

Infectious Disease [ALERT]

Incisive Commentary and Clinical Abstracts on Current Issues in Infectious Diseases

ABSTRACT & COMMENTARY

CDC Update of Notifiable Infectious Diseases

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

SYNOPSIS: CDC has updated the available information regarding reportable infectious diseases in the United States.

SOURCE: Adams DA, Thomas KR, Jajosky RA, et al. Summary of notifiable infectious diseases and conditions — United States, 2015. *MMWR Morb Mortal Wkly Rep* 2017;64:1-143.

CDC has provided an extensive report on notifiable infectious diseases in the United States for 2015. Their 143-page document is daunting to the reader, but, fortunately, the authors provide a section dealing with the highlights of the full report. What follows is a further summarization of selected infectious diseases.

VIRAL INFECTIONS

Arboviral Infections. A total of 2,175 cases of West Nile virus infections were reported in 2015, with 1,455 of these being neuroinvasive and 146 being fatal. California and Texas together accounted for 61% of cases. The incidence of neuroinvasive infections (0.45

cases per 100,000 population) was similar to the median incidence reported from 2002-2014.

Among domestically acquired arboviral infections, La Crosse virus infection was the second most frequently reported. This was followed by infections due to St. Louis encephalitis virus (all 23 cases of which were acquired in Arizona), Jamestown Canyon virus, Powassan virus, and Eastern equine encephalitis virus. The last is rare but fatal: Four of six patients with this infection died.

In the 50 states, one of the 896 cases of chikungunya infection was autochthonously acquired (in Texas).

Financial Disclosure: *Infectious Disease Alert's* editor, Stan Deresinski, MD, FACP, FIDSA, peer reviewer Patrick Joseph, MD, Updates author Carol A. Kemper, MD, FACP, peer reviewer Kiran Gajurel, MD, executive editor Shelly Morrow Mark, editor Jonathan Springston, and AHC Media editorial group manager Terrey L. Hatcher report no financial relationships to this field of study.

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Infectious Disease Alert.

ISSN 0739-7348, is published monthly by AHC Media, a Relias Learning company
111 Corning Road, Suite 250
Cary, NC 27518
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 74008694 Chicago, IL 60674-8694

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However, 237 infections were acquired in U.S. territories, including 227 in Puerto Rico and in the U.S. Virgin Islands.

In 2015, 951 laboratory-confirmed cases of dengue virus infection were reported in the United States, including its territories. Of those cases, 72% were travel-related, most frequently to the Caribbean and the Americas. An outbreak of 200 autochthonous cases occurred in Hawaii on Oahu, while the only other case acquired in a U.S. state was in Florida. The number of cases acquired in the endemic territories of Puerto Rico and the U.S. Virgin Islands was the lowest ever recorded.

Measles. Measles was officially declared to have been eliminated in the United States in 2000. Almost all (97%) cases are now import-associated, meaning that they are imported from abroad, epidemiologically linked to an imported case, or are caused by strains demonstrated by genetic methods to represent an imported genotype. Of the 150 reported cases in 2015, 80% were associated with six outbreaks, the largest of which involved 130 cases and was linked to two Disney theme parks. Cases from that outbreak were seen in seven additional states as well as in Mexico and Canada. Among the 150 cases in 2015, > 80% occurred in individuals who had not been vaccinated or whose vaccination status was unknown. Of note is that an immunocompromised adult with pneumonia died of undiagnosed measles virus infection.

Mumps. Eight outbreaks involving ≥ 20 cases accounted for 53% of the 1,329 cases of mumps reported in 2015; 88% of cases had been fully vaccinated. Seven (88%) of the outbreaks occurred in settings with high likelihood of close contact, including athletic teams, high schools, and universities.

Varicella. Since the change from the single-dose vaccination recommendation to two doses in 2015, the incidence of varicella has decreased 85% to 3.8 per 100,000. Among those for whom the information was available, 49% of cases occurred in children 1-9 years of age. Overall, among those with the

relevant information, 58% had received at least one dose of vaccine and 57% of these had received a second dose. One-fifth of cases were associated with outbreaks. Five percent of cases resulted in hospitalization.

Influenza Virus — Associated Pediatric Mortality. The median age of the 130 reported influenza-associated pediatric deaths in 2015 was 5.4 years (range, 27 days – 17 years). At least one pre-existing condition known to increase the risk of complications of influenza infection was present in 43%, with neurological disease in 18% of the total group. Positive bacterial cultures from normally sterile sites were obtained from 35 (48%) of 73 children, with *Staphylococcus aureus* recovered in 15 (43%) of 35. Twenty-seven (30%) of the 89 children ≥ 6 months of age had been fully vaccinated.

Rabies. Rabies caused two deaths in 2015. A 65-year-old man had been bitten by a dog while abroad, and a 77-year-old woman in Wyoming had a history of contact with a bat.

Human Immunodeficiency Virus (HIV) Infection. In 2015, 33,817 cases of newly diagnosed HIV infection were reported to the CDC, with blacks/African-Americans accounting for 44.5% and with an incidence of 37.7 per 100,000. The following states had incident diagnoses ≥ 15.0 per 100,000: District of Columbia, Florida, Louisiana, Maryland, Mississippi, New York, and South Carolina.

PROTOZOAN INFECTION

Babesiosis. Twenty-four states reported a total of 2,074 cases of babesiosis in 2015, with seven states (Connecticut, Massachusetts, Minnesota, New Jersey, New York, Rhode Island, and Wisconsin) accounting for 1,925 (93%).

Cryptosporidiosis. *Cryptosporidium* is the number one cause of waterborne outbreaks of infection, particularly of those related to recreational exposure to water. Adams and colleagues noted the following characteristics that contribute to this: A single bowel movement may release 10^8 - 10^9 infectious *Cryptosporidium* oocysts; oocysts may be shed for weeks; the infectious dose is

only ≤ 10 oocysts; and the oocysts have a very high tolerance to chlorine.

Cyclosporiasis. Approximately one-third of reported cases of *Cyclospora* infection were associated with international travel. Fresh cilantro imported from Mexico was implicated as the vehicle in 61 restaurant-associated cases in Texas, Georgia, and Wisconsin.

PARASITIC

Trichinellosis. The known sources of the 13 cases of trichinellosis reported to the CDC were bear meat and pork. Two small outbreaks occurred — both the result of eating meat from bears that had been hunted in Alaska.

FUNGAL

Coccidioidomycosis. There was a 36% increase in reported coccidioidomycosis cases in both California and Arizona, which recorded 3,053 and 7,622 cases, respectively. Separately, CDC has reported a dramatic increase in the number of cases in California to 5,372, with a comparably proportionate increase in incidence to 13.7 per 100,000 population.

RICKETTSIAL

Anaplasmosis and Ehrlichiosis. In 2015, 3,656 cases of anaplasmosis were reported in the United States — an increase of approximately 31% over the previous year. In the mid-Atlantic states, there was a 70% increase. There was only a minimal increase in the number of cases of ehrlichiosis, with 1,475 due to *Ehrlichia chaffeensis* and 17 due to *Ehrlichia ewingii*.

BACTERIAL INFECTIONS AND INTOXICATIONS

Botulism. Of the 195 reported confirmed cases of botulism, 135 were instances of infant botulism, while 37 were foodborne and 20 were “other” (including wound botulism). Of the five identified outbreaks, the identified sources were potato salad, beets, and fermented seal flipper.

Shiga Toxin-producing *Escherichia coli* (STEC)

Infection. While the overall incidence of STEC infections was 2.2 cases per 100,000 population, the incidence in children 1.4 years of age was almost four times higher at 8.0 per 100,000. The most serious complication of STEC infection is hemolytic uremic syndrome. This is associated most frequently with STEC O157, but other strains also may produce the toxin. As a consequence, it is recommended that stool specimens from individuals with community-onset diarrhea be tested routinely, not only by culture for the presence of STEC O157, but also by a method that detects either Shiga toxin itself or the gene that encodes it. This does not preclude the need

for serogrouping and determination of the pulsed field gel electrophoresis pattern, both of which are important for epidemiological purposes.

Campylobacteriosis. It is estimated that *Campylobacter* causes 1.3 million illnesses in the United States each year and that most of these are the result of ingestion of domestic contaminated food. Furthermore, approximately 120 individuals die with this infection. Most cases are associated with ingestion of raw milk and undercooked chicken. A preliminary estimate of the incidence in 2015 is 17.7 cases per 100,000 population. Although most cases are sporadic, 35 outbreaks were reported with chicken liver pâté, grilled chicken, raw milk, and irrigation water among the implicated sources.

Cholera. Four of the five reported cases of cholera infection were associated with travel, including two cases related to travel to Haiti, and one each to Cuba and the Philippines. The non-travel case resulted from the ingestion of raw shrimp from the Philippines.

Shigellosis. Taking underdiagnosis into account, it is estimated that *Shigella* causes 500,000 symptomatic infections each year in the United States. During 2015, the incidence of reported cases of shigellosis in the United States was 7.3 per 100,000 population, with the highest incidence in children younger than 10 years of age. Although it may occur as the result of ingestion of contaminated food or water, *Shigella* infection most frequently is the result of person-to-person transmission. One group at increased risk is men who have sex with men.

The scourge of antibiotic resistance has reached *Shigella*, which caused several outbreaks due to multidrug-resistant strains. It is reported that, overall, 2.4% of isolates are resistant to ciprofloxacin, 4.7% to azithromycin, and that 15.3% were resistant to at least both ampicillin and trimethoprim-sulfamethoxazole. Susceptibility testing requires recovery of an isolate in culture so that use of non-culture methods alone is inadequate for management.

Reduced susceptibility of *Shigella* to ciprofloxacin was addressed in a recent CDC Health Advisory (<https://emergency.cdc.gov/han/han00401.asp>), which dealt with an increase in the number of isolates with an MIC of 0.12-1 mcg/mL or higher — which, although within the susceptible range (the current CLSI breakpoint indicates that those with MICs ≤ 1 mcg/mL are susceptible), are significantly higher than that of most clinical isolates with usual MICs ≤ 0.015 mcg/mL. The isolates with an elevated MIC carry plasmid-related quinolone resistance genes that are not present in those with lower MICs.

Although unproven, there is concern that treatment of these strains with a fluoroquinolone may result in reduced efficacy. When antibiotic therapy is indicated (most cases of shigellosis resolve quickly without antibiotic treatment), an alternative to ciprofloxacin should be chosen if the isolate has an MIC \geq 0.12 mcg/mL, and the clinical laboratory should submit it to their public health laboratory.

Salmonellosis. There were 17.2 cases of *Salmonella* infection per 100,000 population in 2015, with the highest incidence in children < 5 years of age. The largest multistate outbreak was due to contaminated imported cucumbers. Some of the other sources included small turtles, pork, live poultry, and crested geckos.

Typhoid. Approximately four-fifths of the 367 cases of typhoid in 2015 were acquired in southern Asia, with visiting family and friends being the greatest risk factor. Overall, approximately 86% of cases were associated with international travel. There has been little change in the total annual number of cases since 2009.

Listeriosis. The incidence of reported *Listeria monocytogenes* infections in 2015 was 0.24 per 100,000 population. CDC has established an enhanced surveillance system, The *Listeria* Initiative, which uses molecular subtyping by pulsed-field gel electrophoresis and whole-genome sequencing for rapid outbreak investigations. Therefore, they recommend that all clinical isolates be submitted for evaluation. CDC indicates that this initiative has assisted in rapid identification of contaminated food sources, allowing them to be removed from the market, as in the case of the outbreak associated with Blue Bell ice cream.

Haemophilus influenzae Disease. The incidence of *Haemophilus influenzae* type B (Hib) infection in children in 2015 was 0.15 per 100,000, with a 99% decrease in those < 5 years of age since the introduction of conjugate Hib vaccines in 1987. However, the incidence among American Indian and Alaskan Native children is significantly higher than in other groups. Nontypeable strains now cause a majority of *H. influenzae* infections in all age groups.

Meningococcal Disease. The incidence of meningococcal disease, which was 0.12 per 100,000 population in 2015, remains at historic lows. However, the occurrence of outbreaks of infection due to *Neisseria meningitidis* serotype B on two college campuses resulted in nine cases, with one death. This and other recent experiences led to the

Advisory Committee on Immunization Practices (ACIP) recommendation that meningococcal serotype B vaccine be administered to young adults 16-23 years of age as well as to certain groups at increased risk of infection and during outbreaks. Separately, CDC recently has warned of the high risk of development of meningococcal disease in individuals receiving eculizumab, despite prior vaccination.

Pertussis. The incidence of pertussis decreased from 10.3 to 6.5 per 100,000 population between 2014 and 2015, a reduction of 37.9%. One-third of cases occurred in those 11-19 years of age, a time of waning immunity. The highest incidence (67.2 per 100,000), however, was seen in infants < 1 year of age. Of the six deaths, three occurred in infants < 3 months of age and three occurred in adolescents with comorbid conditions. Two of the mothers of infants with fatal pertussis had not received Tdap at the recommended time (weeks 27-36) in pregnancy, while the vaccination status of the third was unknown.

Legionellosis. There continue to be yearly increases in the incidence of reported *Legionella* infection, reaching 1.89 cases per 100,000 population (6,079 cases). An outbreak involving 138 cases in the South Bronx was the largest community-associated outbreak since the one in Philadelphia in 1976. A consensus industry standard aimed at risk-reduction was published and is promoted by CDC.

Plague. Colorado and New Mexico each accounted for four of the 16 cases, Arizona and Oregon for two cases each, while California, Michigan, and Georgia had one case each. Four of the 16 cases of plague were fatal.

Brucellosis. The 126 cases of brucellosis were reported primarily from the South Atlantic, West South Central, and Pacific regions, which accounted for two-thirds. Physicians are encouraged to warn their clinical laboratories if they suspect brucellosis to reduce the risk of laboratory-acquired infection.

Tularemia. The 314 reported cases of tularemia in 2015 represent a 74% increase over the previous year. Eight states, led by Colorado (52 cases) and Kansas (34 cases), accounted for the majority of cases, with disproportionate increases in Colorado, Nebraska, South Dakota, and Wyoming — states that apparently had had increases in rabbit populations.

SPIROCHETAL

Leptospirosis. Ninety-six cases of leptospirosis were reported from 10 states, jurisdictions, and territories, with 45 from Puerto Rico, 22 from Hawaii, and 11 from Guam.

MYCOBACTERIAL

Tuberculosis. The incidence of tuberculosis had remained largely unchanged at approximately 3.0 per 100,000 population from 2013-2015, but, compared to 2014, the number of cases increased by 1.6% to 9,557. Two-thirds of cases were foreign-born, with Asians accounting for almost one-half of this group. The incidence in Asians who were foreign-born was 18.2 per 100,000, which can be

compared to 0.6 cases per 100,000 in non-Hispanic whites. Foreign-born individuals account for the majority of cases (total of 63 in 2015) of primary multidrug-resistant (MDR) TB, but the incidence in the general population has remained between 0.9% and 1.3% each year. Sixteen cases of extensively drug-resistant (XDR) TB have been reported since 2009. ■

ABSTRACT & COMMENTARY

Microbiology of Hidradenitis Suppurativa: New Evidence That Anaerobes Predominate

By Richard R. Watkins, MD, MS, FACP, FIDSA

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Dr. Watkins reports that he has received research support from Allergan.

SYNOPSIS: Using metagenomic techniques, investigators determined that two Gram-negative anaerobes, *Prevotella* and *Porphyromonas*, predominate in hidradenitis suppurativa lesions. Two others, *Fusobacterium* and *Parvimonas*, correlate with disease severity.

SOURCE: Guet-Revillet H, Jais JP, Ungeheuer MN, et al. The microbiological landscape of anaerobic infections in hidradenitis suppurativa: A prospective metagenomic study. *Clin Infect Dis* 2017;65:282-291.

Hidradenitis suppurativa (HS) is an incompletely understood and challenging condition for clinicians to manage. The pathogenesis of HS is believed not to be infectious per se, but, rather, to be a chronic inflammatory disease of the terminal hair follicle that predisposes the patient to recurrent skin infections. Guet-Revillet et al hypothesized that anaerobic bacteria are the main drivers of this inflammation and, through the use of molecular techniques, aimed to comprehensively elucidate the microbiology of HS skin lesions.

Severity of HS is based on the Hurley scale: Stage 1 consists of a single lesion or abscess, stage 2 denotes multiple lesions with sinus tracts and scarring, and stage 3 is severe disease with multiple interconnected sinus tracts across an entire area of skin. The investigators prospectively sampled and cultured lesions in 149 patients with different Hurley stages and 175 unaffected samples, which were used as controls. Draining lesions were sampled by swabbing pus, while nondraining lesions were sampled by punch biopsy or needle aspiration. The DNA from the cultured bacteria was extracted and used to construct 16S rRNA gene libraries. High-throughput sequencing then was performed to compare the microbiome of 80 HS lesions to that of 88 control samples.

Anaerobic flora were isolated in 83% of the HS lesions compared to 53% of the controls. In a breakdown by Hurley stage, anaerobes were seen in 54% of stage 1 lesions, 95% in stage 2 lesions, and 100% in stage 3 lesions. *Streptococcus dysgalactiae*, an opportunistic skin pathogen, was isolated from the HS samples but not from the controls. *Staphylococcus aureus* was cultured from some of the HS lesions but was never the predominant organism. Moreover, skin commensals like *Staphylococcus epidermidis* and *Micrococcus spp.* were less abundant in the HS lesions than in the controls. High-throughput sequencing identified 43 taxa that were associated with HS lesions, of which *Prevotella*, *Porphyromonas*, *Fusobacterium*, and *Parvimonas* were the most common. Hurley stage 3 lesions exhibited an increased bacterial diversity compared to stage 1 and 2 lesions, of which the most abundant taxa were *Fusobacterium*, *Parvimonas*, *Streptococcus*, and *Clostridiales*. The microbiome of the HS lesions did not vary according to gender, duration, family history of HS, body mass index, location of the lesion(s), or clinical parameters except for Hurley stage.

■ COMMENTARY

These data are interesting because they represent the most comprehensive analysis of the microbiology of HS lesions to date. The two most common bacteria isolated from the HS lesions, *Prevotella* and

Porphyrromonas, usually are commensals in the mouth and vagina. However, they also are associated with chronic infections like gingivitis and periodontitis. *Fusobacterium*, the most common isolate from Hurley stage 3 lesions, is another commensal in both the mouth and gastrointestinal tract that has been associated with neonatal sepsis, chorioamnionitis, inflammatory bowel disease, and appendicitis. As the authors note, *Fusobacterium* has proinflammatory properties like strong adhesion to epithelial cells, the ability to invade tissues, and biofilm formation that may contribute to the inflammation in HS lesions. These anaerobes overall exhibit lower pathogenicity compared to other skin organisms, such as *S. aureus*. Thus, this may explain the lack of a systematic inflammatory response to HS. Regarding the limitations of the study, it was conducted at a single institution, so the results might not be generalizable to other settings. Also, the investigators collected samples from 149 HS lesions but only analyzed 80 of them, which may have led to selection bias.

So how can the findings of the study be used in clinical practice? Previous investigations have shown that antibiotics with anaerobic activity (e.g., carbapenems) can lead to clinical improvement in HS and, in some cases, remission. TNF- α blockers also have been used successfully to reduce inflammation. Guet-Revillet et al provide a theoretical basis to support the use of antibiotics in the treatment of HS. Further clinical studies are warranted to determine if this approach is indeed efficacious. These studies should be designed to compare commonly prescribed antibiotics (e.g., clindamycin, amoxicillin-clavulanate) vs. placebo in a randomized, blinded fashion. In my practice, I have had some success in treating patients with HS using topical clindamycin, although recurrences unfortunately are common. I also prescribe zinc, which has anti-inflammatory properties, and there is some evidence that 90 mg of zinc gluconate daily can reduce the size of HS lesions. ■

ABSTRACT & COMMENTARY

Autochthonous Crimean-Congo Hemorrhagic Fever in Europe

By Dean L. Winslow, MD, FACP, FIDSA

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

SYNOPSIS: Two patients with Crimean-Congo hemorrhagic fever acquired in Spain are reported. The index patient acquired infection from a tick bite, and the second patient was a nurse who cared for the index patient. The first patient died in the hospital with multi-system organ failure and was diagnosed at autopsy. The second patient recovered with supportive care and was treated with ribavirin, but it was unclear whether the use of ribavirin was helpful.

SOURCE: Negredo A, de la Calle-Prieto F, Palencia-Herrejon E, et al. Autochthonous Crimean-Congo hemorrhagic fever in Spain. *N Engl J Med* 2017;377:154-161.

The index patient was a 62-year-old man from Madrid who presented with a two-day history of fever, abdominal pain, nausea, and diarrhea. After admission to the hospital, he rapidly developed purpuric skin lesions and hematomas at venipuncture sites, had evidence of severe coagulopathy and thrombocytopenia, and required transfer to the ICU. Four days before admission, his family reported that he had walked through fields in the province of Avila in central-western Spain and had removed a tick from his knee. By the seventh day of illness, his condition had deteriorated dramatically, with macroscopic hematuria, worsening purpura, hematomas, fulminant hepatic failure, acute respiratory distress syndrome (ARDS), encephalopathy, hypoglycemia,

and severe metabolic acidosis. After transfer to a tertiary care hospital, he developed shock, acute renal failure, worsening acidosis, and died. Autopsy findings included generalized visceral edema, bloody ascites, extensive cutaneous and visceral hemorrhages, and hepatic necrosis. Retrospective analysis of serum samples obtained on the sixth and eighth day of illness revealed 1.0×10^8 and 1.2×10^9 viral copies of Crimean-Congo hemorrhagic fever (CCHF), respectively.

The second patient was a 50-year-old female nurse who had assisted during the endotracheal intubation of the index patient and during insertion of central venous and arterial lines. Although she did not

sustain a puncture, she reported direct contact of index patient blood with her intact skin. Four days after the reported exposure, she developed fever, arthralgia, and myalgia. The following day, she presented to the hospital with petechiae, thrombocytopenia, and moderately elevated transaminases. On the third day of illness, vaginal bleeding developed. The next day, after her clinicians suspected CCHF, she was started on ribavirin 1,000 mg IV every six hours. On the sixth day of illness, the ribavirin dose was reduced to 500 mg IV every eight hours, and she was transferred to a tertiary care hospital in Madrid. She had mild acute kidney injury, some degree of hypoxic respiratory failure, in part related to a moderate-sized pleural effusion, but did not require mechanical ventilation. Her liver enzymes began decreasing by the ninth day of illness and her platelet count started to increase by day 11. Severe hemolysis necessitated discontinuation of ribavirin on day 9. Analysis of stored samples showed that her CCHF viral load was highest on the second day of illness, at 3.6×10^7 copies/mL. The first negative RT-PCR in serum was observed at day 20. Anti-CCHF antibodies were not detectable initially, but IgM antibodies increased to 1:640 on day 6 and started to decrease at day 15. IgG antibodies rose later and remained constant at 1:640. Vaginal, saliva, conjunctival, and rectal swabs were intermittently positive for CCHF virus by RT-PCR, but all of these body fluids were negative by day 14.

A total of 437 hospital personnel at the various hospitals that cared for these two patients were identified and of these, 386 were deemed to be at high risk of acquiring infection. None were observed to have acquired infection.

■ COMMENTARY

CCHF is a widely distributed viral infection seen in more than 30 countries in Africa, Asia, and the Middle East, but prior to these cases was seen only in the far Southeastern part of Europe (Russia, Ukraine, Bulgaria, Albania, Kosovo, Greece, and Turkey). Humans acquire CCHF through tick bites or contact with viremic animals or humans.

As with other viral hemorrhagic fevers, heroic supportive care often is necessary for survival. It is interesting that the second patient was treated with ribavirin despite numerous studies and a meta-analysis showing that ribavirin is ineffective in CCHF.¹ As my colleagues and trainees know, ribavirin treatment of viral diseases is one of my pet peeves. Ribavirin displays nonspecific antiviral activity against many DNA and RNA viruses in vitro. However, if one determines the TC₅₀ (cytotoxicity) using a sensitive indicator of cytotoxicity, such as a tetrazolium assay (rather than the insensitive trypan blue dye exclusion), one usually finds that the TC₅₀ and IC₅₀ are very close. This is probably because ribavirin is not even acting as a viral polymerase inhibitor, but rather just making the cells sick by nonspecifically altering intracellular nucleotide pools. There is a certain philosophy among many clinicians that it is justifiable to “throw the kitchen sink” at very ill patients. However, I believe that with toxic drugs like ribavirin, this approach has significant potential for harm. ■

REFERENCE

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ABSTRACT & COMMENTARY

Infections Associated With Adventure Travel

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

SYNOPSIS: Some adventure travel is associated with exposure to infectious pathogens. Some adventure-related illnesses can be prevented. Understanding the details of an adventure trip can help focus a differential diagnosis for ill returned travelers.

SOURCE: Gundacker ND, Rolfe RJ, Rodriguez JM. Infections associated with adventure travel: A systematic review. *Travel Med Infect Dis* 2017;16:3-10.

Extreme adventure sports are increasingly popular, and millions of people engage in adventurous activities during vacation travel. While risks of trauma with adventure sports are evident, the infectious risks of such activities have

been less well characterized. Thus, Gundacker and colleagues performed a systematic review of the literature to collate information regarding risks for infection while engaging in adventure sports during travel.

Gundacker focused on the risks associated with water sports (such as rafting and surfing), caving, trekking, cycling, and skiing. A careful literature search yielded 116 relevant articles. Varying with geography, whitewater rafting, caving, and adventure races carried relatively greater risk for infection.

Whitewater rafters are at risk of leptospirosis. With rodents (and possibly dogs, cattle, bats, and sea lions) as a reservoir, leptospirosis exposure occurs in water contaminated with spirochete-infected urine. A Costa Rican outbreak occurred during the rainy season when water levels were particularly high, thus allowing water to wash over land areas that were contaminated with rodent urine. Adventurers were particularly at risk when they swallowed significant amounts of water. Prophylaxis with doxycycline (200 mg weekly for adults) is effective in preventing leptospirosis in travelers who anticipate exposures to contaminated water.

Rafters in Ethiopia and Uganda also have become ill with schistosomiasis. Up to half of participants on some studied trips have been infected. Drying off right after water exposure might decrease the risk of parasite penetration. Post-trip testing (three months after return) and treatment (praziquantel) can reduce the risk of long-term sequelae of *Schistosoma* infection.

[Surfers, windsurfers, and kite-boarders are at risk of superficial trauma and lacerations.]

Travelers in contact with rivers in rugged areas are at risk of gastrointestinal illnesses as well. *Giardia* and norovirus infections have been reported after whitewater rafting trips. Attention to ingesting only boiled, bottled, or purified beverages can reduce an individual's risk, and careful stool hygiene can reduce risks to future travelers.

Rafters to areas of endemic mycosis have become ill with blastomycosis and histoplasmosis after contact with soil on riverbanks. Itraconazole can be effective treatment for mild cases, and amphotericin is used for severe illness.

Surfers, windsurfers, and kite-boarders are at risk of superficial trauma and lacerations. These skin lesions then can become infected with water-associated germs, including *Vibrio*, *Aeromonas*,

Plesiomonas, and *Erysipelothrix*. Third-generation cephalosporins and quinolones can be effective against infections caused by these microbes. Slow-to-heal infected skin lesions might be due to *Mycobacterium marinum*.

[Hikers and trekkers in developing countries and in wilderness areas also are at particular risk for travelers' diarrhea.]

Caving can include exposures to bird droppings containing *Histoplasma* and to bat saliva and/or urine containing rabies. Cryptococcal meningitis occurred in an immunocompromised caver in South America.

Adventure racers are exposed to extreme environmental conditions. Outbreaks of *Campylobacter* enteritis and norovirus gastroenteritis have been described in adventure racers, with approximately 800 individuals affected in a norovirus outbreak.

Hikers and trekkers are, of course, at risk of mosquito-borne illnesses in disease-endemic areas. Malaria, dengue, chikungunya, and Zika are of particular concern. Topical insect repellents (such as 20% picaridin and 25% diethyl-meta-toluamide [DEET]) can reduce insect bites for four to six hours. Repellent use also can protect against tick-borne illnesses. Hantavirus and tularemia also have been reported in trekkers.

Hikers and trekkers in developing countries and in wilderness areas also are at particular risk for travelers' diarrhea. For symptomatic individuals, oral hydration is essential, and loperamide can reduce the frequency or diarrhea in adults. Antibiotics (usually azithromycin; quinolones also are helpful in areas where resistant *Campylobacter* is not common) can reduce the duration of travelers' diarrhea but also carry a risk of fostering the emergence of multidrug-resistant organisms in the gastrointestinal tract; thus, current advice is to use an antibiotic only for severe episodes of travelers' diarrhea.

Cyclists experiencing traumatic accidents involving soil contact are at risk of superinfection not only by skin flora but also by *Sporothrix*, *Nocardia*, and other microbes. ■

Immediate Improvement in Childhood Vaccination

The largest epidemic of whooping cough in seven decades occurred in California from 2010 to 2014. In 2014, the California Department of Public Health (CDPH) reported a peak number of 11,203 cases of pertussis, 456 of which required hospitalization (26% in intensive care); 278 cases were in small infants younger than 4 months of age, three of whom died. One of the worst pockets of sustained pertussis infection was in and around Palo Alto, CA — home of Silicon Valley entrepreneurs and vaccine deniers.

Research has shown that higher per capita income is linked to lower childhood vaccine rates. Previously, Californians were allowed a “personal belief” exemption from childhood vaccination, which effectively created pockets of unvaccinated children throughout the state, especially in more affluent areas. Exercising that right in California was as simple as checking the box on your kid’s school paperwork — with no discussion as to the implications for the child or the community. By 2014, fully 800 schools in California reported non-vaccination rates of 8% or greater — effectively, those schools lacked herd immunity. In reviewing California school system reportable vaccine rates for 2014, some school systems reported 100% measles, mumps, rubella (MMR) vaccine coverage of their students, while one school

reported that only 43.5% of their kids had received MMR. The personal belief exemption was used for 34.8% of their children. Even more startling, one school reported that only 22.7% of their kids had received MMR, and 68.2% of children were exempt for personal belief.

These pockets of unvaccinated children can be linked directly to the observed increase in cases of pertussis and measles. In a *JAMA* review of 1,416 reported measles cases in the United States from 2000 to 2015, 574 cases were unvaccinated.

Seventy percent had claimed non-medical exemption. The measles outbreak at Disneyland in Anaheim, CA, in 2014-2015, which resulted in 125 measles infections, garnered significant media attention and helped to sway public opinion against the anti-vaccine movement. Of the 110 Californians infected with measles at Disneyland, 45% were unvaccinated, most for non-medical exemption. On any given day, only 86% of persons at Disneyland had received MMR — well below the threshold required for herd immunity against measles infection. Imagine this figure when considering that about 44,000 people visit Disneyland every day.

Because of these outbreaks, public health officials lobbied the California State Legislature to remove the personal belief clause for vaccination of school-age children. The result of these efforts was Senate Bill 277, passed in

June 2015, and which took effect in July 2016 — just before the school year began. California SB 277 requires school-age children to receive 10 specific vaccinations before they can attend school or day care in California, and only medical exemption certified by a physician is permissible.

[In April 2017, the California Department of Public Health reported that overall vaccine rates for kindergartners hit an all-time high this year.]

The result has been a welcome success. Already, improvement in vaccine rates in school-age children has been observed. In April 2017, CDPH reported that overall vaccine rates for kindergartners hit an all-time high this year, up from 92.8% in 2015-2016 to 95.6% for 2016-2017.² That amount of 2.8% can make all the difference in terms of herd immunity, especially for an agent as contagious as measles. Despite these efforts, nine counties, all in northern California, still reported 2016-2017 kindergarten vaccine rates below 90% — although this was an improvement from 2015-2016 when 20 counties reported sub-standard vaccine rates. A small number of children (0.6%) still are not vaccinated on entry to kindergarten based on a belief exemption provided by their parents before the legislation went into effect, although these children will be required to show

proof of vaccination when they enter seventh grade.

The effect of these improved vaccine rates has been immediate and substantial: Pertussis rates in California have dropped from 29.3 cases per 100,000 population in 2014 to 1.6 cases per 100,000 population in 2016.

All 50 states allow for medical exemption to vaccination. Forty-eight states allow for some kind of religious exemption (not Mississippi nor West Virginia). As of August 2016, 18 states still allow for personal belief/philosophical exemption, although legislation is being introduced in many states to reduce or eliminate personal belief as an exemption to childhood vaccination.

Steven Novella, from the Science-Based Medicine website, reminds us that the U.S. Supreme Court ruled in 1944 in *Prince v. Massachusetts* that “the right to practice religion freely does not include liberty to expose the community or the child to communicable disease or the latter to ill health or death.” Politically, it has been difficult to eradicate religious exemption from vaccination, although there is no right of citizens to refuse vaccination. But the anti-vaccination effort continues — a veto referendum to allow personal belief as an allowable exemption did not qualify for the California Nov. 8, 2016, ballot, but hundreds of parents have continued to lobby the state capital to repeal California SB 277. Parents also can circumvent the law by choosing to home school their children.

The outbreaks of pertussis in our community — putting kids at risk or keeping some out of school for 25 days — has gone a long way to changing many parents’ minds in our area. Suddenly, pertussis was

a real disease, not just something you read about. But it’s important to remind parents that while vaccination may protect their child, it’s ultimately for the good of the community — it protects all of us, especially the weak, the very young, and the elderly.

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A Better Mosquito Trap

I have always wanted to be one of our county’s sentinel chicken mummies, but San Mateo County has too many takers, and I was told my neighborhood had too many of the “wrong” mosquitoes. For years, scientists have had to resort to the insensitive and labor-intensive process of bleeding sentinel chickens for arboviral infections, such as West Nile virus or, more recently, Eastern equine encephalitis virus in Alabama. Either that, or they hang old-fashioned bug traps in trees, and then an expert has to pick through all the trapped debris, moths, and bugs to find their quarry of interest for testing. But that may change soon.

Young scientists at Microsoft, working on Project Premonition, have designed a prototype “smart” bug catcher that may revolutionize our ability to monitor mosquito populations and mosquito-borne infections. The device is designed to identify and trap only a particular species of mosquito of interest, and ignore everything else. The prototype is constructed of

sturdy plastic that can withstand wind and rain, and has 64 compartments, each with a tiny plastic door, stacked like a small high-rise apartment building. When an insect flies through, an infrared beam records the size and pattern of the shadows of the beating wings. The data are uploaded to the cloud, and the machine can literally teach itself which mosquito is desirable — and the door snaps shut — and which gnat is not. Whenever a mosquito is captured, the time of day, wind speed, temperature, and humidity are recorded.

Ten prototypes are being trialed in Houston this summer, and thus far the machines can capture the right mosquito with 90% accuracy. Insects can be readily collected and tested with the latest molecular techniques for the presence of Zika or any other virus of interest.

Can FMT Restore Gut Flora and Eliminate Resistant Pathogens?

SOURCE: Bilinski J, Grzesiowski P, Sorensen N, et al. Fecal microbiota transplantation in patients with blood disorders inhibits gut colonization with antibiotic-resistant bacteria: Results of a prospective, single-center study. *Clin Infect Dis* 2017;65:364-370.

Ever since the first case landed on our doorstep 24 months ago, our hospital has been vigorously screening at-risk admissions for carbapenemase-producing carbapenem-resistant *Enterobacteriaceae* (CP-CRE). Thus far, we’ve identified nine people, including four travelers hospitalized in India within the previous six months (three with NDM+ *Escherichia coli* and one with NDM+ *Klebsiella pneumoniae*). Four people formed a cluster of suspected transmission of NDM-KP. One elderly Indian woman, returning

from a wedding in India, was found to have been positive for NDM-resistant organisms in 2013 at an outside facility and, although her current tests were negative for carbapenemase-producers, she had four CRE organisms cultured from stool. Several patients required care at a local skilled nursing facility, where they were maintained in strict contact isolation, unable to join in group activities or go to the dining room. It is not known whether such individuals, once colonized, can ever “clear” the resistant organisms from the gut flora, nor whether there is a sufficiently sensitive method for guaranteeing clearance from the gut flora. But there may be hope for these individuals.

Researchers at the University of Warsaw have demonstrated successful clearance of multidrug-resistant organisms (MDRO) from fecal samples in 15 of 20 patients (75%) with hematologic malignancy or stem cell transplants using fecal transplant material. Many of the patients were neutropenic or severely immunosuppressed. Gut colonization included NDM-*K. pneumoniae* (n = 14), ESBL-*E. coli* (n = 11), and two patients each with carbapenem-resistant *K. pneumoniae*, ESBL-*K. pneumoniae*, Metallo beta-lactamase-*Pseudomonas aeruginosa*, carbapenem-resistant *P. aeruginosa*, as well as various other MDRO. Thirteen participants (65%)

were colonized with two or more MDRO.

A total of 25 fecal microbiota transplantations (FMTs) were performed in 20 patients; one patient underwent three separate transplants. Fecal transplant material was obtained from screened donors and administered intra-duodenally via nasogastric tube. Patients fasted for 12 hours before the process, were administered polyethylene glycol, and given a proton pump inhibitor to diminish gastric acid. The first three patients received their FMT just once on one day, and subsequent FMT were performed over two consecutive days. Fecal samples were obtained at one week, one month, and six months and tested by both culture and quantitative PCR for polymerase resistance genes. These results were available for 24 transplants at one month, and 14 at six months.

Complete decolonization was achieved in 15 of the 20 participants (75%), including the individual with multiple attempts. However, none of the three individuals who received a single-day FMT treatment were cleared. In those patients with available fecal data, successful clearance was demonstrated with 15 of 24 transplants at one month (62%) and 13 of 14 transplants (93%) at six months. Most importantly, six of 10 patients with NDM-KP were decolonized, and 11 of 11 patients (100%) with

ESBL-*E. coli* were cleared. Partial eradication of one of two or more organisms was demonstrated in several additional patients.

There was diminished success at clearance of MDRO in patients receiving antibacterials within seven days of their FMT (44%) compared with those not receiving antibacterials (79%). Two patients demonstrated recolonization with the same strain of MDRO after having tested negative at least once, and one patient died of septic shock from OXA-48-*E. coli*, which had been “cleared” from the gut on earlier testing.

It would be beneficial to see these study results repeated, possibly in a less immunosuppressed population. If this approach works, I will be thrilled, but suspect it may not be that easy either to decolonize an individual or demonstrate successful clearance. Since the sensitivity of culture and quantitative PCR is not yet known for this situation, repeated testing over time may reveal occult residual organism in some patients. But a better “test” would be to challenge such patients with broad-spectrum therapy and see what emerges under selective pressure. One limitation to this approach is that some of these patients may have chronic colonization at other sites, such as wounds, trachs, and urinary catheters, not amenable to decolonization. ■

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CME QUESTIONS

1. Which of the following associations have been reported?
 - a. Whitewater rafting; leptospirosis
 - b. Caving; rabies
 - c. River rafting; histoplasmosis
 - d. All of the above
2. Which of the following is correct regarding notifiable infectious diseases in the United States in 2015?
 - a. One-half of measles cases were import-related.
 - b. No cases of measles occurred in individuals who had a history of measles vaccination.
 - c. The majority of mumps cases occurred in individuals with a history of mumps vaccination.
 - d. The change from one to two doses of varicella vaccine was not associated with a further reduction in varicella cases.
3. Which of the following is correct regarding notifiable infectious diseases in the United States in 2015?
 - a. *Cryptosporidium* is the leading cause of waterborne outbreaks of infection.
 - b. There was a significant decrease in the incidence of coccidioidomycosis.
 - c. *Shigella* is most often transmitted by ingestion of contaminated food.
 - d. Shigellosis always should be treated and always with ciprofloxacin.

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.



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