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Severe Acute Respiratory Syndrome (SARS)

SPECIAL REPORT BY MICHELE BARRY, MD

Sources: *MMWR Morb Mortal Wkly Rep*. 2003;52(11):226-228; *MMWR Morb Mortal Wkly Rep*. 2003;52(12):241-248; *MMWR Morb Mortal Wkly Rep*. 2003;52(14):299-302; WHO: www.who.int; CDC: www.cdc.gov/ncidod/sars; Promed: www.promedmail.org; Health Canada: www.sars.gc.ca.

SINCE LATE FEBRUARY 2003, THE CDC AND WHO HAVE BEEN INVESTIGATING a multicountry outbreak of an atypical pneumonia manifested by an illness referred to as severe acute respiratory syndrome (SARS). These initial reports in *MMWR* describe the scope of the outbreak, case definition, and interim infection control guidance for the United States. Continuous daily updates can be obtained from these web sites: www.cdc.gov/ncidod/sars and www.who.int.

Epidemiology and Transmission

The first case of SARS was reported outside China on February 26, 2003. By April 9—in less than 2 months—the number of probable cases from 16 countries had reached 2722 with 106 deaths (3.9%). Initially, some 60-70% of infected people were health care professionals who treated SARS-infected people, and the remaining 30-40% were family members and other close contacts of infected people. However, a recent report from Hong Kong documented spread of the disease within nonrelated tenants of an apartment complex with faulty sewage facilities. The current working hypothesis is SARS is transmitted via large droplets (sneezes, coughs, or bodily fluids). This concept does not account for all the epidemiologic evidence including the people in one Hong Kong housing complex and on one floor of a Hong Kong hotel raising the idea of "super-spreaders" or an undiscovered environmental mode of transmission.

Etiologic Agent

Although the etiologic agent had not been confirmed initially, laboratory data indicate that a coronavirus is most probably the culprit. Coronaviruses are enveloped, single-stranded RNA viruses that infect both humans and animals and have a halo or crown-like corona appearance under electron microscopy. The known human coronaviruses are common causes of mild-to-moderate upper respiratory tract infections and are responsible for approximately one-third of common colds. However, they can cause serious infections of the lower respiratory tract in children and adults and are associated with necrotizing enterocolitis in newborns. Coronaviruses can survive on environmental surfaces for up to 3 hours and can be transmitted person-to-person via droplets, hand contamination,

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Table

CDC Updated Interim Case Definition for Severe Acute Respiratory Syndrome (SARS)*

Suspected case†

Respiratory illness of unknown etiology with onset since February 1, 2003, and the following criteria:

- Measured temperature > 100.4°F (> 38.0°C)
- One or more clinical findings of respiratory illness (eg, cough, shortness of breath, difficulty breathing, hypoxia, or radiographic findings of either pneumonia or acute respiratory distress syndrome)
- Travel within 10 days of onset of symptoms to an area with suspected or documented community transmission of SARS,§ (excluding areas with secondary cases limited to health-care workers or direct household contacts) *or*
- Close contact†† within 10 days of onset of symptoms with either a person with a respiratory illness and travel to a SARS area or a person under investigation or suspected of having SARS

* As of March 22, 2003

† Suspected cases with either radiographic evidence of pneumonia or respiratory distress syndrome, or evidence of unexplained respiratory distress syndrome by autopsy, are designated "probable" cases by the World Health Organization case definition

§ Hong Kong Special Administrative Region and Guangdong province, China; Hanoi, Vietnam; and Singapore.

†† Close contact is defined as having cared for, having lived with, or having had direct contact with respiratory secretions and/or body fluids of a patient suspected of having SARS.

formites, and small particle aerosols.[1,2] The SARS-associated coronavirus was isolated in Vero E6 cells from clinical specimens of 2 patients in Thailand and Hong Kong with suspected SARS. Electron microscopy identified the isolate as a coronavirus and its identity was confirmed by immunostaining, indirect immunofluorescence assays, and RT-PCR and sequencing of a segment of the polymerase gene. Serology performed on paired convalescent and sera confirm antibody responses to the suspected agent. Sequence microarray analysis suggests this new coronavirus is distinct from other coronaviruses and that it may have begun its current course as an animal pathogen.

Clinical Description of SARS

The incubation period for SARS is typically 2-7 days; however, isolated reports have suggested an incubation period as long as 10 days and reports even up to 15 days in recent isolated cases. The illness generally begins with a prodrome of fever (> 100.4°F or > 38.0°C). Fever is often quite high, sometimes is associated with chills and rigors, and might be accompanied by other symptoms, including headache, malaise, and myalgia. At the onset of illness, some persons have mild respiratory symptoms. Typically, rash and neurologic or gastrointestinal findings are absent; however, some patients have reported diarrhea during the febrile prodrome.

After 3-7 days, a lower respiratory phase begins with the onset of a dry, nonproductive cough or dyspnea, which might be accompanied by or progress to hypoxemia. In 10-20% of cases, the respiratory illness has been severe enough to require intubation and mechanical ventilation. The case-fatality rate among persons with illness meeting the current WHO case definition of SARS is approximately 4%.

Chest radiographs might be normal during the febrile prodrome and throughout the course of illness. However, in a substantial proportion of patients, the respiratory phase is characterized by early focal infiltrates progressing to more generalized, patchy, interstitial infiltrates. Some chest radiographs from patients in the late stages of SARS also have shown areas of consolidation.

Early in the course of disease, the absolute lymphocyte count is often decreased. Overall white blood cell counts have generally been normal or decreased. At the peak of the respiratory illness, approximately 60% of patients have leukopenia and thrombocytopenia or low-normal platelet counts (50,000-150,000/mL). Early in the respiratory phase, elevated creatine phosphokinase levels (£ 3000 IU/L) and hepatic transaminases (ALT 2-6 times the upper limits of normal) have been noted. In the majority of patients, renal function has remained normal. The severity of illness may be highly variable, ranging from mild illness to death. Although most close contacts of patients with SARS have remained well, other close contacts have reported a mild, febrile illness without respiratory signs or symptoms, suggesting the illness might not always progress to the respiratory phase.

Treatment

Treatment regimens have included several antibiotics to presumptively treat known bacterial agents of atypical pneumonia. Therapy also has included antiviral agents such as oseltamivir or ribavirin. Steroids have also been administered orally or intravenously to patients developing acute respiratory distress syndrome. At present, the most efficacious treatment regime, if any, is unknown, and supportive therapy is recommended by CDC. In

Hong Kong and Canada, intravenous ribavirin had been recommended in presumed SARS cases in dosages of 33 mg/kg (max 2 g) IV loading dose following by 16 mg/kg (max 1 g) every 6 hours for 4 days then 8 mg/kg (max 0.5 g) every 8 hours for 3-6 days depending on clinical response. The CDC has not officially recommended use of ribavirin or steroids but does recommend use of antibiotics for community-acquired atypical pneumonia until the agent is definitely documented.

In the United States, clinicians who suspect cases of SARS are requested to report such cases to their state health departments. CDC requests that reports of suspected cases from state health departments, international airlines, cruise ships, or cargo carriers be directed to the SARS Investigative Team at the CDC Emergency Operations Center (telephone, [770] 488-7100).

Clinicians evaluating suspected cases should use standard precautions (eg, hand hygiene) together with airborne prevention (N95 or higher efficiency particle prevention respirator) and contact precautions (gowns and gloves). Until mode of transmission has been defined more precisely, eye protection should also be worn. CDC infection control guidelines for SARS in the inpatient and outpatient setting can be found on the following web site: www.cdc.gov/ncidod/sars/infectioncontrol.htm.

Travel Advisories

Table 2

Cumulative Number of Reported Cases of Severe Acute Respiratory Syndrome (SARS)

From: Nov 1, 2002[1] to: April 3, 2003

Country	Cumulative number of case(s)	Number of deaths	Local chain(s) of transmission[2]
Australia	1	0	None
Belgium	1	0	None
Brazil	1	0	None
Canada	62	6	Yes
China	1190	46	Yes
China, Hong Kong Special Administrative Region	734	17 *	Yes
China, Taiwan	14	0	Yes
France	3	0	None
Germany	5	0	None
Italy	3	0	None
Republic of Ireland	1	0	None
Romania	1	0	None
Singapore	98	4	Yes
Switzerland	2	0	None
Thailand	7	2	None
United Kingdom	3	0	None
United States	85[A§]	0	Being determined
Vietnam	59	4	Yes
TOTAL	**2270**	**79**	

Notes:

Cumulative number of cases includes number of deaths.

As SARS is a diagnosis of exclusion, the status of a reported case may change over time. This means that previously reported cases may be discarded after further investigation and follow-up.

1. The start of the period of surveillance has been changed to November 1, 2002, to capture cases of atypical pneumonia in China that are now recognized as being cases of SARS.
2. National public health authorities report to WHO on the areas in which local chain(s) of transmission is/are occurring. These areas are provided on the list of *affected areas*.

A§ Due to differences in the case definitions being used at a national level, probable cases are reported by all countries except the United States of America, which is reporting suspect cases under investigation.

* One death attributed to Hong Kong Special Administrative Region of China occurred in a case medically transferred from Vietnam.

At this writing, there are no travel restrictions directly related to SARS; however, a CDC travel advisory recommends that individuals who are planning nonessential or elective travel to mainland China, Hong Kong, Vietnam or Singapore may wish to postpone their trip (for updates see www.cdc.gov/travel). Canada has had a cluster of cases in Toronto but has not been added to the CDC list as of this printing. All Canadian cases have been linked to foreign travel or exposed health care workers.

Specific guidelines for airline crew and flight personnel of commercial flights have been developed (www.cdc.gov/ncidod/sars/ flightcrewguidelines.htm) as well as for air evacuation aircraft www.cdc.gov/ncidod/sars/airtransport-sarspatients.htm). CDC's Division of Global Migration and Quarantine has sent quarantine officials to provide health alert notices (25,000 daily) to returning travelers on airplanes, cargo ships or cruise ships from infected areas and board airplanes or ships to assess ill travelers. Fact sheets for travelers can be obtained from the CDC web page. (www.cdc.gov/ncidod/sars) Each country is handling travel and case contacts in their particular fashion and travelers should check web sites before leaving as quarantines and mask requirements may occur at airports. For WHO to issue global travel warnings for specific geographical areas is unprecedented even during the years of the smallpox eradication campaign. Daily advisories and press releases are posted on www.who.int.

COMMENT BY MICHELE BARRY, MD, FACP

Readers should note the mortality rate of 3-4% may understate actual rate for SARS because many patients who have been infected are healthy, relatively young, health care workers with case detection occurring in the context of a closely watched epidemic and health care setting. Should SARS continue its spread, older and sicker patients with comorbid diseases may contract the disease, treatment resources may fall, and mortality rates could increase. In less than 2 weeks due to amazing global collaboration, the virus has been identified, the genome has been sequenced and diagnostic tests have been developed. In the coming weeks, it will be crucial to develop and use diagnostic tests to apply quickly in hospitals and possibly airports.

Key questions and developments to watch:

- The transmissibility of SARS during the incubation period *before* symptoms occur. Is transmissibility large or small droplets, airborne, or by fecal-water contamination?
- Are there super-spreaders—and what makes one a super-spreader?—more virulent strain, higher inoculum, etc.
- Do ribavirin or steroids have an effect on mortality or morbidity?
- Will public health authorities impose travel bans or strict quarantines?
- Can a vaccine be developed by next winter? ■

References

1. Sizun J, et al. *J Hosp Infect*. 2000;46:55-60.
2. Ijaz MK, et al. *J Gen Virol*. 1985;66:2743-2748.

Peanuts, Allergy, and Travel

ABSTRACT & COMMENTARY

Synopsis: *Repeated injections of a monoclonal anti-IgE antibody markedly decreased the sensitivity of peanut-allergic patients to subsequent peanut exposure. Since fatal anaphylaxis to peanuts can occur following inadvertent ingestion of small amounts of peanut antigen, this treatment might be very useful for peanut-allergic travelers who will be exposed to foods of uncertain purity.*

Source: Leung DYM, et al. *N Engl J Med*. 2003;348:986-993.

TNX-901 IS AN IgG_1 MONOCLONAL ANTI-IGE ANTIBODY that hinders binding of IgE to mast cell and basophil receptors. A multicenter, randomized, double-blind, dose-ranging interventional trial was done in 84 peanut-allergic patients. Following a series of subcutaneously injected TNX-901 doses, subjects were orally challenged with peanuts. The threshold at which subjects responded with a sensitivity reaction was noted. There was a significant positive correlation between the dose of TNX-901 and the increase in reaction threshold. At the highest dose tested, the mean dose of peanuts to which subjects reacted increased from 178 mg (about half a peanut) to 2805 mg (about 9 peanuts).

COMMENT BY PHILLIP R. FISCHER, MD, DTM&H

Approximately 15% of individuals have allergic disease, and food allergies are a significant problem for some of these people. Peanuts are among the foods most likely to trigger serious reactions, and fatal anaphylaxis is a possible outcome. In a series of 7 cases of fatal anaphylaxis, each individual was atopic with a prior history of anaphylaxis; triggering foods included peanuts (4 cases), pecan, crab, and fish.[1] In a separate report of serious anaphylactic reactions in children (6 fatal and 7 near-fatal), each affected child was previously known to have food allergies, and most were asthmatic; triggering foods included nuts (6 cases) and peanuts (4 cases) as well as milk and eggs (fewer cases).[2] Some children are allergic to multiple different foods, and significant exposures are

commonly inadvertently related to hidden or unknown food ingredients.[3] While milk and egg allergies commonly resolve during childhood, peanut allergies often persist throughout life.

It is particularly concerning that reactions to peanuts can occur after exposure to very small amounts of allergen.[4] While most significant exposures result from inadvertently eating food that contained peanut material, some authors have expressed concern that air filters in commercial aircraft have been found to contain peanut allergen and are only changed every 5000 hours.[5] Many peanut-sensitive travelers fear exposure to peanuts during air travel as well as when eating foods of unknown composition during their trips. Some airlines have offered peanut-free flights to help allay these fears.

In the context of travel, the recent *New England Journal of Medicine* paper offers great hope to peanut-allergic individuals. Leung and associates found that peanut-sensitive patients were much less likely to respond to peanut exposure 2-4 weeks after completing a course of 4 subcutaneous injections at 4-week intervals of TNX-901. In fact, subjects increased their threshold of response to a level that could likely not occur due to inadvertent ingestion on an airplane or by eating food contaminated with peanuts during processing. If further studies confirm these findings, this "peanut allergy vaccine" could markedly decrease both anxiety and the risk of fatal anaphylaxis in peanut-sensitive travelers.

Similarly favorable results with a different anti-IgE product have been reported for asthma treatment. As reported in the *New York Times* (March 11, 2003), however, commercial and marketing decisions might delay further study and the potential availability of any of these products for peanut-allergic individuals.

So, what can peanut-sensitive travelers do right now while they await the availability of anti-IgE products? First, they should continue to pay attention to food preparation and labeling in an effort to avoid inadvertent ingestion of peanut-containing products. Second, they can be reassured to know that fatal reactions rarely occur in people without previous knowledge of their food allergy. Furthermore, fatal outcomes are rare when epinephrine is given within 30 minutes of the inciting ingestion. Epinephrine is the treatment of choice for anaphylaxis, and at-risk travelers should have epinephrine available during trips while realizing that they should check expiration dates to ensure that the epinephrine is still effective at the time they travel. Travel medicine practitioners can seek a history of serious allergic reactions and provide epinephrine when indicated, along with documentation of the need for this injectable product to help travelers avoid delays when crossing international borders. Travelers can also be advised that *epinephrine reaches a peak plasma concentration more quickly (8 vs 34 minutes) following intramuscular rather than subcutaneous injection.*[6]

While presumptive treatment of allergic reactions is useful, it would be better to prevent the development of allergies. What causes food allergies in the first place? Parallel to the TNX-901 article, the *New England Journal of Medicine* published a paper reviewing epidemiologic associations with the development of peanut allergy in children.[7] There was no link between pediatric peanut allergy and preceding prenatal exposure to maternal dietary factors. There was, however, a link between the use of peanut oil on inflamed skin during the first 6 months of life and subsequent peanut allergy. Similarly, peanut allergy was more common in children who had used soy milk or soy formula. Pending interventional studies, it might be wise for infants to avoid the topical use of humidifying lotions that contain peanut oil, and it could be sensible to limit the use of soy formulas to those children with clear-cut need for them.

Does vaccination prompt people to develop allergies? A recent, detailed review concluded that "large well-controlled epidemiologic studies do not support the hypothesis that vaccines cause allergies."[8] Furthermore, another recent report showed that routine childhood vaccination actually protects against the development of atopy in the first years of life.[9] Travel medicine providers need not shy away from appropriate vaccination due to concerns about stimulating allergic disease.

In summary, there is exciting progress in the management of individuals with peanut allergy. At the same time, travel medicine practitioners should continue their efforts to provide appropriate pretravel guidance that includes the provision of appropriate medication and counsel for allergic travelers, and they should continue giving pretravel vaccines without fear that vaccines cause allergies. ■

References

1. Yunginger JW, et al. *JAMA*. 1988;260:1450-1452.
2. Sampson HA, et al. *N Engl J Med*. 1992;327:380-384.
3. Sicherer SH, et al. *Pediatrics*. 1998;102(1):e6.
4. Hourihane JO, et al. *Clin Exp Allergy*. 1997;27:634-639.
5. Jones RT, et al. *J Allergy Clin Immunol*. 1996; 97:abstract 961.
6. Simons FE, et al. *J Allergy Clin Immunol*. 1998;101: 33-37.
7. Lack G, et al. *N Engl J Med*. 2003;348:977-985.
8. Offit PA, et al. *Pediatrics*. 2003;111:653-659.
9. Gruber C, et al. *Pediatrics*. 2003;111:666.

W135 Meningococcal Disease: A New Vaccine for Africa

ABSTRACTS & COMMENTARY

Synopsis: *A case of* Neisseria meningitidis *W135 in a traveler to Morocco is reported, but it was last year's epidemic of W135 meningococcal meningitis in Burkina Faso that led to the development of a new trivalent vaccine (A/C/W135) for use in Africa. So far this year, more than 500 deaths due to meningitis have occurred in Burkina Faso.*

Sources: Wilder-Smith A, et al. *J Travel Med*. 2003;10:59-61; WHO CSR and Epidemiological Bulletin, 7 March 2003. www.who.int/csr/don/en/.

A HEALTHY BRITISH JOURNALIST FLEW FROM LONDON to Morocco. She remained in Morocco for 10 days before traveling on to Japan. After an 11-day stay in Japan, she flew to Singapore. During the flight, she began having fever, chills, and rigors. After arrival, she went to her hotel and was later found semiconscious by her friend. On admission to the hospital, she was in shock with a generalized petechial rash. Antibiotics were begun and her CSF culture subsequently grew *Neisseria meningitidis* W135. She recovered fully and eventually returned home to England.

Wilder-Smith and associates postulate that this traveler was most likely exposed to *N meningitidis* W135 in Morocco, a predominantly Muslim country. However, exposure from close proximity to a W135 carrier during her airplane travel is another possibility they discussed. Their search of the literature did not reveal any previous reports of W135 meningitis in either Morocco or Japan. Singapore has reported W135 disease, but all cases have been related to the Hajj pilgrimage or close contacts of returning pilgrims.

The Ministry of Health in Burkina Faso has reported a total of 3691 cases of meningococcal disease with 542 deaths since the outbreak began in January 2003. Samples from the outbreaks confirm *N meningitidis* serogroups A and W135. The number of cases and deaths will no doubt continue to rise. By April of last year, Burkina Faso had reported a total of 11,247 meningitis cases with at least 1300 deaths. *N meningitidis* W135 was confirmed in 147 of the 175 positive specimens sent to their national laboratory network. The remaining specimens were either serogroup A, or both A + W135 agglutination.[1]

COMMENT BY MARY-LOUISE SCULLY, MD

Meningococcal disease associated with large epidemics in the African "meningitis belt" has historically been caused by *N meningitidis* serogroup A and, less often, serogroup C strains. Recent reports of significant meningococcal disease outside the traditional "belt" of Africa should heighten our awareness of the growing meningococcal disease risk in other parts of Africa.[2,3] The case of W135 meningitis in the British traveler to Morocco perhaps reflects future changes in the epidemiology of African meningococcal disease and its implications for travelers.

The epidemic potential of *N meningitidis* W135 became evident during the 2000 and 2001 Hajj seasons when W135 meningitis occurred in Saudi Arabia and internationally in Hajj pilgrims and their contacts. As a result, vaccination with quadrivalent (A/C/Y/W135) vaccine is now a requirement for a Hajj visa.[4] Some postulate that Muslims from Africa introduced this strain to the Hajj pilgrimage. Indeed, sporadic disease due to *N meningitidis* W135 has been reported in Africa since 1981 and a vaccine trial in 1996 found high levels of W135 carriage in asymptomatic Gambian children.[5] Molecular analysis of the W135 Hajj-associated isolates found this strain to be associated with the ET-37 complex, a clone that has been circulating globally since at least 1970.[6]

The 2002 outbreak of W135 meningitis in Burkina Faso was the first report of epidemic disease in Africa due to this strain. Until now, available international meningococcal polysaccharide vaccines were either monovalent, bivalent (A/C) or quadrivalent (A/C/Y/W135). However, the cost of the quadrivalent vaccine ranges from $4 to $50 per dose and is out of reach for most African countries. Three group C meningococcal conjugate vaccines (MCC) are licensed internationally. MCC is now part of the national immunization program in the United Kingdom and has resulted in a significant reduction in group C meningococcal disease in their country. Unfortunately, none of these vaccines provides protection against serogroup B meningococci strains circulating in Australia, Europe, North America, and South America. Group B polysaccharide is poorly immunogenic, even when conjugated to a protein carrier.

In response to the unexpected 2002 outbreak of W135 meningitis in Burkina Faso, the World Health Organization (WHO) and its partners in meningitis preparedness began intense negotiations to provide an affordable W135 meningitis vaccine to African countries. With unprecedented speed, the WHO, GlaxoSmithKline, and the Bill & Melinda Gates Foundation are making available a new trivalent vaccine to cover serogroups A, C, and W135. Already 500,000 doses of the newly licensed

trivalent vaccine (A/C/W135) have arrived in Burkina Faso and a mass vaccination campaign is underway in hopes of abating the outbreak now in progress. In all, 3 million doses of the new trivalent vaccine will be available at reduced cost to African countries.[7] The vaccine is being distributed through the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control (ICG) to countries that submit requests and meet the criteria for a meningococcal outbreak. ■

References

1. Meningococcal disease, serogroup W135, Burkina Faso. Preliminary Report, 2002. *Wkly Epidemiol Rec*. 2002; 77:152-155.
2. Molesworth AM, et al. *Trans R Soc Trop Med Hyg*. 2002;96:242-249.
3. Fischer PR. *Travel Medicine Advisor Update*. 2002; 12:33-35.
4. Gold R. *Clin Infect Disease*. 2003;36:684-686.
5. MacLennan JM, et al. *Lancet*. 2000;356:1078.
6. Mayer L, et al. *J Infect Dis*. 2002;185:1596-1605.
7. www.who.int/mediacentre/release/2003/pr9/en/print.html.

Quinolone Resistance in *Campylobacter jejuni*

ABSTRACT & COMMENTARY

Synopsis: *Overall, quinolone resistance among isolates of* Campylobacter jejuni *from returned Finnish travelers increased during a 5-year period. The countries at highest risk for quinolone resistance are Thailand, India, and China. These findings indicate a need to reconsider the choice of antibiotics for self-treatment of traveler's diarrhea in some countries.*

Source: Hakanen A, et al. *Emerg Infect Dis*. 2003;9(2): 267-270.

A TOTAL OF 354 *Campylobacter jejuni* ISOLATES COLlected from travelers returning to Finland were evaluated for ciprofloxacin resistance. All subjects had traveled within 2 weeks of isolate collection. The specimens were collected from 1995 to 1997 and 1998 to 2000 by the laboratory staff of a hospital in Helsinki, who also determined minimal inhibitory concentrations (MICs) of ciprofloxacin and nalidixic acid for *C jejuni* isolates. Of these, 319 isolates were attributed to 40 specific countries of origin. Because of multiple destinations in the travel history, 22 isolates were attributed at the continent level, and the origins of 13 isolates were unknown.

Ciprofloxacin resistance in the *C jejuni* isolates was demonstrated in 49% of all isolates. Forty percent of the isolates collected from 1995-1997 were resistant compared with 60% obtained from 1998-2000. In a comparison by continent, Asia showed a significant increase in quinolone resistance from 45% to 72% between the two periods. There were very few isolates from North America; therefore, ciprofloxacin resistance for the two periods (0 and 67% respectively) may not be an accurate reflection of resistance. Although less dramatic, isolates from Africa and Europe also demonstrated increase in ciprofloxacin resistance.

There were 205 isolates collected from 1995-1997 and 149 isolates from 1998-2000. The most common countries of origin during the first period (1995-1997) for the *C jejuni* isolates were Spain (20%), India (9%), Thailand (8%), and Turkey(8%). The most common countries of origin during the second period were Spain (25%), Thailand (22%), Portugal (4%), and Tunisia (4%).

Hakanen and colleagues derived rate ratios for acquiring ciprofloxacin-resistant *C jejuni* from various destinations based on the number of trips to those destinations. The rate ratios show that the risk of acquiring quinolone-resistant *C jejuni* is highest in Thailand, followed by India and China. *The risk of acquiring ciprofloxacin-resistant C jejuni from Thailand appeared to be 10 times the rate in Spain or Portugal*.

■ COMMENT BY LIN H. CHEN, MD

C jejuni is a motile, curved, Gram-negative rod, found worldwide and with numerous animal reservoirs. Human infections typically result from ingestion of contaminated water and food, in particular contaminated meat, but can also result from ingestions of unpasteurized milk.[1] In developing countries, *C jejuni* is frequently isolated from asymptomatic persons, and it is a common cause of diarrhea in early childhood—especially those younger than 2 years old.[2,3] An epidemiologic review following laboratory surveillance of *Campylobacter* in the United Kingdom indicated a high risk of campylobacteriosis in persons who had traveled to Indonesia (Bali), Singapore, the Philippines, followed by Thailand, Nepal, Sri Lanka, and Malaysia.[4] Pakistan, Bangladesh, India, South America, and Africa also had greater risk than travel to other countries or domestic travel.

Clinical symptoms usually present after an incubation period of 2 days after exposure, although this ranges from 1 to 7 days.[1] *C jejuni* may cause an enteritis or colitis affecting the jejunim, ileum, or colon. Acute symptoms can last up to 1 week, associated with fever, abdominal cramping, and stools ranging from loose to watery to frankly bloody. Symptoms are often self-limited. However, local spread can occur resulting in complications such

as cholecystitis, pancreatitis, and peritonitis. *C jejuni* is one of the more common triggers of the Guillain-Barré syndrome. Organisms can be excreted for a mean of 16 days following convalescence.[5]

Treatment of *C jejuni* is primarily symptomatic and supportive, including hydration and replacement of electrolytes. Antibiotics are reserved for severe clinical presentations including high fever, bloody diarrhea, copious amounts of stool, or lack of response to conservative treatment. A number of antibiotics have been effective in the past, although erythromycin and ciprofloxacin have been drugs of choice.[6] Antibiotic treatment does not prolong carriage, and erythromycin actually eliminates the organism from stool by 72 hours.[7]

Resistance among human isolates of *C jejuni* has previously been traced to the use of antibiotics in food animals.[6] Unfortunately, quinolone resistance in *C jejuni* is now widespread, as encountered by Finnish travelers. The study demonstrates a significant increase in resistance during the 5-year period, and identifies countries associated with high risk for acquiring quinolone-resistant *C jejuni*: Thailand, India, and China. Because of its convenient dosing and good tolerance, azithromycin is already being recommended as a self-treatment for moderate cases of traveler's diarrhea in travelers going to Thailand. The same recommendation may be applied to other countries as quinolone resistance emerges.

What other drugs are effective against *C jejuni*? Erythromycin (or another macrolide) is again the drug of choice, but resistance is also emerging. Aminoglycosides, chloramphenicol, clindamycin, nitrofurans, and imipenem should still be effective against *C jejuni* in severely ill patients.[3] ■

References

1. Blaser MJ, et al. *JAMA*. 1987;257:43-46.
2. Coker AO, et al. *Emerg Infect Dis*. 2002;8:237-243.
3. Allos BM. *Clin Infect Dis*. 2001;32:1201-1206.
4. The Campylobacter Sentinel Surveillance Scheme Collaborators. *J Travel Med*. 2003;10:136-138.
5. Wassenaar TM, Blaser MJ. *Microbes Infect*. 1999;1:1023-1033.
6. Engberg J, et al. *Emerg Infect Dis*. 2001;7:24-34.
7. Anders BJ, et al. *Lancet*. 1982;1:131-132.

CME Questions

5. Severe Acute Respiratory Syndrome (SARS) is:

a. only contagious by face-to-face large droplet exposure and contamination.
b. fatal in 10% of cases of health care workers exposed.
c. due to occasional prolonged incubation and is a differential diagnostic consideration for a patient with travel to Hong Kong 1 month prior who presents with an acute upper respiratory infection.
d. due to a coronavirus, which is similar to the common cold virus.

6. The following statement is correct regarding *C jejuni*:

a. *C jejuni* is still universally sensitive to macrolides.
b. Quinolone resistance in *C jejuni* does not occur in developed countries.
c. *C jejuni* infection usually causes severe intractable diarrhea in developing countries.
d. *C jejuni* strains from Thailand are especially sensitive to fluoroquinolones.
e. The mainstay of treatment for *C jejuni* enteritis is supportive therapy.

Answers: 5. (d); 6. (e)