zoster Increases After Zoster Vaccination in Patients Taking Immunosuppressive Medications

By Richard R. Watkins, MD, MS, FACP

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Dr. Watkins reports that he has received research support from Forest Pharmaceuticals.

SYNOPSIS: In adults >18 years, taking immunosuppressive medications at the time of zoster vaccination increased the risk for herpes zoster for up to 6 weeks afterward (adjusted odds ratio, 2.99; 95% CI, 1.58-5.70).

SOURCE: Cheetham TC, et al. Risk of herpes zoster and disseminated varicella zoster in patients taking immunosuppressant drugs at the time of zoster vaccination. *Mayo Clin Proc* 2015;90:865-873.

Currently, the live zoster vaccine is recommended for all adults older than age 50 years. However, live vaccines are generally contraindicated for immunocompromised patients such as those with HIV, malignancy, or those receiving high-dose corticosteroids. The generally accepted recommendation for patients taking < 20 mg/d of prednisone for fewer than 14 days is that the zoster vaccine is safe, while patients taking higher doses or longer courses should wait until steroids have been stopped for a month. Cheetham and colleagues sought to further delineate the risks associated with administering the zoster vaccine to patients taking corticosteroids and other immunosuppressant drugs.

The study was conducted by using data derived from a vaccine safety database maintained by the CDC and several managed care organizations. Adults aged 18 years and older who received the zoster vaccine were included in the analysis. The types of immunosuppressant medications used by patients in the study included oral corticosteroids, non-biological disease-modifying antirheumatic drugs (DMARDs), and anti-rejection drugs. Those on immunosuppressant drugs were further characterized as current users, defined as having the drug dispensed between 30 days before and 5 days after vaccination, or remote users, defined as having the drug dispensed between 365 days and 30 days before vaccination. The primary outcomes measured were diagnosis of disseminated varicella zoster virus (VZV) of the central nervous system, lungs, or heart, and diagnosis of zoster within 1 to 42 days following vaccination.

Of 277,358 patients who received the zoster vaccine, 14,554 (5.2%) had an immunosuppressant drug dispensed between 365 days before and 5 days afterward. In the current users group, the median daily prednisone dose for low-dose corticosteroids (< 20 mg/d) was 17.5 mg and the duration was 8 days, while for the high-dose group (> 20 mg/d) the median dose was 35 mg and the duration was 28 days.

During the 42-day window, no cases of disseminated VZV were identified in either the current or remote users groups. In the current user group, 25 cases of herpes zoster occurred, compared to 17 in the remote user group. The odds ratio for herpes zoster for the current vs. remote group was 2.97 (95% CI, 1.61-5.51).

■ COMMENTARY

Herpes zoster can be a very debilitating disease, and the introduction of an effective vaccine has been welcomed in the clinic. However, physicians are challenged to decide which patients should and should not be vaccinated, especially among those who are immunosuppressed. The evidence has been conflicting, with some studies showing an increased risk of developing zoster while on corticosteroids, while others reported no additional risk. Thus, the new study by Cheetham and colleagues is pragmatic because it provides further guidance about who should receive the zoster vaccine and when. The main finding of the study was the slightly increased risk of herpes zoster in the current users of immunosuppressant drugs for 42 days following zoster vaccination. The authors hypothesized that it was unlikely the herpes zoster experienced by the patients was caused by the vaccine strain due to the relatively short incubation period. In other words, it seems implausible that the Oka VZV strain could migrate to a dermatome and reemerge as a herpes zoster rash in only 42 days. A better explanation is that the herpes zoster was due to reactivation of latent zoster virus. Further research to test this hypothesis seems warranted.

There were a few limitations to the study. First, despite a large database of patients who received the zoster vaccine, the overall number of cases of herpes zoster in both the remote and current immunosuppressant drug groups was small (n = 42). Second, the investigators did not report whether any of the patients had their immunosuppressant drugs filled by pharmacies outside the database network, which would have led to bias toward the null hypothesis. Third, the investigators counted a drug being dispensed as a surrogate for the patient actually taking it, which might not always have been true. Finally, it is possible that some patients stopped their immunosuppressant drugs prior to zoster vaccination and did not inform their physician.

The take-home point from this study is that patients on immunosuppressive drugs (including low-dose corticosteroids) at the time of zoster vaccination seem to be at increased risk for herpes zoster. We now have evidence that these patients should be off their immunosuppressive drugs for at least four weeks prior to vaccination. ■

ABSTRACT & COMMENTARY

Community-acquired Pneumonia Requiring Hospitalization in Adults

By Dean L. Winslow, MD, FACP, FIDSA

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Dr. Winslow reports no finanical relationships relevant to this field of study.

SYNOPSIS: An active population-based surveillance of community-acquired pneumonia (CAP) requiring hospitalization in adults 18 years of age and older was conducted in five hospitals in Chicago and Nashville. The incidence of CAP requiring hospitalization was highest in older adults. Despite extensive diagnostic testing, no pathogen was identified in most patients. Respiratory viruses were identified more frequently than bacteria.

SOURCE: Jain S, et al. Community-acquired pneumonia requiring hospitalization among U.S. adults. *N Engl J Med* 2015;373:415-427.

From January 2010 through June 2012, a total of 2488 (of 3634 eligible) adults were enrolled in an active population-based surveillance of community-acquired pneumonia (CAP) requiring hospitalization in adult patients. Patients who had recently been hospitalized or who were severely immunosuppressed were excluded. Blood, urine, respiratory, and pleural specimens were systematically collected for testing by culture, serology, antigen detection, and molecular diagnostic methods. In addition to routine bacteriological methods and urine antigen testing for *S. pneumoniae* and *Legionella pneumophila*, a variety of real-time PCR assays were systematically

performed on respiratory samples and pleural fluid (when available).

Of the 2488 enrolled patients, independent review of X-rays by a panel of study radiologists concurred with the radiographic diagnosis of pneumonia in 2320 (93%). The mean age of patients was 57 years. Seventy-eight percent of patients had some underlying medical condition (most commonly chronic lung disease, heart disease, immunosuppression, or diabetes). Twenty-one percent of patients required intensive care unit (ICU) admission, and 2% died. Incidence rates of CAP requiring hospitalization ranged from 6.7 cases/10,000 adults per year in patients ages 18-49, to 164.3 cases/10,000 adults per year in patients 80 years of age or older.

Of the 2259 patients who had radiographic evidence of pneumonia and specimens available for both bacterial and viral testing, a pathogen was detected in 38%, one or more viruses in 23%, bacteria in 11%, bacterial plus viral pathogen in 3%, and fungal or mycobacterial pathogen in 1%. Of the potential pathogens identified, the most common were rhinovirus in 9%, influenza virus in 6%, and *Streptococcus pneumoniae* in 5%. Less common pathogens included human metapneumovirus (4%), respiratory syncytial virus (RSV) (3%), and parainfluenza virus (3%). Interestingly, *Mycoplasma pneumoniae*, *Staph. aureus*, adenovirus, *Legionella*, and *Enterobacteriaceae* were each found in < 2% of cases. A large peak of infection occurred during the winter of 2010-11 and was associated with a large number of influenza cases and smaller peaks of *S. pneumoniae* and *S. aureus* cases.

[The study highlights the burden of pneumonia requiring hospitalization, particularly in older adults, as well as the low frequency of identification of a pathogen (particularly a bacterial one) despite the use of sensitive methods.]

■ COMMENTARY

This is an interesting surveillance study conducted by the Centers for Disease Control (CDC) in two large U.S. cities during a two-year period. The study highlights the burden of pneumonia requiring hospitalization, particularly in older adults. This study also emphasizes that, even when extremely sensitive molecular diagnostic tests are used, a pathogen can be identified in only a minority of cases of CAP, and that viral pathogens are more common than bacterial ones. This study is a nice companion piece to the paper published by this same group at CDC earlier this year that focused on CAP requiring hospitalization in children.[1] ■

REFERENCE

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ABSTRACT & COMMENTARY

"Only Skin Deep" — Preventing and Managing Dermatologic Problems in Travelers

By Philip R. Fischer, MD, DTM&H

Dr. Fischer is Professor of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN.

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

SYNOPSIS: Skin infections and infestations account for significant concern among returned travelers. Appropriate diagnosis and treatment makes long-term morbidity unlikely.

SOURCE: Monsel G, Caumes E. What's new in travel-associated dermatology? *J Travel Med* 2015;22:221-224.

An international network of clinics seeing international travelers identified skin conditions as a major cause of travel-related medical consultations.[1] Helpfully, the current review provides clinically relevant details about travel-related dermatologic problems.

Skin and soft-tissue infections are the main dermatologic concern among returned travelers. Group A Streptococcus and *Staphylococcus aureus* are common causative pathogens. Some methicillin-resistant *S. aureus* carry a cytotoxin (Panton-Valentine leucocidin) that can destroy white cells and cause tissue necrosis; these cytotoxic organisms are especially likely to be transmitted to other people after return from travel. Long-term travelers often develop staphylococcal furuncles that can persist for several months and only fully resolve after return to the home country.

Relevant to sports enthusiasts traveling to Brazil, hookworm-related cutaneous larva migrans is commonly identified in travelers who have been in Brazil. This "creeping dermatitis" can be associated with furuncles. Treatment is with either ivermectin or albendazole.

Larvae of some insects can burrow into skin, causing tungiasis and myiasis. More novel species are being reported to cause these bothersome local lesions.

[... 20% of travel-related medical consultations are for skin problems, and the majority of those skin problems are due to infections and infestations.[1]]

■ COMMENTARY

Eric Caumes, editor-in-chief of *Journal of Travel Medicine*, and Gentiane Monsel provide a great editorial overview of travel-related skin problems. This is important, since 20% of travel-related medical consultations are for skin problems, and the majority of those skin problems are due to infections and infestations.[1] In addition, several other original research papers in the July-August 2015 issue of *Journal of Travel Medicine* provide new information about skin problems related to international travel.

Eli Schwartz's group in Israel reviewed 90 patients who returned from foreign trips with myiasis.[2] Most had been in Latin America, and many had been at Madidi National Park in the Amazon region of Bolivia. Some flies deposit eggs directly on human skin, and then the larvae burrow into the skin; other flies deposit their eggs onto drying clothes that are subsequently put on skin and allow the larvae to embed. In areas where both sorts of transmission occur, prevention can be achieved both by the use of insect repellents and by ironing clothes that have been dried outside (especially on the ground). More than 10% of patients had been incorrectly initially diagnosed as having furunculosis and had been given unnecessary antibiotics. With correct diagnosis, manual extraction was effective — even though about one-fourth of patients required surgical intervention to facilitate larval removal.

Sand fleas can cause a similar infestation, tungiasis. In this situation, female sand fleas lay their eggs in the human epidermis. Developing baby fleas remain burrowed in the skin to cause irritating local lesions, often on the toes. Seven individuals in a group of 16 backpacking travelers to Madagascar presented to the same French clinic with sand fleas (mean of 1.7 embedded fleas per traveler) on their toes.[3] Wearing open-toed shoes was a risk factor for acquisition of *Tunga penetrans*. Wearing closed shoes and/or using DEET-containing insect repellant on exposed feet would likely have prevented these infestations. Treatment was successful with simple excision.

Infectious disease practitioners providing pre-travel care should also warn travelers about other dermatologic risks. Sunburn should be prevented by appropriate use of clothes and sunscreen, but even severe cases are still reported.[4] The infectious risks of tattoos are well-known, but it is also possible that even henna tattoos can lead to severe contact dermatitis, especially when black henna is used.[5] The skin can also be the portal of entry for marine envenomations, such as occur with lionfish in the Caribbean; immersion of the affected body part in non-scalding hot water for 30-90 minutes can inactivate the venom.[6] ■

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ABSTRACT & COMMENTARY

Scrub Typhus and the Brain

By Joseph E. Safdieh, MD

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Dr. Safdieh reports no financial relationships relevant to this field of study.

This article originally appeared in the August 2015 issue of Neurology Alert.

SYNOPSIS: Scrub typhus infections involve the nervous system in a majority of cases and should be suspected in patients who live in, or are returning from, endemic regions with a compatible clinical syndrome.

SOURCE: Misra UK, et al. Neurological manifestations of scrub typhus. *J Neurol Neurosurg Psychiatry* 2015;86:761-776.

Rickettsial diseases are bacterial infections transmitted to humans through bites from infected ticks, lice, fleas, or mites. Rickettsial diseases manifest in three forms, including typhus, spotted fever, and scrub fever. The most common rickettsial disease in the United States is Rocky Mountain spotted fever, caused by *Rickettsia rickettsii*. Other rickettsial diseases occur with more frequency in other parts of the world and can cause neurologic manifestations including meningoencephalitis. Scrub typhus is caused by *Orientia tsutsugamushi* and is endemic in northern Japan, northeastern Russia, parts of Australia, Pakistan, and India. Scrub typhus has varied clinical manifestations from a nonspecific febrile illness to severe multi-organ failure, with scattered reports of neurologic involvement as well. The diagnosis is often delayed, leading to poor outcomes including death. Scrub typhus responds well to antibiotic therapy, so it is important to make the proper diagnosis.

In this paper, the authors present a cross-sectional study evaluating the medical and neurologic manifestations of scrub typhus at a tertiary care teaching hospital in North India. Over the course of 2 years, 37 patients were identified. There was no gender predilection. Median age of the patients was 37 years. The median course of illness was 2 weeks. All patients had fever and myalgias. The vast majority of patients had headache, respiratory symptoms, and altered sensorium (> 80%). Typical eschar skin lesion was present in only half of the patients, as was nuchal rigidity. Eight patients (22%) had seizures as part of their disease course. Other clues to the diagnosis included lymphadenopathy (65%), vomiting (73%), hepatomegaly (35%), and focal weakness (38%). Almost all patients were anemic, half demonstrated thrombocytopenia, and half demonstrated leukocytosis. Elevated ALT was present in 89% of the patients.

Twenty-eight of the 31 patients with altered sensorium underwent lumbar puncture. In those patients, the mean cerebrospinal fluid (CSF) white blood cell count was 112 with a predominantly lymphocytic pleocytosis as well as elevated protein. Patients with altered sensorium but normal CSF were classified as experiencing an encephalopathy syndrome as opposed to a meningoencephalitis syndrome. Many of the patients with meningoencephalitis presentation experienced at least 10 days of progressive symptoms, suggesting a subacute meningitis. MRI scan was performed in most patients, and was normal in all but one patient who demonstrated meningeal enhancement. No patients had parenchymal lesions. EEG demonstrated slowing in 25% of encephalitic patients, but none demonstrated epileptiform activity.

All patients were treated with oral doxycycline and ultimately all patients recovered, although patients with a higher degree of disability on admission were more likely to recover slowly. Most patients improved rapidly within 48 hours of doxycycline therapy.

■ COMMENTARY

This is an important study for a number of reasons. For neurologists who practice in countries where scrub typhus is endemic, this paper provides significant data as to the typical presentation, signs, diagnostic testing, and prognosis of patients. For other neurologists, this paper educates us about this important Rickettsial illness, especially the rapid globalization of the world's population. While it is unlikely that a neurologist in the United States would see this illness, it should be considered in the differential diagnosis of febrile encephalopathy or meningoencephalitis in patients who have travelled to endemic regions. This is especially important, as

this disease is rapidly and easily treatable with oral doxycycline but can be fatal without treatment. It is important for U.S. neurologists to stay informed about the various infections that can affect the central nervous system, regardless of the endemic territories. Today, infectious diseases are all global. ■

ABSTRACT & COMMENTARY

Influenza Vaccination: Updated Information for 2015-16

By Stan Deresinski, MD, FACP, FIDSA

Dr. Deresinski is Clinical Professor of Medicine, Stanford University.

Dr. Deresinski reports no financial relationships relevant to this field of study.

SOURCE: Centers for Disease Control and Prevention. Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2015–16 Influenza Season. 2015;64:818-825. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6430a3.htm?s_cid=mm6430a3_w.

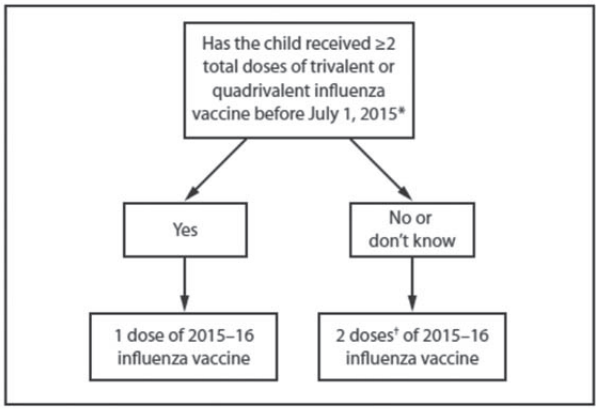
The Centers for Disease Control and Prevention (CDC) has published updates of last year's recommendations of the Advisory Committee on Immunization Practices (ACIP) for the use of seasonal influenza vaccines. The following is a selection of some of the most pertinent ones.

• Antigenic composition of U.S. seasonal influenza vaccines for 2015-16.

U.S.-licensed trivalent influenza vaccines will contain hemagglutinin (HA) derived from an A/California/7/2009 (H1N1)-like virus, an A/Switzerland/9715293/2013 (H3N2)-like virus, and a B/Phuket/3073/2013-like (Yamagata lineage) virus. These are changes in the influenza A (H3N2) virus and the influenza B virus as compared with the 2014–15 season. Quadrivalent influenza vaccines will contain these vaccine viruses, and a B/Brisbane/60/2008-like (Victoria lineage) virus, which is the same Victoria lineage virus recommended for quadrivalent formulations in 2013–14 and 2014–15.

[U.S.-licensed trivalent influenza vaccines will contain hemagglutinin (HA) derived from an A/California/7/2009 (H1N1)-like virus, an A/Switzerland/9715293/2013 (H3N2)-like virus, and a B/Phuket/3073/2013-like (Yamagata lineage) virus.]

Figure 1. Influenza vaccine dosing algorithm for children aged 6 months through 8 years — Advisory Committee on Immunization Practices, United States, 2015–16 influenza season



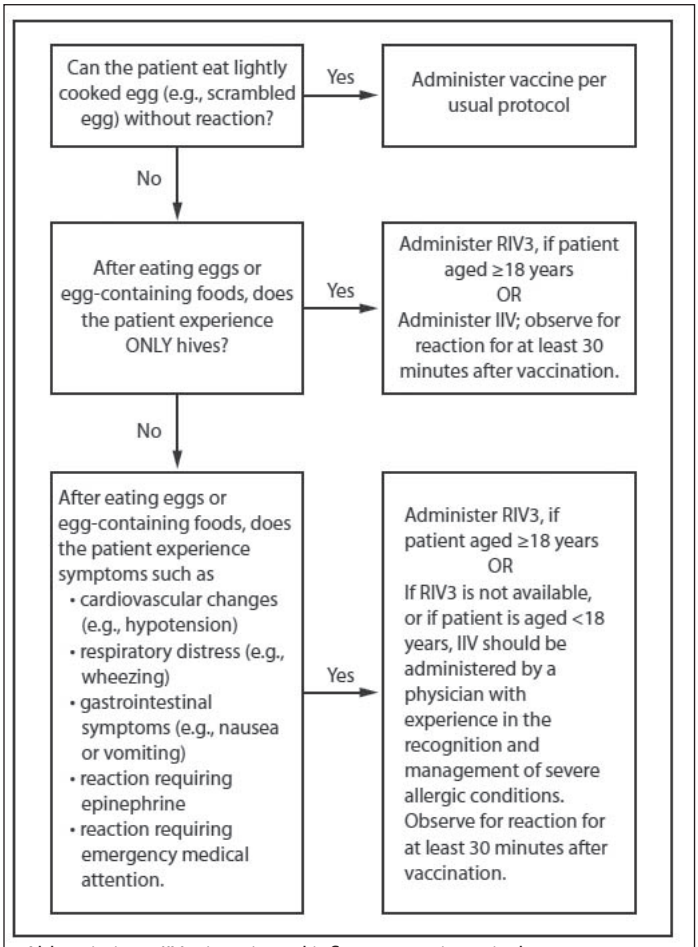
* The two doses need not have been received during the same season or consecutive seasons.
† Doses should be administered ≥4 weeks apart.

Source: Centers for Disease Control and Prevention

• New vaccine products.

Among the new products expected to be available for the 2015-16 season, one is of interest because of its novel method of vaccine delivery. Afluria (inactivated influenza vaccine, bioCSL, Inc., King of Prussia, Pennsylvania) uses a needle-free jet injector rather than a needle for intramuscular vaccine delivery. It is approved for adults aged 18 through 64 years for whom it may be delivered either by the Stratis injector or with a sterile needle and syringe — all other inactivated influenza vaccines are approved for administration by sterile needle and syringe only. The

Figure 2. Recommendations regarding influenza vaccination of persons who report allergy to eggs*† — Advisory Committee on Immunization Practices, United States, 2015–16 influenza season



Abbreviations: IIV = inactivated influenza vaccine, trivalent or quadrivalent; RIV3 = recombinant influenza vaccine, trivalent.
* Persons with egg allergy may tolerate egg in baked products (e.g., bread or cake). Tolerance to egg-containing foods does not exclude the possibility of egg allergy (Erlewyn-Lajeunesse et al., Recommendations for the administration of influenza vaccine in children allergic to egg. BMJ 2009;339:b3680).
† For persons who have no known history of exposure to egg, but who are suspected of being egg-allergic on the basis of previously performed allergy testing, consultation with a physician with expertise in the management of allergic conditions should be obtained prior to vaccination. Alternatively, RIV3 may be administered if the recipient is aged ≥18 years.
Source: Centers for Disease Control and Prevention

Stratis injector is a reusable spring-powered device which injects the vaccine through a single-use sterile needle-free syringe into the deltoid muscle. While local reactions are more frequent with administration by the Stratis injector than in those vaccinated with a sterile needle and syringe, most such reactions resolve within 3 days. Antibody levels after administration by either technique are similar.

• An update of the recommendations for determination of the appropriate number of vaccine doses for children 6 months through 8 years of age (*see Figure 1*).

The change in vaccine composition for 2015–16 means that for 2015–16, ACIP recommends that children aged 6 months through 8 years who have previously received ≥ 2 total doses of trivalent or quadrivalent influenza vaccine before July 1, 2015, require only 1 dose for 2015–16. The two previous doses need not have been given during the same season or consecutive seasons. Children in this age group who have not previously received a total of ≥ 2 doses of trivalent or quadrivalent influenza vaccine before July 1, 2015, require 2 doses for 2015–16. The interval between the 2 doses should be at least 4 weeks.

• New recommendations for the use of live attenuated influenza vaccine (LAIV) and inactivated influenza vaccine (IIV) when either is available.

In the absence of data demonstrating consistent greater relative effectiveness of the current quadrivalent formulation of LAIV, preference for LAIV over IIV is no longer recommended. ACIP will continue to review the effectiveness of influenza vaccines in future seasons and update these recommendations if warranted.

• Influenza vaccination of persons with a history of egg allergy.

With the exceptions of recombinant influenza vaccine (RIV3, Flublok) and cell-culture based inactivated influenza vaccine (ccIIV3, Flucelvax, Novartis, Cambridge, Massachusetts), currently available influenza vaccines are prepared by propagation of virus in embryonated eggs. Nonetheless, severe allergic and anaphylactic reactions are rare. The 2015-16 recommendations are contained in Figure 2. ■

Updates

By Carol A. Kemper, MD, FACP

TB Screening for High-Tech Workers

Source: ProMED-mail post. Tuberculosis – India (03): National TB control program assessed. July 11, 2015. www.promedmail.org.

We're seeing only the tip of the iceberg in Silicon Valley. In my infectious disease practice in Mountain View, CA, we've seen nine new cases of *M. tuberculosis* infection (MTb) in the past few months. Two cases were clearly reactivation TB in older Filipinos who have been in the United States for many years. But seven cases are young Asian Indians, all in their 20s or early 30s, working or going to school in the Silicon Valley. Six were male. At least four of these individuals are here on a student or work visa — which requires no TB screening for entry into the United States. Six had pulmonary involvement, and two were sputum smear-positive, including one patient with drug resistance. The other smear-positive case was a young graduate student at one of the state schools in San Jose who was ill, with 35 pounds of weight loss, hoarseness, and cough for four months before presenting for care and being diagnosed with pulmonary and laryngeal MTb — the most highly contagious form for the disease. His smears were 4+ smear-positive on presentation, and remained positive for weeks on therapy. He had declined to pay for student health insurance, and had been reluctant to seek medical care.

It is no surprise we are seeing these kinds of cases in Silicon Valley, especially after reviewing recent reports from India. A draft Indian public health report for the "Revised National TB Control Program" (or what is referred to as RNTC), leaked by authorities in India, suggests that MTb may be close to out of control in some parts of India. While the WHO global TB report suggests that cases of TB in India have steadily declined during the previous 10 years, other data suggest this is the result of under-diagnosis and under-reporting.

Approximately two million cases of MTb were diagnosed in India in 2013, representing one-fourth of the world's cases, and resulting in approximately 270,000 deaths. The recent draft report states that perhaps as many as 1,000,000 additional cases are undetected or unreported. The RNTC program is overwhelmed and underfunded. Delays in procurement of medications are frequent, and sufficient laboratory facilities and technology are lacking. Most importantly, many labs are not able to perform necessary screening tests for susceptibility, and therefore cases of drug resistance may be missed or mis-treated. One-third of cases are empirically treated without microbiologic diagnosis. And private hospitals have no obligation to participate in the care of these patients.

In addition, MDR- and XDR-TB is emerging as a major threat in India. Officially 2.2% of new MTb cases in India are MDR. This is considered an under-estimate, since many cases have no susceptibility testing performed. And the RNTC program lacks adequate resources and facilities to manage these more complex cases.

I make an argument that immigration reform measures and H-IB visa policy, currently being pushed by the high-tech industry, need to incorporate adequate screening measures for MTb. In their push for adequate skilled workers, tech companies are overlooking an important contagious disease and neglecting the health of their future work force.

Cellulitis or Pseudocellulitis?

Source: Strazzula L, et al. Inpatient dermatology consultation aids diagnosis of cellulitis among hospital patients: A multi-institutional analysis. *J Am Acad Dermatol* 2015;73:70-75.

Cellulitis remains a leading cause of hospitalization, and data suggest, with our increasingly obese, diabetic population, the incidence is increasing. Mean hospital stays are estimated at seven days. However, accurate diagnosis of cellulitis can be a challenge — and studies have suggested that up to 28% of hospital cases of cellulitis may be misdiagnosed. Pseudocellulitis, which is

[... accurate diagnosis of cellulitis can be a challenge — and studies have suggested that up to 28% of hospital cases of cellulitis may be misdiagnosed.]

a non-infectious, non-necrotizing condition, can mimic cellulitis in many ways, also presenting with warmth, redness, swelling, pain, and even fever and leukocytosis. Distinguishing the two conditions is an important challenge to physicians and infectious disease specialists caring for these patients in the hospital. Over-diagnosis and over-treatment of cellulitis in the outpatient setting may also be common: A recent British study found that 100% of patients referred to a primary care doctor for evaluation of cellulitis were diagnosed with cellulitis, compared with only 10% of those referred to dermatology.

A retrospective review of 1430 inpatient dermatology consults performed at several major medical centers throughout the United States found that 74 (5.1%) were requested for evaluation of cellulitis. Presenting signs and symptoms, risk factors, and outcomes were reviewed and compared for diagnosis of cellulitis vs. pseudocellulitis. Nearly three-fourths (74.3%) of the possible cellulitis cases evaluated were found to have alternate conditions. The most common diagnosis was stasis dermatitis (31%), followed by contact dermatitis (14.5%) and inflammatory tinea (9%). Other diagnoses included drug eruption, erythema chronicum migrans, psoriasis, vasculitis, and lymphedema. One-third were found to have more than one of these diagnoses. Skin biopsies were performed in only one-third of the patients, and the rest were diagnosed based on dermatologic expertise.

Risk factors and presenting signs and symptoms for patients with cellulitis and pseudocellulitis were similar — and, therefore, may not be reliable diagnostic cues. Interestingly, only 5% of those with cellulitis presented with leukocytosis, compared with 16% of those with pseudocellulitis.

These dermatologists argue that clinicians would be wise to consider alternate diagnoses when evaluating patients with cellulitis, and inpatient dermatology consultation may be helpful in distinguishing infectious cellulitis from non-infectious cases. As someone who sees an awful lot of cellulitis, I'd like to know what the dermatologists seem to know — especially since the patients presented similarly, and most did not have skin biopsies performed.

Screening for Creutzfeldt-Jakob Disease Before Invasive Procedures

Source: Brown P, Farrell M. A practical approach to avoiding iatrogenic Creutzfeldt-Jakob disease (CJD) from invasive instruments. *Infect Control Hosp Epidemiol* 2015;36(7):844-848.

The use of dedicated equipment and surgical instruments for patients with proven Creutzfeldt-Jakob disease (CJD) is standard practice, with incineration of all materials with body fluid or tissue contamination. But problems arise when patients with unproven or unsuspected disease undergo invasive procedures. What about those who have not yet been diagnosed?

These authors suggest a relatively low-cost pre-emptive screening approach may be helpful. Any patient with dementia or cerebellar signs (even if another diagnosis seems likely) being considered for any invasive procedure should have routine screening of spinal fluid for 14-3-3 protein. Based on reports of the specificity (> 90%) and sensitivity of the test, this simple screening tool could significantly reduce iatrogenic risk in hospitals. Alternatively, a test detecting aberrant prior protein in nasal washings may prove useful.

[Based on reports of the specificity (> 90%) and sensitivity of the test, this simple screening tool could significantly reduce iatrogenic risk in hospitals.]

A recent 10-year longitudinal study of neurologic patients in Europe examined the utility of the 14-3-3 protein and other dementia markers in patients with neurologic disease.[1] A huge number of cerebrospinal fluid samples were analyzed (n= 29,022). The 14-3-3 proved to be a useful biomarker, with an overall specificity of 90%. In patients with neurodegenerative disease, the specificity of the 14-3-3 prion screening test was 95-97%, compared to that found for other acute neurologic diseases (82-85%).

Hospital infection control programs will have to consider alternate scenarios for risk as well, such as those patients with characteristic symptoms with a negative screening test but nonetheless suspected of having CJD; asymptomatic persons who carry the PrP(sc) gene mutation; and/or asymptomatic individuals who have received potentially contaminated human growth hormone, dural grafts, or blood products. ■

1. Stoeck K, Sanchez-Juan P, Gawinecka J, et al. Cerebrospinal fluid biomarker supported diagnosis of Creutzfeldt-Jakob disease and rapid dementias: A longitudinal multicentre study over 10 years. *Brain* 2012;135(Pt 10):3051-3061.

CME INSTRUCTIONS

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CME QUESTIONS

1. Which of the following is correct with regard to *Borrelia miyamotoi* infection?

A. It is associated with positive EIA tests for *Borrelia burgdorferi*.

B. Infection is seldom associated with fever.

C. Its hallmark skin lesion is erythema migrans.

D. It most often causes acute meningoencephalitis.

2. Which of the following is correct with regard to adults hospitalized with acute community-acquired pneumonia in the report by Jain et al?

A. *Streptococcus pneumoniae* was recovered from 43% of patients.

B. A pathogen was identified in 82% of patients.

C. *Enterobacteriaceae* were recovered from < 2% of patients.

D. Fungi accounted for 8% of infections.

3. Fly and flea larvae can embed and grow in human skin. Preventive measures include all of the following *except*:

A. wearing closed-toe shoes

B. using insect repellent

C. ironing clothes before wearing them

D. ingesting garlic daily during travel

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 latest 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