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Infectious Disease [ALERT]

Incisive Commentary and Clinical Abstracts on Current Issues in Infectious Diseases

ABSTRACT & COMMENTARY

Clindamycin vs. Trimethoprim-Sulfamethoxazole for Uncomplicated Skin Infections

By Dean L. Winslow, MD, FACP, FIDSA

Dr. Winslow is Chairman, Department of Medicine, Santa Clara Valley Medical Center, Clinical Professor of Medicine and Pediatrics (Affiliated), Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine.

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

SYNOPSIS: Five hundred twenty-four children and adults with either cellulitis or abscesses larger than 5 cm (smaller for children) were enrolled in a multisite prospective study of clindamycin vs. trimethoprim-sulfamethoxazole dosed for 10 days. Cure rates did not differ between the treatments, and rates of adverse events were similar in the two groups.

SOURCE: Miller LG, et al. Clindamycin versus trimethoprim-sulfamethoxazole for uncomplicated skin infections. *N Engl J Med* 2015;372:1093-1103.

Five hundred twenty-four patients (including 155 children) were enrolled in a prospective, double-blinded, randomized trial of clindamycin vs. trimethoprim-sulfamethoxazole in uncomplicated skin infections. Fifty-three percent had cellulitis, 31% had abscesses, and 16% had mixed cellulitis/abscess. *Staphylococcus aureus* was isolated from 41% of patients, and 77% of these were methicillin-resistant *S. aureus* (MRSA). Overall cure rates were 80% in the clindamycin group and 78% in the trimethoprim-sulfamethoxazole group. Cure rates did not differ significantly between the two antibiotics in the subgroups of children, adults, and abscess vs. cellulitis. Rates of adverse events were similar in the two groups.

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Editorial E-Mail:
shelly.mark@ahcmedia.com

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While this study is a bit difficult to interpret due to a mix of cellulitis (non-suppurative) and abscess (suppurative), the data are important since it is a large study and addresses a real-world question of which of two reasonable choices of antibiotics works best in uncomplicated skin infections commonly encountered in the primary care and emergency department (ED) setting.

It could be argued that inclusion of a placebo arm would have been helpful since previous studies suggest that incision and drainage alone is appropriate treatment for small abscesses and antibiotics are not necessary. However, an earlier study performed in children demonstrated that abscesses larger than 5 cm were often associated with treatment failure unless adjunctive antibiotics were administered.[1] As expected, cultures were not obtainable in patients with cellulitis without abscess (and presumably were almost always due to beta-hemolytic streptococci). The surprisingly high response rate of cellulitis to trimethoprim-sulfamethoxazole suggests that the historical concern about poor activity of trimethoprim-sulfamethoxazole against streptococci may be unfounded. Interestingly, a recent study showed that *S. pyogenes* are generally trimethoprim-sulfamethoxazole susceptible if low-concentration thymidine agar is used for susceptibility testing.[2]

The rates of *S. aureus* resistance to clindamycin and trimethoprim-sulfamethoxazole were 5.2% and 0.2%, respectively, and although a slightly lower cure rate was seen with clindamycin in those rare clindamycin-resistant strains of Staph (73% with clindamycin vs. 92% with trimethoprim-sulfamethoxazole), this should not necessarily preclude the empiric use of clindamycin in uncomplicated skin infections where close follow up can be assured. Interestingly, no cases of *C. difficile* infection were seen in either arm of the study, suggesting that this is not a serious concern in this relatively young and healthy population when only a 10-day course of therapy is prescribed.

The results of this study did reinforce a couple of things I teach the residents and fellows.[1] Clindamycin is a great antibiotic for skin (and bone) infections as long as one knows that the *Staph. aureus* is susceptible in vitro. Clindamycin is just as effective and as well tolerated as linezolid — and much less expensive.[2] It adds further evidence to support my dislike of the common ED practice of prescribing both cephalexin and trimethoprim-sulfamethoxazole to patients with skin infections. (My fear is that when a patient treated with this combination develops a rash, then they are often labeled for life as being "allergic to beta-lactam antibiotics *and* sulfonamides.") This should reassure the practitioner that despite our previous concerns, trimethoprim-sulfamethoxazole probably treats uncomplicated streptococcal skin infections adequately. ■

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ABSTRACT & COMMENTARY

The Response to Ebola in the United States — Current Status and Lessons Learned

By Stan Deresinski, MD, FACP, FIDSA

Dr. Deresinski is Clinical Professor of Medicine, Stanford University; Associate Chief of Infectious Diseases, Santa Clara Valley Medical Center.

Dr. Deresinski has served as a one-time consultant for Cubist and Bayer.

SYNOPSIS: Much was learned in the United States in dealing with the fear of Ebola virus infection — but can we avoid wasteful panic with the next outbreak of a novel pathogen?

SOURCE: Koonin LM, Jamieson DJ, Jernigan JA, et al. Systems for rapidly detecting and treating persons with Ebola virus disease — United States. *MMWR Morb Mortal Wkly Rep*. 2015;64(8):222-225.

The Ebola outbreak in West Africa appears to be winding down, and the panic in the United States spread by cable news and politicians (a strong argument for urgent improvements in science teaching in the United States) appears to have subsided. Given the enormous efforts put forth and money wasted for activities within this country, it is a good time to review the current status of activities here.

Since August 2014, exit screening procedures for international flights leaving countries with Ebola activity (Liberia, Sierra Leone, Guinea — and for several months ending in January 2015, Mali) include administration of a health questionnaire, measuring body temperature, and, if fever is detected, assessment of the likelihood of the fever being caused by Ebola. Travelers who have fever or symptoms compatible with Ebola or who report a high risk for exposure to Ebola are, as a consequence, denied boarding on international flights.

Travelers to the United States from Liberia, Sierra Leone, or Guinea are all routed to one of five international airports — JFK (New York City), Dulles (Washington D.C.), Liberty (Newark), O'Hare (Chicago), or Hartsfield-Jackson (Atlanta). Those with a possible Ebola exposure risk are further evaluated by onsite CDC public health officers. Individuals with symptoms such as fever undergo additional assessment and may be referred for care at a local hospital.

State and local health authorities are notified by CDC within hours of individuals who require monitoring. Monitoring continues until 21 days after their departure from one of the target countries, during which time they are required to measure their temperature at least twice daily. Some with greater exposure, such as those who provided health care to an Ebola patient, must also report twice daily to public health authorities, including once with direct visual contact. Anyone who develops Ebola-compatible symptoms is immediately referred for medical assessment at a health care facility.
Acute health care facilities (AHCF) serve one of three roles in dealing with Ebola: frontline health care facilities, Ebola assessment hospitals (EAH), and Ebola treatment centers (ETC). Although patients with possible symptomatic infection are generally referred to higher level facilities, they may in some cases initially may be dealt with at acute health care facilities — most acute hospitals with emergency departments meet criteria for this designation (assuming, of course, proper training of personnel). AHCFs should be prepared to rapidly identify and isolate patients who might have Ebola, promptly inform the hospital/facility infection control program and state and local public health agencies, and quickly transfer these patients to an EAH or ETC.

EAH facilities are able to safely provide care until an Ebola diagnosis is confirmed or excluded, and manage other conditions present (e.g., malaria) until, in confirmed cases, transfer to an ETC where they may receive comprehensive care for the duration of illness. As of February 18, 2015, there were 55 U.S. hospitals with designated Ebola treatment centers. Three U.S. biocontainment units (Emory University Hospital, the National Institutes of Health Clinical Center, and Nebraska Medicine) also serve as Ebola treatment centers.

The Office of the Assistant Secretary for Preparedness

and Response (ASPR) at the Department of Health and Human Services is taking this tiered approach further by developing a regional approach. As many as 10 Ebola treatment centers with enhanced ability to care for patients with highly infectious diseases, including Ebola, will be designated to serve as regional Ebola and other special pathogens treatment centers. These centers will be able to receive patients with confirmed illness from anywhere in the United States, as well as patients who have been medically evacuated from outside of the United States. Patients with confirmed Ebola will be preferentially referred to one of these regional centers, as necessary. In addition, CDC Ebola response teams are deployed by request to any Ebola treatment center or hospital with a confirmed or highly suspected case of Ebola to provide technical assistance for infection control procedures, clinical care, and logistics of managing a patient with Ebola.

What have been the results of these activities? From October 11, 2014, through January 31, 2015, a total of 7,587 persons arriving from affected countries have been screened upon entry to the United States. Of these, 543 (7.2%) were referred to onsite CDC screening at the airport for additional exposure risk assessment. At the time of assessment, 12 (0.16%) travelers were referred for medical evaluation at a local hospital, and none had Ebola diagnosed. During October 11, 2014–January 31, 2015, at least 136 persons were identified as "persons under investigation" (PUIs) (individuals with an epidemiologic risk factor within the preceding 21 days with symptoms compatible with Ebola). None of these persons under investigation had Ebola; the most common diagnoses were malaria and influenza.

In December 2014, Gregg Gonsalves, taking lessons from dealing with the panic that accompanied the early years of the AIDS epidemic in the United States, addressed the Ebola panic by saying that, "We all have to become activists if we are to protect the public health from being used as a tool to serve primarily political purposes, as it has been over the past few weeks in the United States."[1] In other words, don't let the politicians and cable news bloviators run the asylum. ■

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ABSTRACT & COMMENTARY

Rectal Colonizing *E. coli* Cause Most Infections Following Transrectal Biopsy of the Prostate

By Richard R. Watkins, MD, MS, FACP

Division of Infectious Diseases, Akron General Medical Center, Akron, OH; Associate Professor of Internal Medicine, Northeast Ohio Medical University, Rootstown, OH

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

SYNOPSIS: An observational cohort study found that rectal colonizing strains of *E. coli* are the source for most fluoroquinolone-resistant post-transrectal prostate biopsy infections. Pre-procedure screening cultures should be considered.

SOURCE: Liss MA, et al. Clinical and microbiological determinants of infection after transrectal prostate biopsy. *Clin Infect Dis* 2015;60:979-987.

The incidence of infections following transrectal prostate biopsy (TPB) has been increasing, especially from strains of fluoroquinolone-resistant *Escherichia coli*. This has led some urologists to try alternative approaches to traditional fluoroquinolone prophylaxis, such as pre-procedural rectal swab cultures to guide individual antibiotic selection. Liss and colleagues investigated whether these colonizing rectal *E. coli* strains were associated with TPB infections.

The study was conducted at the San Diego Veterans Affairs Medical Center between January 1, 2010, and February 6, 2014. Patients who were undergoing TPB had a pre-procedure rectal culture done as part of a quality-improvement program. After the

procedure, the patients were followed for post-TPB infections, defined as a presentation to the emergency department with lower urinary tract symptoms, fever, and/or chills within 7 days of the TPB. These clinical isolates of the patients with infections were captured for genetic analysis. The association of fluoroquinolone-resistant *E. coli* rectal colonization with post-TPB infection was determined by comparing the infection rate among carriers to noncarriers. Clonal similarity was assessed between the pre-TPB rectal culture and the post-TPB infection culture. The characteristics that distinguished infectious isolates from colonizing isolates were elucidated using a subset of colonization isolates. These were obtained from patients who did not develop post-TPB infections and all the post-TPB infection isolates (urine and blood), regardless of whether the source patient underwent pre-biopsy rectal culture. Of note, not every patient had a rectal culture despite its being part of the biopsy protocol due to logistical reasons (e.g., lack of culture media).

Of the patients who underwent TPB, 15% carried fluoroquinolone-resistant rectal *E. coli* before biopsy. Post-TPB infection was more common in those who were colonized (13/121 [10.7%]) vs. non-colonized (8/649 [1.2%]; P < 0.001). Risk factors for post-TPB infection included hospitalization in the last year (OR, 4.5; 95% CI, 1.1-19.4; P = 0.04) and colonization with fluoroquinolone-resistant *E. coli* (OR, 4.55; 95% CI, 1.2-18.2; P = 0.03). Twenty percent of patients received supplemental prophylactic antibiotics in addition to ciprofloxacin, of which a single dose of intramuscular ampicillin was the most common agent prescribed (151/160; 94%). The infection rate was similar among patients who did and did not receive supplemental antibiotics (2.5% vs 2.7%, respectively; P = 0.83). Finally, the tested virulence genes did not differ significantly between the colonization and infection isolates (P = 0.73).

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This study provides the first direct evidence that a patient's own microbiota is the source for most infections following a TPB. This finding implies, but does not prove, that rectal bacteria are directly introduced into the blood, urine, and/or prostate tissue by the biopsy needle. Furthermore, the antibiotic-resistant *E. coli* that cause these infections can be identified prior to the procedure by a rectal culture. So what are the clinical implications of this study? It is likely premature to recommend rectal cultures for all patients for whom a TPB is planned. However, this approach is reasonable for select patients, such as those hospitalized in the past year or at high risk for having fluoroquinolone-resistant pathogens (e.g., recent fluoroquinolone use, history of a fluoroquinolone-resistant pathogen, travel to a country with a high prevalence of fluoroquinolone-resistant organisms, and immunocompromised patients at increased risk for sepsis). Another scenario could be as part of an infection control policy if the institution had an especially high rate of post-TPB infections.

The main disadvantage of rectal cultures is the additional cost. However, this must be balanced against the costs associated with TPB infections, such as emergency department visits and hospitalizations. Further cost-benefit studies are warranted to clarify this issue. Moreover, additional prospective, randomized studies are needed to determine whether choosing a pre-procedure antibiotic based on a rectal culture will lead to better outcomes while minimizing additional antibiotic usage. ■

ABSTRACT & COMMENTARY

Typhoid Vaccination

By Stan Deresinski, MD, FACP, FIDSA

Dr. Deresinski is Clinical Professor of Medicine, Stanford University; Associate Chief of Infectious Diseases, Santa Clara Valley Medical Center.

Dr. Deresinski has served as a one-time consultant for Cubist and Bayer.

SYNOPSIS: Vaccination against typhoid continues to be important for many travelers to at-risk countries in Asia, Africa, and Latin America.

SOURCE: Jackson BR, Iqbal S, Mahon B. Updated recommendations for the use of typhoid vaccine — advisory committee on immunization practices, United States, 2015. *MMWR Morb Mortal Wkly Rep.* 2015;64:305-308.

While only approximately 400 cases of typhoid fever are diagnosed and reported each year in the United States, nine of 10 occur in returned travelers, three-fourths of whom had been in India,

Pakistan, or Bangladesh, and with the majority having visited family and friends. While the number of cases is small, the infection can be life-threatening. Furthermore, the frequency of antibiotic resistance, including to fluoroquinolones, is increasing among isolates of Salmonella serotype Typhi.

There are currently two modestly protective vaccines available in the United States — each with an overall estimated protective efficacy of approximately 50%. Furthermore, the vaccines provide no or very limited protection against Paratyphoid infection at a time when the incidence of disease due to Paratyphoid A is increasing. Despite this relatively limited protection, vaccination is recommended for travelers to a number of countries in Asia, Africa, and Latin America — the individual countries can be seen at the CDC web site.[1] The vaccines are a Vi capsular polysaccharide vaccine for intramuscular administration (Typhim Vi) and an orally administered live-attenuated vaccine (Vivotif) derived from the Ty21a strain of Salmonella serotype Typhi. The latter should not be administered to immunocompromised individuals and should not be given together with antibacterial agents.

The Vi vaccine is administered as a single injection, while the attenuated Ty21a vaccine is contained in an enteric-coated capsule (which must be kept refrigerated, but not frozen). A single capsule of Ty21a is taken with water that is less than 37.0°C approximately one hour before a meal on alternate days for a total of four doses. Vi should be administered at least two weeks prior to potential exposure, while Ty21a administration should be completed at least one week before potential exposure.

In addition to vaccination of travelers to at-risk countries, CDC also recommends immunization of individuals, such as household contacts, with close exposure to chronic typhoid carriers. In addition, microbiologists and other laboratory workers routinely exposed to cultures of Salmonella serotype Typhi or specimens containing this organism, or who work in laboratory environments where these cultures or specimens are routinely handled, should be vaccinated.

The manufacturer of the Vi polysaccharide vaccine recommends a repeat dose every two years after the primary dose if continued or repeat exposure is expected. In contrast, the manufacturer of Ty21a recommends revaccination with the entire four-dose series every five years if continued or repeated exposure to Salmonella serotype Typhi is expected.

The relatively poor protection provided by these vaccines highlights the importance of the use of discretion by travelers in attempting to avoid potentially contaminated food and water. ■

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ABSTRACT & COMMENTARY

Pneumonia in U.S. Children Requiring Hospitalization

By Dean L. Winslow, MD, FACP, FIDSA

Dr. Winslow is Chairman, Department of Medicine, Santa Clara Valley Medical Center, Clinical Professor of Medicine and Pediatrics (Affiliated), Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine.

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

SYNOPSIS: Two thousand six hundred thirty-eight children with a clinical diagnosis of community-acquired pneumonia (CAP) were enrolled in a prospective surveillance study. Eighty-nine percent had radiographic evidence of pneumonia. The median age of children hospitalized was 2 years, with the highest rates seen in children younger than 2 years. Respiratory viruses were the most commonly detected pathogens.

SOURCE: Jain S, et al. Community-acquired pneumonia requiring hospitalization among U.S. children. *N Engl J Med* 2015;372:835-845.

Two thousand six hundred thirty-eight of 3803 eligible children were enrolled from January 2010 through June 2012 in a prospective study of children younger than 18 years old requiring hospitalization at three children's hospitals in the United States (Memphis, Nashville, and Salt Lake City). Children with recent hospitalization or severe immunosuppression history were excluded.

Blood and respiratory specimens were collected for pathogen detection by traditional cultures and PCR. Chest X-rays were independently reviewed by a panel of study radiologists.

Eighty-nine percent of children hospitalized had radiographic evidence of pneumonia. The mean age was 2 years old. Twenty-one percent of children required admission to intensive care units, 7% required mechanical ventilation, and 3 children (1%) died. Thirty-three percent of children had underlying asthma or reactive airway disease, and 21% of children younger than 2 years old had a history of preterm birth. Among the 2222 children with radiographic evidence of pneumonia, a viral or bacterial pathogen was detected in 81%, one or more viruses in 66%, bacteria in 8%, and both bacterial and viral pathogens in 7%. The overall incidence of CAP requiring hospitalization in children was 15.7 cases/10,000 children and the highest rate was in children younger than 2 years, in whom the rate was 62.2 cases/10,000 children.

Respiratory syncytial virus (RSV) was more common in children younger than 5 years of age than in older children (37% vs. 8%), as were adenovirus (15% vs. 3%), and human metapneumovirus (HMPV) (15% vs. 8%). Together, HMPV, adenovirus, parainfluenza virus, and coronavirus accounted for one-third of pathogens detected, with the highest rates seen in children younger than 5 years old. As expected, RSV peaked sharply in the winter months. Human rhinovirus was detected in 27% of children with pneumonia. Bacterial pathogens were detected in 15% of children with pneumonia. Streptococcus pneumoniae was detected in just 79 cases (2%) and was roughly equal in younger and older children. *Mycoplasma pneumoniae* was more common in children older than 5 years of age than in younger children (19% vs. 3%).

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This paper presents a nice update on the etiology of CAP in children requiring hospitalization and used modern sensitive laboratory methods to reveal an etiology of infection in a high percentage of patients studied. The study reinforces the importance of CAP requiring hospitalization being of much higher incidence in very young children. Of note in this study was the predominance of viral vs. bacterial pathogens identified in this study (71% vs. 15%), with some overlap in cases in which both viral and bacterial pathogens were identified. The predominance of viral pathogens, especially in young children, was striking and likely reflects both the direct effects (and herd immunity effects) of the use of both pneumococcal conjugate vaccine and HiB vaccine. It should also be noted that this study took place after the 2009-2010 pandemic of Influenza A (H1N1), which would have made the incidence of I\ influenza virus more common than was seen in this study. ■

ABSTRACT & COMMENTARY

Caring for Unaccompanied Central American Immigrant Children

By Lauren M. Carlson, Sherrill (Charlie) Rose, and Philip R. Fischer, MD, DTM&H

Lauren Carlson and Sherrill (Charlie) Rose are students at Mayo Medical School in Rochester, MN. Dr. Fischer is Professor of Pediatrics, Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN.

Ms. Carlson, Ms. Rose, and Dr. Fischer report no financial relationships relevant to this field of study.

SYNOPSIS: Physicians can improve the health of unaccompanied Central American immigrant children by ensuring appropriate vaccination, by identifying culturally and linguistically appropriate community resources, and by becoming involved in patient advocacy.

SOURCE: Robinson LK. Arrived: The crisis of unaccompanied children at our southern border. *Pediatrics* 2015;135:205-207.

With 60,000 children arriving in the United States through the southern border within the first eight months of 2014, physicians voiced desires to understand more about the situation of these immigrants and to find appropriate ways to help. Many of the unaccompanied children and young families are arriving from Guatemala, El Salvador, and Honduras, countries facing extreme poverty and violence. A few media and public officials have suggested that these children pose a public health threat. One response, on behalf of medical providers, is to identify the facts and to share this information

with the local community, including the difference between serious and nonserious conditions, as well as opportunities for treatment. Unaccompanied children entering the country undergo health screening and vaccination through the U.S. Department of Health and Human Services (HHS), including a tuberculosis screen, urine pregnancy test for girls older than 9 years of age, and multiple critical vaccinations appropriate for a catch-up schedule identified by the Advisory Committee on Immunization Practices.

Robinson identifies three important responses by U.S.-based physicians: to vaccinate, to know your community resources, and to advocate. Identification of a catch-up immunization schedule for children is crucial, and although immigrants may not be eligible for federal assistance programs, they may be eligible for local charity care and the Centers for Disease Control and Prevention's Vaccines for Children program. In addition to identifying local organizations serving Spanish-speaking populations through the process of clinical care and satisfaction of other essential needs, use of interpreter services and Spanish screening forms are aspects of providing culturally and linguistically appropriate resources through a clinic. Advocacy may take many forms, such as medico-legal partnerships to improve awareness of immigrant rights, as well as supporting greater access to services, both legal and medical, for immigrants and underserved populations in general. Looking ahead, providers have an opportunity to support immigrants in breaking the barrier of health care access.

■ COMMENTARY

There is an ongoing need for pediatricians and infectious disease physicians to consider the special needs of immigrant children in the United States. To this end, the author offers compelling direction on how to begin the process of improving the health of Central American child immigrants to the United States. Issues of immunization and infectious disease are vitally important for immigrant children. At the same time, though, infectious disease physicians can also promote overall health among vulnerable child immigrants.

It is important for physicians to be able to identify the unique health risks of a population and also to be able to separate legitimate health risks and need from health concerns that are primarily media-driven. In addition to the author's examples of spurious connections between immigrant children and both H1N1 and Ebola, we have also seen attempts to make connections between immigrants and the recent measles and enterovirus outbreaks. The Health and Human Services Department and the CDC have denied any connection between the immigrant children and either measles or enterovirus outbreaks in the United States. In the case of measles, World Health Organization records show that from 2009-2013, the last five years for which data are available, measles vaccine rates in El Salvador, Honduras, and Guatemala have often exceeded rates in the United States.

Although Central American countries have generally strong vaccination rates, it does appear that there is greater year-to-year variation in vaccination rates in Central American countries than in the United States. During that five-year period, U.S. rates ranged from 90-92%, while rates in Central America ranged from 85-99%. These fluctuations may show that vaccination rates in Central America are more vulnerable to external influence, such as economic instability or sociopolitical factors. Also, children in migration are presumably at higher risk for missing routine preventive health care, and factors such as whether children are coming from urban or rural settings may also influence their access to care. Physicians should not assume that a child from Central America has been vaccinated but should instead rely on vaccination records when they are available and initiate catch-up vaccination schedules when necessary. Suggested schedules are available from the CDC.[1]

Beyond initiating catch-up vaccinations, physicians should be aware of and screen as needed for infectious diseases for which Central American immigrants may be at risk but for which no vaccine is readily available, such as Chagas disease, HIV, intestinal parasites, and sexually transmitted infections (STIs). Current HHS practices include a urine pregnancy test for girls older than the age of 9, which illustrates a need for STI screening as well, especially because of the high potential for rape before or during the journey to the border. It may be useful for physicians to research the particular endemic diseases in the country of origin as well as countries passed en route to the United States. For example, an estimated 1.98%, 3.05%, and 3.37% of immigrants from Guatemala, Honduras, and El Salvador, respectively, are infected with *Trypanosoma cruzi*, the causative agent of Chagas disease.[2] Chagas disease is considered a neglected tropical illness. There are no guidelines for routine screening, although it may be warranted in this high-risk population, especially because infection is only curable in the acute phase and can lead to lifelong cardiac complications. Comorbid infections can worsen the prognosis for diseases like Chagas; for example, co-infection with HIV and Chagas hastens progression of illness.

Screening guidelines for Chagas infection should be considered as part of an effort to treat congenitally infected infants. All immigrant mothers should possibly be screened, as screening guidelines exist for babies born to seropositive mothers to be tested at 9 months of age. Antiparasitic treatment is indicated for all patients with acute disease, including congenital infections, and is advised for patients with chronic disease who are up to 18 years of age; even though there is no FDA-approved treatment for Chagas, nifurtimox and benznidazole have proven efficacious.[3] Concerned physicians can advocate for an improvement of existing screening guidelines and treatment availability and can also educate fellow providers and the patient population about the disease.

Other important factors that impact the health of Central American children include language barriers and the resurgence of family detention centers. Many Central American immigrants speak only indigenous languages and require translation services. In addition, as immigrant families and children are detained in institutional settings, there will be added risk for contracting diseases such as TB that flourish in some detention centers. ■

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Infectious Disease [ALERT]

Updates

By Carol A. Kemper, MD, FACP

Legionella Revisited

Euser SM, de Jong S, Bruin JP, et al. Legionnaires' disease associated with a car wash installation. *Lancet.* 2013;382:2114.

van Heijnsbergen E, et al. Confirmed and potential sources for Legionella reviewed. *Environ Sci Technol* 2015 April 1 (Epub ahead of print).

Environmental investigation has shown that Legionella organisms may be found throughout nature, as well as colonizing drinking water systems and other man-made water structures that either mist, bubble, or spray water. When and why these organisms become infectious to humans is not always clear. The Netherlands have been performing source investigations and environmental surveillance for Legionella organisms for many years through a National Legionella Outbreak Detection Programme, and have uncovered some surprising sources for human infection.

Recent investigation examined the case of an 81-year-old man who presented to a hospital with fever and bilateral pulmonary consolidation, subsequently confirmed to be due to *L. pneumophila* serogroup 1 strain based on urinary antigen testing and isolation of the organism from respiratory secretions. Following a 24-day hospital stay, he was discharged to home. The Legionella Outbreak Detection Programme investigates all potential sources for human infection and, in this case, examined 26 samples collected from four potential sources: the home taps and shower; the taps and shower at a hotel where the patient stayed; a fountain near the hotel; and a car wash where he washed his car with a hand-held power hose. All of the samples from the home, the hotel, and the fountain were negative. But two samples taken from the car wash were positive for *L. anisa* and a sample from the car wash hose contained *L. pneumophila*, which appeared identical to the patient's isolate based on amplification fragment length polymorphism testing. The temperature of the hose was 21.5°C (70.7°F). This finding suggests the car wash was the source for the patient's infection.

Retrospective examination revealed two patients diagnosed with Legionellosis three years earlier who reported using the same car wash. At that time, investigation of the car wash turned up only a single positive sample for *L. anisa*. Samples from various car wash installations taken throughout the Netherlands between 2002 and 2010 found that two of 11 were positive for non-pneumophila Legionella spp. Such car washes are used throughout the Netherlands, and could serve as a source of Legionella infection. This information could lead to regular inspection of car wash installations,

recommendations for routine maintenance and disinfection, and equipment modification.

Treatment of Latent Tuberculosis

Goswami ND, et al. Predictors of latent tuberculosis treatment initiation and completion at a U.S. public health clinic: A prospective cohort study. *BMC Public Health* 2012;12:468-475.

Initiation — and completion — of self-administered treatment for latent tuberculosis (TB) infection (LTBI) remains a challenge for clinicians. Treatment for LTBI is considered optional, even for those with recent exposure and skin test conversion who may be at the highest risk for active TB (approximately 50% within two years of exposure). Public Health Guidelines "strongly recommend" treatment for such cases, somewhat more exuberant than the standard "recommended" treatment for LTBI, but hardly requisite.

These authors investigated demographic, medical, and behavioral factors associated with a willingness to initiate and continue treatment for LTBI in adults (18 years or older) attending a public health TB clinic in Raleigh, NC. Between 2008 and 2009, 496 adults met the CDC guidelines for LTBI treatment, and upon entry to the clinic, were interviewed, counseled, and provided a self-administered questionnaire which inquired as to their health, social factors, and attitude toward TB and treatment. All medications were provided free of charge through the clinic on-site pharmacy. Primary endpoints were the number of people who initiated treatment (as defined by picking up at least one month of medication), and the number who completed treatment (defined as picking up 9 months of INH medication within a 12-month period or 4 months of rifampin within a 6-month period).

Of the 496 participants, 87% were racial/ethnic minorities and 65% were foreign born. Nearly two-thirds were referred to the clinic by their employers for screening and evaluation, and 19% were identified during contact investigations. Only 130 (26%) persons started LTBI treatment, and 70 (14%) completed therapy. Half (52%) of those receiving INH completed treatment, and 61% of those receiving rifampin completed treatment. Nearly two-thirds of those receiving INH completed at least 6 months of treatment, although compliance with both regimens diminished over time. Seven of 99 (7%) persons receiving INH were switched to rifampin, and 1/31 (3%) receiving rifampin was switched to INH.

In multi-variate analysis, factors independently associated with treatment initiation included close contact with a TB case, a non-employment reason for screening, lower education level, and having a regular physician. Persons with underlying medical conditions, who were considered a greater risk for TB reactivation, were more likely to complete treatment than those at lower risk (45% vs 17%, $P < .01$). While income/geographic factors did not appear to influence a willingness to start treatment, persons living in higher income areas were more likely to complete their treatment than those in lower income areas (81% vs 42%, $P = .08$).

Other studies have demonstrated higher rates of treatment initiation than this. And yet, I can vouch for the difficulty in convincing people about the benefits of LTBI treatment — even those at greater risk for reactivation — but especially those who are younger, healthy, born outside the United States, and have unremarkable chest radiographs. Even when we know it's the right thing to do — and the patient is at higher risk for reactivation — there are just no teeth to the current Public Health recommendations. How are clinicians supposed to encourage people to accept treatment for LTBI when there is no imperative to do so?

Transmission of *Clostridium difficile* from Asymptomatic Carriers

Curry SR, et al. Use of multilocus variable number of tandem repeats analysis genotyping to determine the role of asymptomatic carriers in *Clostridium difficile* transmission. *Clin Infect Dis* 2013;57(8): 1094-1102.

Active surveillance and expedited infection control contact precautions have been shown to reduce the risk of nosocomial transmission of MRSA and other hospital-acquired organisms. While newer molecular screening techniques using PCR allow for more rapid screening for *C. difficile* colonization, questions remain about whether such surveillance is of sufficient value to justify the expense and the burden to the microbiology laboratory.

These experts examined both stool and environmental *C. difficile* isolates from hospital patients screened for clinical purposes, as well as *C. difficile* isolates detected from peri-rectal swab samples, initially collected for the purposes of screening patients for vancomycin-resistant Enterococcus (VRE). Multilocus variable number of tandem repeats analysis (MLVA) was employed to examine the genetic relationship between the isolates, and to craft a minimum spanning tree, looking for temporal associations between genetically similar isolates.

For the first portion of the study, clinical stool specimens from 158 patients were positive for *C. difficile* toxin; isolates were obtained from 92% of these cases for analysis. Of these 158 patients, 56 (43%) were considered hospital-onset (HO-CDI), while 57 (46%) were considered acquired at another institution or relapsors, 34 (22%) were considered carriers; and 13 (10%) were consider community-acquired.

In addition, screening tests performed on 4979 specimens from 3006 patients were positive for toxigenic *C. difficile* strains in 422 specimens, yielding 417 *C. difficile* isolates. Not surprisingly, the presence of *C. difficile* in a sample was strongly associated with the presence of VRE. Of the 314 patients with toxigenic *C. difficile* strains, 38% also had VRE. In addition to these, environmental isolates were collected.

In all, 739 isolates were examined by MLVA, yielding 524 unique genotypes. Of these, 230 formed 78 complexes of highly related isolates; carrier strains were important to the creation of 5 of these complexes. The 027-genotype 1 strain made of 41% of the isolates — these were broken into 170 genotypes and 26 complexes for analysis.

Of the 56 cases of HO-CD, nearly one–third (30%) were associated with other cases of *C. difficile* infection, and another third (29%) were related to carriers identified during surveillance screening. Of those cases related to colonized subjects, 9 of the cases were classified as non-ward transmissions, 2 as ward-transmissions, 2 as environmental transmissions (from a prior bed occupant); and 2 were indeterminate. This study also demonstrated that colonized individuals can serve as an important source for environmental contamination, perhaps weeks before transmission occurred. In addition, the incubation period for active *C. difficile* infection may be greater than 1 week prior to the onset of symptoms. One patient's screening tests were positive 35 days prior to collection of a positive clinical specimen for symptoms, and was the presumed source for one other HO case. Seven symptomatic patients tested positive on screening surveillance samples 8 to 28 days prior to their diagnosis.

Through sophisticated genetic analysis and modeling of a huge number of clinical, surveillance, and environmental *C. difficile* isolates, this study demonstrates that asymptomatic colonization and/or colonization prior to the onset of symptoms was an important source for 59% of the cases of HO-CDI at their facility. Even the best infection control program cannot capture asymptomatic colonization with *C. difficile* without benefit of a surveillance program. ■

CME INSTRUCTIONS

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

1. Read and study the activity, using the provided references for further research.
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CME QUESTIONS

1. Which of the following is correct regarding the risk of infection after transrectal biopsy?

A. Rectal colonization with any enteric bacteria is associated with a reduced rate of infection.

B. Rectal colonization with antibiotic-resistant bacteria is associated with a reduced rate of infection because of the loss of fitness and reduced virulence resulting from carriage of resistance determinants.

C. Patients with rectal colonization with fluoroquinolone-resistant *E. coli* were more likely to develop infection after biopsy.

D. Rectal colonization with fluoroquinoloine-resistant Pseudomonas were found to be at greatest risk of infection.

2. Which of the following is true regarding the findings of Miller et al about the treatment of uncomplicated skin infections?

A. Clindamycin was significantlysuperior to trimethoprim-sulfamethoxazole.

B. Trimethoprim-sulfamethoxazole was significantly superior to clindamycin.

C. Trimethoprim-sulfamethoxazole was entirely ineffective in the treatment of cellulitis.

D. There was no overall significant difference in outcomes with use of either antibiotic regimen.

3. In terms of infectious illnesses, immigrant children arriving unaccompanied from Central America are most likely to:

A. need updated immunizations

B. have asymptomatic Chagas disease

C. be ill with HIV/AIDS

D. serve as a reservoir for enterovirus D68 infection

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

[IN FUTURE ISSUES]

Is Combination Antifungal Therapy of Invasive Aspergillosis More Effective Than Monotherapy?

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents