

La Otra Cara de la Moneda: Enfermedades Infecciosas que nos Amenazan Cuando Visitamos a Norteamérica (The Other Side of the Coin: Dangerous Infectious Diseases of North America for Colombian and Latin American Travelers)

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Doctors are aware of medical risks for the traveler, often considered in the context of a north American or European traveling to a tropical region where exotic and unusual pathogens lurk to prey upon the unwary, immunologically inexperienced. As the title suggests, this is only a part of the story. Europeans and north Americans do enjoy a life relatively free of traditional pathogens, thanks in part to the medical profession, but in larger part to the engineers and public health laws which see to it that the water and food supplies are safe and that sewage and waste are reduced to innocuous landfill and water. Many urban – and rural – areas in the tropics pose no special threat to the traveler, either, but stereotypes die hard, and blame is painted with a broad brush. So too, the stereotyping of North America as a disease free zone.

Many Colombians visit the United States for business and pleasure, activities that take them primarily to the cities such as Miami and New York City. However, there is much to see outside of Miami and New York City, and the tourist from Cali, Popayán, Tumaco may confront infectious agents not present back home. I would like to describe a few of the pathogens found in the United States, some of which might not be encountered in Colombia, or at least not in urban Colombia.

Before addressing geographically circumscribed pathogens, the threat of sexually transmitted diseases to the solitary traveler must be mentioned – STDs certainly are not geographically circumscribed! Seeking solace from strangers often translates into acquisition of a sexually transmitted disease. Of those infectious diseases reported to the US public health, STDs head the list. Gonorrhea levels have decreased from the epidemic proportions seen in the 1960s and 1970s, but gonorrhea as well as chlamydia, HSV and HPV are widespread and common problems in the United States. Although not the most common, HIV should be recognized as the most serious of the STDs extant in the United States today. The dictum “buyer beware” certainly applies to anyone who purchases sexual favors.

Another very real issue is the presence of multidrug-resistant bacteria in the United States. The prevalence of multi-drug resistant bacteria is high in many medical center intensive care units, and Colombian physicians caring for patients who have received care at major medical centers in the United States should be on the alert for colonization of returning patients by multi-drug resistant bacteria such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Enterobacter* species, and vancomycin-resistant enterococci. The major risk for

acquisition of these pathogens would a stay in an intensive care following solid organ transplantation or other extensive surgery, but any patient undergoing surgery or staying in a hospital may become colonized or infected.

Food and Water Borne Infections

The gulf waters of Florida and other southern states are a major source of delicious oysters for restaurants throughout the United States. The gulf waters, particularly during the warm summer months, also are a source of non-cholera Vibrio, and one of these, *Vibrio vulnificus*, has a predilection for infecting and causing a fulminate infections in persons with cirrhosis. Individuals with known chronic liver disease should be advised to eschew raw seafood, especially fresh oysters as a matter of principle. If he must have his oysters, recommend oysters Rockefeller as an alternative.

There are many other pathogens that may make their way into the food and water supply. Giardiasis is considered the most common intestinal parasite to cause sporadic disease, but cryptosporidiosis, cyclosporiasis (outbreaks attributed to.....imported fruit!), and rarely other parasites such as toxoplasma and trichinella are encountered. Usually not in the best restaurants. Enteric bacterial pathogens such as *Salmonella*, *Campylobacter*, *Shigella* may also be acquired, and various strains of *E. coli* may produce turista.

Not so common but with potential for severe complications is

Escherichia coli 157:H7. Apple cider as well as hamburger has been implicated as a vehicle for this Escherichia that may precipitate a hemolytic uremia syndrome. The organism is an inhabitant of the intestinal track of ruminants and is passed to humans through contamination of surface water or via contaminated, under cooked meat. Hamburger rather than steak is a vehicle because the organism is spread throughout the hamburger patty whereas it remains on the surface of the steak. The *E. coli*157:H7 is destroyed on the cooked surface but survives at the center of rare hamburgers. This has led to laws prohibiting the sale of hamburgers less than medium done. The diagnosis of *E. coli* 157:H7 requires special studies not generally available in standard microbiologic laboratory. Although treatment is supportive, diagnosis is important because it may be the clue to a source of exposure for others.

Tick-Borne Diseases

Tick-Borne Diseases in the United States
Babesiosis
Colorado Tick Fever
Ehrlichiosis
Lyme Disease
Rocky Mountain Spotted Fever
Tularemia
Tick paralysis

There are a number of tick-borne diseases endemic to the United States. The tick vector, *Ixodes scapularis*, is the vector for Lyme disease, Ehrlichiosis, Babesiosis, and may transmit Rocky Mountain Spotted Fever. These diseases are circumscribed by the geographic distribution of the ticks and natural mammalian hosts (rodents such as the white-footed deer mouse, rat and chipmunk) and acquisition generally involves hiking or camping in rural areas. Because the white-tailed deer has served as the host for these ticks but does not seem to be infected. However, re-population of suburban areas of the northeastern United States with white-tailed deer is considered a key factor in the emergence of these diseases as the deer's habitat merges with that of humans. Colorado Tick fever is a benign disease still diagnosed primarily in the western United States, whereas tularemia has been diagnosed throughout the United States. Tularemia, caused by *Francisella tularensis*, is interesting because it is a distinctly north american pathogen. Many cases are acquired not by a tick bite (several varieties serve as vectors) but by the handling of infected animal skins and carcasses. Tick paralysis is a toxin mediated disease, which may occur after a prolonged tick bite. The paralysis can be severe to the point of respiratory failure, but rapidly resolves with removal of the tick.

Lyme disease has been diagnosed in areas throughout the US, the epidemiology closely linked to the habitat of the white-tailed deer. *Borrelia burgdorferi*, causes a chronic infection with several clinically distinct manifestations, including a variety of neurologic complaints. Because of the chronicity and the protean manifestations, it is a common diagnostic consideration. The pathogen can be isolated but the mainstay of diagnosis is the combination of an enzyme-linked immunoassay for screening and a western blot test for confirmation. Treatment of the acute or early stages of the disease is quite good, but the later stages require prolonged courses of antibiotic.

There are two types of **Ehrlichioses**, Human Granulocytotropic Ehrlichiosis (HGE), caused by *Ehrlichia phagocytophilia* – group, and Human Monocytotropic Ehrlichiosis (HME), caused by *Ehrlichia chaffeensis*. Most cases occur in the late spring and early summer, although they may occur year around. These infections are relatively newly recognized, and the epidemiology and spectrum of disease may be incompletely defined. The clinical spectrums range from asymptomatic seroconversion to a fatal overwhelming infection; immunosuppressed patients are at particular risk for fatal outcomes. Fever, headache, rigors, myalgia are typically present – all nonspecific. The presence of leukopenia and thrombocytopenia are seen in more than 50% of cases. The diagnosis, based on serology, must be made retrospectively as treatment should be given early in the disease. HGE can be diagnosed by the presence of ehrlichial morulae in peripheral blood neutrophils. The treatment of choice is tetracycline, and rifampin is also active in vitro. Unlike *R. rickettsii*, which it clinically and epidemiologically overlaps, *Ehrlichia* spp. is not susceptible to chloramphenicol.

Although the name **Rocky Mountain Spotted Fever** conjures up a disease of the mountains of Western USA, most cases of are reported today from the South Atlantic states. This disease, caused by *Rickettsia rickettsii*, is much feared because of a significant morbidity

and mortality. RMSF is heralded by fever, myalgia and headache with the characteristic rash developing some days later. The rash typically begins on the wrists and ankles and moves centrally and often involves the palms and soles. Atypical presentations are common, the appearance may be delayed for a week or more, and some patients develop no rash, the rocky mountain “spotless” fever; the absence of rash, so characteristic of RMSF challenges the clinician because the symptoms and signs are so non-specific. Diagnosis is generally established after the fact as treatment must be given as promptly as possible. The timing of treatment is critical to a successful outcome, especially in fulminate cases, which lead to death within a few days. Doxycycline has been the treatment of choice, but other tetracyclines and chloramphenicol are alternatives and a number of other agents are also likely to be effective although as yet are unproven. The diagnosis is confirmed by serology after the patient recovers.

Babesiosis in the United States is caused by *Babesia microti* (the US indigenous version of malaria). Clinical disease – fever, shaking chills, malaise, myalgias, headache, abdominal pain, etc – is thought to occur in a minority of infected persons. There is a correlation between age and symptoms – the older the patient, the more likely or more severe the symptoms. Asplenic patients are at particular risk for fulminate infection with severe hemolytic anemia. Untreated infection may persist for months with recrudescence episodes. Diagnosis is usually based on observation of the parasite in blood smears, although an indirect immunofluorescent antibody assay is available at the CDCP in Atlanta, Georgia. Clindamycin and oral quinine is recommended for 7-10 days; other regimens such as atovaquone and azithromycin have been successful.

Environmental Exposures

A diverse group of infections can be grouped epidemiologically into environmentally acquired infections. Most of these are acquired by inhalation of the pathogen, but ingestion and direct inoculation are also routes of infection. Along with the clinical presentation, the travel or exposure history is helpful (and often critical) in arriving at a timely diagnosis. These include the pathogens listed in the following table.

Environmental Exposure-Related Pathogens
<p>Geographic Fungi</p> <ul style="list-style-type: none"> - Coccidioides Immitis - Histoplasma Capsulatum - Blastomyces Dermatitidis <p>Francella Tularensis Yersinia Pestis Hantavirus</p>

Hantavirus Pulmonary Syndrome

Hantaviruses have been recognized for many years, as a virus without a disease throughout the United States, and as a cause of a hemorrhagic fever in Korea and other parts of Asia. It was only after a climatic changes caused an increase in *Peromyscus maniculatus*, the deer mouse, and movement into human dwellings in the southwest and to cause multiple infections in a short time that Hantavirus pulmonary syndrome emerged as a recognized entity. The virus, now called the *Sin nombre virus*, (with variants, Black Creek Canal and Bayou viruses), has been found in many parts of the United States. Humans acquire the infection by breathing aerosols containing rodent urine or feces, for example, by cleaning a barn or house in which the deer mouse has invaded. The true incidence of human disease is unknown, as many cases presumably are undiagnosed. The onset of disease begins with a fever and myalgias, occasionally with abdominal pain followed 4-5 days later by cough and dyspnea rapidly leading to respiratory insufficiency. Thrombocytopenia and an elevation of hematocrit (ascribed to hemoconcentration) are characteristic laboratory findings. The chest x-ray shows interstitial edema or a picture typical of adult respiratory distress syndrome. The diagnosis should be suspected in any previously healthy patient who develops adult respiratory distress syndrome with no obvious cause and a history of possible exposure to rodents. Confirmation of the diagnosis is based upon ELISA IgM and IgG antibodies, tests available in the United States through the Public Health Department. Treatment is supportive; no specific antiviral therapy is available.

Plague (*Yersinia pestis*)

Sylvatic plague persists in the southwestern states among rodents, ground squirrels and prairie dogs. Each year a few cases occur in humans, secondary to bites by fleas from diseased rodents and occasionally from handling of dead animals. The most common syndrome is the bubonic form, but septicemic and pneumonic forms also occur. The bubos generally develop in the regional lymph nodes proximal to the site of the inciting flea bite. Plague may be rapidly fatal, but even in the slower paced infection, delays in diagnosis may occur with poor outcome if the patient is a tourist who has returned home to a non-endemic area. Obviously, critical to the diagnosis is epidemiologic information about potential exposure. Diagnosis is with culture of an aspiration from the bulbo or blood. The standard treatment has been streptomycin, but chloramphenicol and tetracycline are also effective.

Geographic fungi

Within the United States, Blastomycosis, coccidiomycosis and histoplasmosis are considered to be geographic fungi, that is fungi pathogenic for humans but with limited geographic distribution. Blastomycosis is relatively uncommon, occurring most frequently in persons with a history of recreational or occupational outdoor exposure to moist soils in the Mississippi, Ohio and St. Lawrence river basins. Coccidiomycosis is acquired in the lower Sonoran life zones – arid regions with limited rainfall, hot summers and alkaline soil. In the United States, this would be the southwestern states (and in Colombia in the

northeastern deserts). Histoplasmosis is more ubiquitous, but most cases occur in the same distribution as blastomycosis.

Something New - West Nile Fever

One of the recent “new” infections to emerge did so in the environs of New York City. Mistaken at first for a resurgence of Saint Louis Encephalitis virus, a strain of the West Nile Virus (WNV) proved to be the cause of a major - and fatal - epidemic among birds in the area with spill over into humans. WNV is a flavivirus belonging taxonomically to the Japanese encephalitis subgroup that includes the serologically closely related SLE virus, Kunjin virus, Murray Valley encephalitis virus, and others. The remarkable aspect of this infectious disease is that it has never been encountered in the Western Hemisphere

WNV was first isolated in the West Nile Province of Uganda in 1937. The first recorded epidemics occurred in Israel during 1950-1954 and in 1957. Epidemics have been reported in Europe in the Rhone delta of France in 1962 and in Romania in 1996. The largest recorded epidemic occurred in South Africa in 1974. It is unclear whether the virus that caused this outbreak is a previously identified strain of WNV or a new variant.

Laboratory studies conducted at CDC have identified the etiologic agent responsible for the human arboviral encephalitis outbreak in the NYC area as WNV. Confirmation of the genetic identity as WNV has been performed independently by collaborators at the United States Army Medical Research Institute for Infectious Diseases. WNV-specific gene sequences have been amplified by RT-PCR performed on RNA extracted from autopsy specimens (six case-patients). Sequences of genome fragments of WNV isolated from dead birds and mosquitoes are identical to gene sequences from the human autopsy specimens. Antigenic mapping of these isolates has been performed using a panel of monoclonal antibodies (Mabs) developed by CDC or provided by collaborators at the University of Queensland, Australia. These envelope (E)-glycoprotein specific Mabs, capable of distinguishing WN, Kunjin, and St. Louis encephalitis viruses, confirmed the sequence identification of these isolates as WNV.

Conclusion

Fortunately, most of the infections mentioned above are uncommon to rare in occurrence. Because treatment is available and timely diagnosis can avoid significant morbidity and mortality, the clinician should be alert to the characteristics and exposure history suggestive of specific infections. In a world where global travel is commonplace, all physicians must be aware of the unusual. Zebras may be rare but they exist!

Suggested Reading

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