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Infectious Diseases in the Balkans

SPECIAL REPORT

By Stan Deresinski, MD, FACP

Editor's Note: Please see the special map supplement of the *Balkans*, which accompanies this article, enclosed with this issue of *Infectious Disease Alert*.

We have previously reviewed potential infectious hazards faced in the Balkans. Given the current events in that area, including the refugee crisis, the influx of NATO and relief personnel, and the possible introduction of land forces, a large number of individuals will be put at risk. For that reason, an update appears warranted.

Arboviruses and Hemorrhagic Fever Viruses

Arboviruses and hemorrhagic fever viruses causing human disease in the Balkans include tick-borne encephalitis (TBE), Crimean-Congo hemorrhagic fever (CCHF), sandfly fever (Naples strain), and West Nile and hantaviruses.¹

Tick-Borne Encephalitis (TBE). TBE viruses comprise a complex that includes eight human pathogens: Central European encephalitis (CEE), Russian spring-summer encephalitis (RSSE), Kyasur Forest disease, Omsk hemorrhagic fever, Powassan, Langat, Louping ill, and Negishi. However, the degree of homology among these viruses is such that only two, CEE and RSSE, can be considered as clearly distinct organisms.² These have also been termed, respectively, TBE Western subtype and TBE Eastern subtype; both subtypes are present in eastern Europe.⁶⁸

The tick vector, of the *Ixodes ricinus*, is also the vector for *Borrelia burgdorferii* as well as *Babesia* spp. in Europe. *Ixodes persulcatus* also serves as a vector for TBE. Outbreaks of CEE and RSSE have also resulted from ingestion of unpasteurized sheep or goat milk or cheese. In eastern Croatia, most cases occur between April and August.³ In general, RSSE is reported to occur from May to August while CEE extends its season into October.

Infection, if symptomatic (this is the case in only approximately

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20%), may cause a biphasic illness, with headache, myalgia, and radiculopathy during the initial viremic phase. Aseptic meningitis is the most common clinical form of disease, occurring in approximately two infections in 1000. After initial improvement, patients suffer the abrupt onset of high fever, severe headache, and, in some cases, progressive neurologic deterioration and death. The biphasic pattern is more commonly associated with infection with the Western, rather than the Eastern, subtype of the virus. In a series of 92 cases in eastern Croatia, approximately 10% of 92 recognized cases presented with aseptic meningitis while the remainder had acute meningoencephalomyelitis. One-third had disturbed consciousness; 3.3% died.³

Approximately 85-130 cases of Central European TBE occur per annum in Yugoslavia, primarily in the northwestern area in hilly and mountainous regions of Slovenia as well as on the plains of Slovenia and Croatia. Sporadic cases have, however, also been reported from along the Adriatic coast of Croatia and in Bosnia, as well as other areas.⁴

An effective and well-tolerated vaccine is available in Europe (FSME-Immun Inject; Immuno, Vienna).^{5,6}

Crimean-Congo Hemorrhagic fever (CCHF). CCHF virus is a member of the Nairovirus genus of the bunyavirus family and is transmitted by infected

Hyalomma species ticks or by direct contact with animal tissues. Tick-infested migrating birds appear to play an important role in the geographic dissemination of the virus. Nosocomial transmission may also occur.⁷

Asymptomatic infection is uncommon. After an incubation of 2-5 days (tick transmitted) or 5-9 days (nosocomial transmission), the onset of symptoms is abrupt, with chills and high fever, severe headache and low back pain, epigastric and joint pain, and flushing of the face and chest with palatal hyperemia and petechiae. Bradycardia may occur. Leukopenia is present and thrombocytopenia are common.

The illness may have a biphasic character. At 3-5 days after onset, capillary leak and disseminated intravascular coagulation with hemorrhagic manifestations may occur. Severe hepatocellular dysfunction may also be evident. The death rate varies widely. CCHF virus is susceptible in vitro to ribavirin.⁸

Hantavirus Infection: Epidemic Nephropathia and Hemorrhagic Fever with Renal Syndrome (HFRS). Hantavirus infection poses a clear risk; British soldiers developed HFRS in Bosnia in 1995.⁹ Hantaviruses causing human disease in the Balkans include Hantaan, Dobrava/Belgrade, and Puumula. All may cause HFRS; Puumula is more frequently associated with epidemic nephropathia than the others.¹⁰⁻¹⁶ The normal vertebrate hosts and sources of human infection are arvicolid and murid rodents with transmission occurring via their aerosolized excrement.

Hantavirus. Infections occur in both urban and rural areas throughout the Balkans, both sporadically and in epidemic fashion, primarily from May to November.¹⁷ An epidemic of HFRS in 1986 caused more than 150 people to be hospitalized and 11 to die.¹⁸ An epidemic occurred in 1989 with 226 cases serologically documented. The fatality rate was 6.6%.

The usual incubation period is 12-21 days. Infection is commonly asymptomatic or associated with only mild self-limited symptoms, especially in those infected with Puumula virus. Puumula is also more likely to cause nephropathia epidemica, characterized by early renal involvement, often with transient renal insufficiency. Some individuals, usually among those infected with Hantaan or Belgrade virus, however, develop severe disease characterized, after a mild prodromal stage, by abrupt onset of chills, high fever, lethargy, headache and ocular pain, nausea and vomiting, backache, and flushing of the face, neck, and shoulders. Leukocytosis is commonly present at this stage.

The onset of severe signs and symptoms coincides with clearance of virus from the blood at the time of the appearance of antibody, suggesting that they may be the result of immune complex deposition. At 5-7 days after

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onset, patients may become hypotensive as the result of the development of a diffuse capillary leak with ensuing oliguria. Hypertension is, however, common during both the oliguric and diuretic phases.

Thrombocytopenia occurs and the development of petechiae is common.

Clinically significant hemorrhagic manifestations, resulting from disseminated intravascular coagulopathy and endothelial injury, however, occur in only 10% of severe cases. Death may ensue. Survivors generally improve rapidly, with diuresis being a harbinger of recovery.^{19,20}

Early (within 5 days of onset) treatment of hantavirus infection in China with ribavirin appears to improve outcome, but its role in the treatment of infection with the virus endemic in the Balkans is unclear.

Sandfly fever. Among the other viral infections that may be encountered in this area is sandfly fever. Approximately 51.4% of healthy residents of the Adriatic island of Mljet had neutralizing antibody to the Naples strain of the sandfly fever virus.²¹ This phlebovirus usually causes asymptomatic infection or a mild self-limited illness, although it may cause aseptic meningitis.

West Nile fever. Infection with West Nile fever virus, a member of the Japanese B encephalitis virus complex of flaviviruses, is transmitted by *Culex* mosquitoes; its usual vertebrate hosts are wild birds.² West Nile fever has been documented in Albania. After an incubation period of 1-6 days, a febrile illness similar to that of mild dengue may occur; rash emerges toward the end of the febrile period in approximately 50% of patients. Neurological manifestations, including meningitis and meningoencephalitis, usually occur predominantly in the elderly. However, meningitis occurred at all ages in a large outbreak in Romania in 1996.

Other Viral Infections

Hepatitis viruses. Hepatitis virus infections of all sorts have a high prevalence in parts of the Balkans. Among a group of 500 pregnant Albanian refugees, HbsAg was detected in 13.4%, anti-HBc in 70.8%, anti-HAV in 96.2%, anti-HDV in 0.4%, and anti-HEV in 2%.²² A separate study of Albanian refugees found the prevalence of HbsAg to be 19% and anti-HAV to be 96%.²³ In contrast, however, a serosurvey of 2142 apparently healthy individuals in Slavonski Brod, Croatia, found that only 1.8% had detectable HbsAg.²⁴

Among 203 Croatian patients with chronic HCV infection, 61.1% were infected with genotype 1b, 26.1% with 3a, and 10.8% with 1a.²⁵ Antibody to hepatitis E was detected in 4.9% of 350 southern Albanian refugees.²⁶ HGV RNA was detected in seven (11.9%)

and HGV E2 antibody in 20 (33.9%) of 59 Slovenian hemodialysis patients.²⁸

HIV. The prevalence of HIV infection among 551 injection drug users from the area of Belgrade tested between 1987 and 1992 was 43.7%, but HIV prevalence was only 4.6% among individuals from other urban areas.²⁸ Similarly, a report published in 1990 indicated that nearly 50% of injection drug users imprisoned in Belgrade were HIV infected.²⁹ It is of interest that the protective CCR5D32 homozygous mutation was present in only two (0.5%) of 385 nonHIV-infected individuals in Slovenia.³⁰

Childhood viruses. The lack of vaccination against childhood diseases in many areas will lead to a resurgence of these diseases. It was reported in 1992 that 41.3% of recent Albanian emigres to Italy lacked antibody to poliovirus type 3 and that 21% lack antibody to poliovirus type 1.³¹ An outbreak of wild type 1 poliovirus infection, which began in Albania in 1996, subsequently spread to Yugoslavia and Greece.³² Of 145 affected patients who were identified, 87 had persisting paralysis and 16 died.

In 1976, an outbreak of rubella in Croatia affected 2746 individuals, 79.1% of whom were male.³³ In April 1996, four British military helicopter ground crew deployed to Bosnia-Herzegovina developed rubella.³⁴

Rabies. Rabies is endemic in the Balkans. Dog bites were reported by 62 British soldiers during the first six months of their peacekeeping mission in Bosnia.³⁵

Bacterial infections. Anthrax and brucellosis remain potential hazards and outbreaks of tularemia have been reported).^{4,36-38} Typhoid fever occurs, sometimes in epidemic form.³⁹

Tuberculosis is highly prevalent; 0.55% of Yugoslav immigrants to Switzerland between 1988 and 1990 had radiographic evidence of pulmonary tuberculosis.^{40,41} Leprosy is reported in the Balkans.^{42,43}

An outbreak of infection due to *Vibrio cholerae* 01 El Tor occurred in Albania (and Italy) in 1994. All isolated strains were resistant to tetracycline, streptomycin, spectinomycin, trimethoprim, and sulfathiazole.⁴⁴ As of press time, the Balkans are not on the USPHS list of "cholera-infected countries."

The conditions of crowding, poverty, and inadequate hygiene provide a circumstance ideal for lice infestations and, therefore, the likelihood of infection with the agent of trench fever, *Bartonella quintana*.

Spirochetal infections. Spirochetal infections that may be encountered include syphilis, leptospirosis, and Lyme borreliosis disease.⁴⁵ Lyme disease is highly endemic in Slovenia and is undoubtedly present elsewhere in the Balkans as well.⁴⁶ *Borrelia* spp. were isolated from the midgut of 69 (10%) of 363 ticks (*I. ricinus*), including 26 (13%) of 206 nymphal stage organ-

isms in Slovenia.⁴⁷ Of 60 isolates that were speciated using PCR, 53% were *Borrelia afzelii*, 33% were *Borrelia garinii*, and 8% were *B. burgdorferii* sensu stricto. In 1994, *B. burgdorferii* sensu lato was isolated from 231 patients with erythema migrans at the University Medical Center in Ljubljana, Slovenia. Observations suggest that early infection might be milder in Slovenia than in the United States.^{49,50}

Rickettsial infections. Rickettsial infections represent potential hazards in this region. A serosurvey involving 231 individuals in northwestern Bosnia-Herzegovina found that 61.5% had complement-fixing antibody to *R. typhi*, 4.3% to *Rickettsia prowazekii*, 1.7% to *R. conorii*, and 19.0% to *C. burnetii*. Testing by an indirect immunofluorescent assay found somewhat different results, with 37.7% being positive for *R. typhi*, 1.6% for *R. conorii*, and 22.4% for *C. burnetii*.⁵⁰ A survey of residents of coastal Croatia found that 4.2-5.0% had antibody to *R. conorii*.⁵¹

Brill-Zinsser disease (recrudescing typhus) may still be seen in individuals from areas with previously active foci of infection and louse-borne typhus was widespread in Bosnia during, and for at least a decade after, the second World War. In addition, more than 57 outbreaks were documented to have occurred between 1957 and 1980.⁴ Murine typhus may also be encountered; 63-68% of inhabitants of the northern Dalmatian islands had detectable antibody to *R. typhi*.⁵²

Rickettsia akari, the agent of rickettsialpox, has been recovered from a patient in Croatia.⁵³

Human granulocytic ehrlichiosis is present in Slovenia.^{54,55}

Mycoses. Seventeen patients with rhinosporidiosis were identified in northern Serbia over a two-year period; all had bathed in the same stagnant lake.⁵⁶

Parasitic infections. Intestinal infestations with *Enterobias vermicularis*, *Ascaris lumbricoides*, *Trichuris trichiura* (as well as *Giardia lamblia*) are highly prevalent among school-age children in many areas of Serbia.⁵⁷ Stool examination of 5981 school children in central Serbia from 1984-1993 found the following prevalences: *Entamoeba histolytica*, 0.02%; *G. lamblia*, 6.8%; *Hymenolepis nana*, 0.06%; *E. vermicularis*, 14.7%; *A. lumbricoides*, 3.3%; and *T. trichura*, 1.8%.⁵⁸

Yugoslavia, along with Greece, Spain, and northern Portugal, has the highest rates of echinococcosis due to *Echinococcus granulosus* in Europe. The areas with the highest prevalence within Yugoslavia are Dalmatia and Montenegro.⁵⁹ *Taenia saginata* and *T. solium* infection, including cysticercosis, may occur. Approximately 4.7% of swine in one area had serological evidence of *Trichinella spiralis* infection and human trichinosis was

seen.⁶⁰ Another study found that 22% of grazing pigs and 1.67% of pigs raised on small farms were infected.⁶¹ Hookworm has been endemic in Yugoslavia.

Heterophyiasis (dwarf fluke infection), which results from ingesting raw or undercooked freshwater cyprinoid or salmonoid fish (salted and pickled fish may also be risky) containing metacercariae, is seen.⁴

The seroprevalence of toxoplasmosis in female residents of Belgrade ages 15-45 years was reported in 1998 to be 77%.⁶² The incidence of congenital toxoplasmosis in Slovenia was reported in 1992 to be three per 1000 live births.⁶³

Leishmaniasis, both cutaneous and visceral, may be acquired in Yugoslavia.^{65,66} Cutaneous leishmaniasis is said to be currently rare in continental areas where it had previously been endemic but is still a risk in some coastal regions and on islands in the Adriatic. More than 200 cases of visceral leishmaniasis were reported from 1940-1980, but this infection is now only infrequently identified.⁴

The first human case of babesiosis in Europe was reported from Yugoslavia in 1957.⁶⁶ Most European cases are due to *Babesia divergens*, a cattle pathogen. The infection is transmitted by *I. ricinus*.

Envenomation. Venomous snake bites pose a danger in the Balkans. Physicians at the Clinical Hospital in Split, Croatia, encountered 389 victims bitten by the horned viper between 1980 and 1996.⁶⁷

Prevention of Infectious Illness in the Balkans

All childhood vaccines should be up to date; fully vaccinated adults should receive a polio vaccine booster prior to travel. Measles and diphtheria-tetanus toxoid boosters may also be indicated. Consideration should be given to receiving vaccination against tick-borne encephalitis virus (not available in the United States), as should rabies vaccination. Typhoid vaccination is indicated and hepatitis A vaccination are indicated; hepatitis B vaccination is desirable. Influenza vaccination should be used in season. Those working in refugee camps should consider meningococcal vaccination, as well as pneumococcal vaccination.

Food should be well cooked. Precautions should be taken with drinking water. Protection against insect and arthropod bites is important. Long-sleeved shirts and long pants should be worn, DEET-containing insect repellent should be used, and permethrin should be applied to clothing. Inspection for the presence of ticks should be performed regularly. This is of great importance given the large number of potentially tick-borne diseases that may be encountered such as TBE, Lyme disease, human granulocytic ehrlichiosis, rickettsial

infections, babesiosis, and tularemia. The Lyme disease vaccine available in the United States is not effective in preventing infection by the *Borrelia* species most encountered in Europe.

An antibiotic, such as a fluoroquinolone, should be carried, along with loperamide, for empiric treatment of diarrheal illness. After return, medical evaluation, including PPD testing, may be indicated. ❖

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Deadly Legionella Outbreak at a Flower Show in The Netherlands

SPECIAL REPORT

Source: Legionellosis outbreak at a flower show. ProMED-mail; April 5, 1999; <http://www.healthnet.org/programs/program.html>.

This report describes an outbreak of at least 231 cases of Legionnaire's disease following a flower show in Bovenkarspel, The Netherlands, which attracted up to 12,000 people per day during the last week of February. Twenty-one people have died to date. Preliminary studies suggest that the organism was spread by a warm-water whirlpool spa in the consumer products show, which was held concurrently with the flower show, and which attracted another 80,000 people. A water sample from the spa was positive for *Legionella* by PCR assay, although cultures were negative.

Epidemiological studies of a cohort of people who attended the exhibit, as well as all 1500 employees, are ongoing. Since this outbreak, *Legionella* has been isolated in a second spa in The Netherlands, prompting notification of the 40 or more people who had recently used the jet massage equipment.

■ COMMENT BY CAROL A. KEMPER, MD

A similar outbreak of *Legionella anisa* infection occurred in San Jose, Cali., in 1988 among 34 of 56 people attending a conference in a local hotel.¹ *L. anisa* was isolated from a decorative fountain in the hotel lobby where a luncheon had been set up for the conference attendees. In contrast to the outbreak described above, most of the victims experienced an acute febrile respiratory illness with fairly rapid resolution of symptoms, usually within five days of onset—otherwise known as Pontiac fever. The attack rate was high (82%) and rapid in onset (within 56 hours). Serological studies of hotel employees found positive antibody titers to *L. anisa* in 42%.

Investigations of the San Jose outbreak revealed no set schedule for fountain maintenance, which used recirculated water with no disinfecting chemicals. The fountain was cleaned by mopping the tile floor with municipal hot water and running it through the jets, which permitted persistence of the organism. In contrast to the ongoing outbreak in The Netherlands, *L. anisa* infection does not progress to pneumonia and has not been associated with death.

Legionella infection has been transmitted in other settings during demonstrations of new hot tub and spa equipment when chlorination is often disregarded because the equipment is being used solely for demonstration purposes. The deadly outbreak in The Netherlands should serve as a severe reminder that disinfection protocols are necessary for all spas, fountains, and misting devices used in public places. ❖

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Hansen's Disease is Still With U.S.

ABSTRACT & COMMENTARY

Synopsis: *Hansen's disease continues to be transmitted at an unabated rate along the Gulf coast of Texas.*

Source: Taylor JP, et al. A continuing focus of Hansen's disease in Texas. *Am J Trop Med Hyg* 1999;60:449-452.

Taylor and colleagues at the Texas Department of Health reviewed all 810 cases of Hansen's disease reported to them for the years 1973 through 1997. During this time, the average number of cases reported annually ranged from 18-54, with 26-42 cases reported annually during the most recent period of 1993 through 1997. The average annual incidence rates ranged from 1.9-2.4 cases per million population. The areas of highest incidence were clustered along the Gulf coast, with one county (Goliad) having an average annual incidence rate of 96.1 cases per million. Seventy-seven percent of patients were white (51% Hispanic), 19% Asian, and 3.0% were African-American; 63% were male. Relative to the general population of the state, Asians and Hispanics were overrepresented among the cases and African-Americans were underrepresented.

The median age at onset of disease was 44 years (range, 2-87 years). Fifty-three percent were born in the United States, with two-thirds of those born in Texas. Approximately one-fourth each were born in Mexico and other countries—most commonly Vietnam, India, Phillipines, and Cambodia. Of the 56% who experienced the onset of their disease after arrival in the United States, 23% did not become ill until 10 years or more after migration. The diagnosis was made within one year of onset of illness in 56%. Three-fourths had multibacil-

lary disease; loss of sensation was noted at diagnosis in 46% and deformity in 10%. A potential human source of infection was identified for 23%.

■ COMMENT BY STAN DERESINSKI, MD

I once went to a Willie Nelson/Jerry Jeff Walker concert at Stanford. The sight of thousands of people in Palo Alto wearing cowboy boots and hats and waving stuffed armadillos was entrancingly bizarre. But this report has caused the intrusion of this memory into my consciousness. More than two decades ago, 4.7% of armadillos caught in the Gulf coast area were found to be leprosy.¹ The same year, leprosy was reported in Texas armadillo handlers and is also believed to occur in the adjacent state of Louisiana.^{2,3} However, while transmission from armadillos remains a possibility in some cases, this source cannot account for more than a tiny fraction of cases. Although leprosy has been assumed to be the result of person-to-person contact, the mechanism of transmission remains uncertain. The transmission by inhalation of organism from environmental sources remains a theoretical possibility.

There were 3.7 million registered cases of Hansen's disease in the world in 1990, with a planetary prevalence of 7.10 cases per 10,000 population.⁴ In 1998, the regions with the highest detection rates of new cases of Hansen's disease were some Pacific islands, southeastern and western Africa, and southeast Asia.⁵ Sixteen countries accounted for 92% of registered cases: Bangladesh, Brazil, Cambodia, the Democratic Republic of Congo, Ethiopia, Guinea, India, Indonesia, Madagascar, Mozambique, Myanmar, Nepal, Niger, Nigeria, Phillipines, and Sudan.⁶

Taylor et al point out that the incidence of Hansen's disease in Texas has not changed significantly over the last six decades, although the proportion of cases born outside either the United States or Mexico has increased to 23.1% from less than 1.0%. In contrast to other states, such as Hawaii and Florida, the number of indigenous cases has not decreased in Texas, which now reports more than 60% of the indigenous cases in the United States, but only 25% of the total cases.⁷ The annual number of reports of Hansen's disease in the years 1991 through 1995 ranged from 136-187.⁸

It is ironic that there has been no significant decrease in the number of autochthonously acquired Hansen's disease cases in Texas over the decades at the same time

that the number of cases worldwide is decreasing in response to the eradication activities of the World Health Organization. This plan is based primarily upon enhanced case finding and administration of appropriate therapy.⁶ Maybe they can try it in Texas. ♦

References

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CME Questions

30. Which of the following is *incorrect* about Pontiac fever?

- a. It is caused by at least four different species of Legionella, including *L. anisa*.
- b. It results in a self-limited febrile respiratory illness.
- c. It is characterized by severe pulmonary infiltrates, which may be fatal.
- d. It causes rapid onset of symptoms.

31. Which of the following is *not* transmitted by a tick?

- a. Tick-borne encephalitis
- b. Crimean-Congo Hemorrhagic fever
- c. Hantavirus
- d. Babesiosis
- e. Tularemia

32. Which of the following is *correct*?

- a. There has been no transmission of Hansen's disease within the United States since 1936.
- b. Most cases of Hansen's disease in Texas are the result of eating armadillos that have been killed on the highway.
- c. The regions of the world with the highest incidence of new cases of Hansen's disease include some Pacific islands.
- d. Approximately 95% of patients with Hansen's disease in Texas are of Hispanic ethnicity.

In Future Issues:

Surviving Ebola Virus

Risk of HIV-related Illness and Nadir CD4 Counts

Source: Miller V, et al. *Ann Intern Med* 1999;7:570-577.

Using surveillance data collected during a large-scale, prospective observational study (EuroSIDA), Miller and colleagues assessed the evolving risk of opportunistic infection and disease progression in patients with advanced HIV infection. Data on a total of 7333 subjects from 52 clinics across Europe who either had persistently low CD4 cell counts ($< 50/\text{mm}^3$) or CD4 counts greater than $200/\text{mm}^3$ were compared. The latter group was divided into four subgroups: those with a history of a nadir CD4 cell count less than $50/\text{mm}^3$, between $50-99/\text{mm}^3$, $100-149/\text{mm}^3$, or greater than $150/\text{mm}^3$. Viral load data were not available on sufficient numbers of patients for analysis. Patients were followed until they developed an AIDS defining event or death; the data were censored once an individual's CD4 count fell below 200 or rose above $50/\text{mm}^3$. The median duration of follow-up for patients with CD4 counts greater than $200/\text{mm}^3$ was 16 months vs. six months for those with CD4 counts less than $50/\text{mm}^3$.

The overall rate of disease progression was about 20 times higher for patients with CD4 counts persistently below $50/\text{mm}^3$ compared with those with CD4 cells who were now greater than $200/\text{mm}^3$. The event incidence rate was 72.9 per 100 patient-years in patients with fewer than 50 CD4 cells vs. 3.9 per 100 patient-years in patients with CD4 counts presently greater than $200/\text{mm}^3$.

Even for those patients who had now reached higher CD4 counts, a previously low nadir CD4 count defined a modestly increased risk of disease and death. For

example, the event incidence rate for patients whose CD4 counts were now greater than $200/\text{mm}^3$, but which had been below $50/\text{mm}^3$ in the past, was 5.9 per 100 patient-years compared with 8.1 for those with nadir counts of $50-99/\text{mm}^3$ and 3.7 for those whose counts had never fallen below $150/\text{mm}^3$. Older age was also significantly associated with disease progression.

Lower nadir CD4 cell counts were also associated with more rapid disease progression, varying from as little as a medium of 2-3 months for patients with a history of CD4 cell counts less than $100/\text{mm}^3$ compared with 15 months for those whose CD4 count had always been greater than $150/\text{mm}^3$. In contrast to what we see in the United States, the most frequent illnesses, in descending order, were esophageal candidiasis (20%), *Kaposi sarcoma* (13%), *Pneumocystis carinii* pneumonia (13%), and pulmonary tuberculosis (8%). Patients who have previously had extremely low CD4 cell counts in the past remain at increased risk for opportunistic infection and disease progression, although this risk is substantially smaller than those with persistently low CD4 cell counts below $50/\text{mm}^3$. ■

VRE for the Birds?

Source: Schwalbe RS, et al. *Lancet* 1999;353:722.

While the emergence of vancomycin-resistant strains of enterococcus (VRE) as the result of selective pressure in hospitals is of significant concern, evidence suggests that resistant enterococci are being introduced into the human population from a number of potential sources. Animal feed is believed to be a significant factor in the transmission of resistant enterococci from animals to humans in European countries. Schwalbe and colleagues suc-

cessfully isolated numerous colonies of *E. faecium* from a bag of chicken feed commercially prepared in the United States. All of the colonies had a similar electrophoretic pattern and were resistant to ampicillin, gentamicin, streptomycin, and vancomycin, but not quinupristine/ dalbapristine. Although the isolation of enterococcus from chicken feed is apparently not unusual, the origins of this highly resistant VRE remain uncertain but represent a clear transmission risk for humans. ■

Amantadine and Aspiration Pneumonia

Source: Nakagawa T, et al. *Lancet* 1999;353:1157.

This fascinating study from Japan assessed the frequency of pneumonia in 163 elderly stroke victims randomized to receive amantadine 100 mg daily or no intervention. Stroke victims, especially those with basal ganglia impairment, often have swallowing disorders and are at increased risk for aspiration pneumonia. Nakagawa and colleagues wondered whether amantadine, which facilitates the release of dopamine from dopaminergic nerve terminals, may improve the swallow reflex in patients with a history of cerebral infarction.

Eligible subjects were ambulatory and immunocompetent. During a follow-up period of up to three years, patients receiving amantadine were at significantly less risk for pneumonia. Only five of 83 patients (6%) receiving amantadine vs. 22 of 80 (28%) receiving no active therapy developed pneumonia ($P = 0.0001$). Amantadine deserves further attention in high-risk populations with selective swallowing disorders at risk for aspiration. ■