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Ventilator-Associated Pneumonia: Translating Risk Assessment into Prevention

ABSTRACT & COMMENTARY

Source: Cook DJ, et al. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. *Ann Intern Med* 1998; 129:433-440.

Cook and colleagues prospectively followed 1014 patients who underwent mechanical ventilation for at least 48 hours in a multicenter study of nosocomial pneumonia in intensive care units in Canada and France. They used four different definitions of pneumonia, including a blinded adjudication panel, modified CDC criteria, a Clinical Pulmonary Infection score, and the results of bronchoalveolar lavage or protected specimen brush cultures. A large number of independent variables were recorded; these included demographics, underlying diagnoses, several illness severity measures (e.g., Apache II score, Glasgow coma score), feeding method, and drug exposures. Variables associated with pneumonia on univariate analysis were entered into a multivariate analysis, as well as a Cox hazard model, in order to assess the influence of independent variables over time.

Of the 1014 patients, 17.5% developed pneumonia; the overall incidence was 14.8/1000 patient days. The daily risk of pneumonia peaked on day 5 (3.3% per day) but decreased rapidly thereafter, to a risk of 1.3% per day by day 15. The majority of independent predictors of pneumonia were related to underlying illness, including burns, trauma, central nervous system disease, respiratory disease, and cardiac disease. Witnessed aspiration (risk ratio 2.3, CI 1.1-4.7) and receipt of paralytic agents (RR 1.6, CI 1.03-2.4). Receipt of antibiotics had a protective effect (RR 0.37, CI 0.27-0.51), which however, declined with time in the ICU; a significant protective effect was no longer demonstrable by day 15. The risk factors for pneumonia were the same no matter which of the four diagnostic criteria were used.

COMMENT BY ROBERT MUDER, MD

This study of ventilator-associated pneumonia is notable for its

INSIDE

size, its prospective, multicenter design, the complexity of the data base, and the rigor of the statistical analysis. Its results are likely to be generalizable to critical care units in other large tertiary care centers. This study was conducted concurrently with a randomized trial of sucralfate vs. ranitidine for prophyaxis of gastrointestinal bleeding (which, incidently, found no difference in pneumonia between the treatment groups).

Although this study sheds considerable light on the complex interrelationships between risk factors for nosocomial pneumonia in the ICU, it is less clear how this data can be used to decrease the risk of pneumonia. The greatest risk is conferred by the patient's underlying condition—this cannot, of course, be modified. The potentially modifiable risk factors are aspiration, exposure to paralytic agents, and exposure to antibiotics.

It is well known that aspiration increases the risk of pneumonia in virtually every setting; measures to decrease the risk of aspiration are clearly warranted. However, it is not clear how this should be accomplished. The study found no relationship between nasoenteral alimentation and pneumonia, for example. Indeed, the existing literature on this relationship is conflicting. The relationship between pneumonia and paralytic agents is a bit puzzling; paralytic agents predispose to pneumonia by inhibiting cough reflex and preventing effective swallowing. However, it is not clear how this would adversely affect a patient who had already been intubated, in whom effective coughing was prevented by the endotracheal tube. Cook et al did not specify which paralytic agents were used, but some agents could have adverse effects on gastrointestinal motility, facilitating reflux of gastric contents into the upper aerodigestive tract.

Cook et al found a protective effect of antibiotic exposure, and this was most pronounced during the first ten days of ICU stay. The most likely explanation for the waning of the protective effect over time is that the risk of pneumonia itself decreased rapidly after day 5. Patients received a wide variety of antibiotics, and many received multiple agents. Cephalosporins were given most often (63% of patients). Some comparative trials (using a variety of regimens) have shown that prophylactic antibiotics reduce the incidence of pneumonia in ICU patients,[1,2] while others have not.[3] Not surprisingly, use of prophylactic antibiotics may increase the risk of colonization by multiresistant organisms. Thus, the precise role of antibiotic prophylaxis in this setting is uncertain. There is a great need for well-designed clinical trials to assess the efficacy of antibiotic prophylaxis in the ICU and to determine the "best" regimen for prevention of pneumonia. Any study should also carefully assess the effect of prophylaxis on carriage of and infection with multiresistant organisms in both pulmonary and extra-pulmonary sites. ❖

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Persistent Babesial Parasitemia

ABSTRACT & COMMENTARY

Synopsis: *Untreated, asymptomatic babesial infection may persist for many months. Treatment with clindamycin and quinine reduces the duration of parasitemia, but infections can still recrudesce.*

Source: Krause PJ, et al. Persistent parasitemia after acute babesiosis. *N Engl J Med* 1998;339:160-165.

Krause and associates performed a prospective study from 1991 to 1996 to detect seroconversion and illness among the residents of communities in

southeastern Connecticut and Block Island, RI. Forty-six babesia-infected subjects were identified and were monitored every three months for up to 27 months by thin blood smears, polymerase chain reaction (PCR) assays, serology, and questionnaires.

Approximately 25% of infections were detected through a serologic survey, in which the subjects were minimally symptomatic and were not treated. Another 25% of infections were detected in a survey of patients already diagnosed with Lyme disease. These patients did not receive specific antibabesial therapy because their symptoms had improved with treatment for Lyme disease. The remaining 50% of the subjects had symptoms of acute babesiosis and were treated with clindamycin 600 mg and quinine 650 mg orally every eight hours for 1-2 weeks. Almost half of these treated subjects developed drug-related side effects from therapy.

Babesia parasites were initially detectable by microscopy in all treated subjects and two of the untreated subjects, but no parasites could be found one week after the onset of illness. Babesial DNA was detectable for a mean of 16 days in the subjects treated with clindamycin and quinine, compared to 82 days in the untreated subjects. Serology correlated initially with babesial DNA detection but remained positive longer than did babesial DNA. Serology correlated with babesial DNA detection initially but remained positive longer than babesial DNA.

Sixteen of the 46 patients in the study appeared to be coinfected with the Lyme spirochete, and only two received antibabesial therapy. Comparisons of babesial DNA persistence did not show an increase in the subjects coinfected with Lyme disease. However, serum obtained from one subject reacted against the Lyme spirochete as well as the agent of human granulocytic ehrlichiosis; babesial DNA was detectable in this case for 208 days.

Among the subjects who did not receive specific antibabesial treatment, the subjects in whom babesial DNA was detectable for three months or more had symptoms of babesiosis for a mean of 114 days. In the subjects in whom babesial DNA was undetectable at three months, babesial symptoms were only present for a mean of 15 days.

Interestingly, one subject had recrudescent disease after two years. He was initially asymptomatic, but babesial DNA was detected during the 5th and 17th months after microscopic detection of parasites. He then had symptoms of babesiosis, with 3% parasitemia, and responded to a one-week course of clindamycin and quinine. At that time, he was diagnosed with a primary intracapsular renal tumor. Six weeks later (27 months after initial parasitemia), he was found to have 1% parasitemia, and therapy was administered for yet another week with resolution of parasitemia.

COMMENT BY LIN H. CHEN, MD

Babesiosis is a tick-transmitted zoonosis caused by one of several intraerythrocytic protozoa in the genus *Babesia*. The organisms usually associated with human disease are *B. microti* (rodents), *B. bovis*, *B. divergens*, *B. bigemina* (cattle), and the recently identified, transfusion-acquired WA-1 strain. (See also Deresinski, S. *Infect Dis Alert* 1997;16(18):141-142.) Similar to Lyme disease and human granulocyte ehrlichiosis, the organisms are transmitted by *Ixodes dammini* in the northeastern United States. The most common host for *I. dammini* is the white-footed mouse, *Peromyscus leucopus*. The vector for WA-1 is felt to most likely be *Ixodes pacificus*,[1] and the vector for *B. divergens*, the most commonly involved pathogen in Europe, is thought to be *Ixodes ricinus*.[2] The nymphal form of the tick is the usual vector, and they are most active from May to July.

The majority of babesiosis cases in humans have occurred in the northeastern United States, especially coastal Massachusetts, Connecticut, Rhode Island, and New York.[4,8] Sporadic cases have been reported from other states, including Wisconsin, Missouri, Washington, and California.[5-7] Rare cases have also been reported from Europe, including France, Great Britain, Ireland, and Yugoslavia (the very first human case in 1957),[2] and one case has been reported from Taiwan.[10]

The clinical manifestations of babesiosis range from an asymptomatic course to a malaria-like illness with hemolysis, fever, and hemoglobinuria.[1] Seroepidemiologic studies in the United States have shown most infections to be self-limited and often subclinical.[3,9] In contrast, human infections reported from Europe have occurred mainly in asplenic patients, resulting in a fulminant course and a mortality rate higher than 50%.[1,2]

The diagnosis of babesiosis can be made by detection of parasites in blood smears or quantitative buffy coat methodology, by an indirect immunofluorescent assay for serum antibodies, or by detection of circulating babesia DNA using the PCR technique. Treatment with clindamycin and quinine is usually reserved for the patients with significant symptoms, the elderly, asplenic individuals, and immunocompromised patients.[1,4] Severe, fulminant cases are treated with exchange transfusions.[1,2]

This study by Krause et al makes several important observations. First of all, babesial DNA determination by PCR appeared to be a more sensitive test for detection of infection than microscopic identification of the parasite on blood smears. DNA also persisted longer and correlated with symptoms of babesiosis. Second, treatment with clindamycin and quinine shortened the duration of babesial DNA detection; however, almost half the treated subjects developed side effects related

to antimicrobial therapy. Third, coinfection with *Borrelia burgdorferi* did not appear to prolong the duration of babesial DNA detection, although coinfection with *B. burgdorferi* and the agent of human granulocyte ehrlichiosis may have prolonged the period of babesial DNA circulation in one subject. Finally, recrudescent disease appeared to be a possibility more than two years after initial infection, as described in one patient.

For the travel medicine practitioner, the following inferences can be made: 1) Babesiosis, often a mild, self-limiting infection, may become more persistent than previously believed; 2) Perhaps patients diagnosed with babesiosis should be treated more aggressively (e.g., even those with only mild symptoms); 3) For those patients with a history of a tick bite and/or patients diagnosed with Lyme disease or human granulocyte ehrlichiosis, one should consider testing for babesiosis to assess whether additional antibabesial therapy might also be appropriate; 4) The asplenic patient poses a greater risk for severe babesiosis and must be vigilant both during and after travel in endemic areas. *(Dr. Chen is Clinical Instructor, Harvard Medical School and Travel/Tropical Medicine Clinic, Lahey Hitchcock Medical Center.)* ❖

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Summaries from the 38th Interscience Conference on Antimicrobial Agents and Chemotherapy: Part II

CONFERENCE COVERAGE

Note: *The following summaries represent a selection of papers from those presented at the 38th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) held September 24-27, 1998, in San Diego, CA. It is important to recognize that many of these summaries are extracted only from the published abstracts, and it is possible that some of the material may have differed at the time of presentation. —Stan Deresinski, MD, FACP*

Viral Pathogens

Influenza

Two agents are currently available for the prophylaxis and treatment of influenza A virus infections. Consistent with previous reports, amantadine use was associated with a significantly greater incidence of CNS adverse effects than was the use of rimantidine in elderly nursing home residents. *(Abstract H-73.)*

Several new agents, active against both influenza A and B virus, are in clinical trials. Zanamivir, a selective inhibitor of the neuraminidase of both types of influenza virus, was evaluated in a placebo-controlled, randomized trial involving more than 1200 patients with acute influenza. The median time to symptom improvement was one day shorter in those receiving active drug (6 days vs 7 days in placebo recipients; P = 0.012) and was 2.7 days shorter in a subset of "at risk" patients (5.3 vs 8 days; P = 0.016). Virological studies in a subset of 40 patients demonstrated more rapid clearance of viral shedding in zanamivir recipients; emergence of resistance during therapy was not detected. *(Abstract H-67.)* Similar results were obtained in a Southern Hemisphere study. *(Abstract H-56.)*

GS4104 (Ro 64-0796) is a prodrug of GS4071,

another influenza A and B virus neuraminidase inhibitor. In a randomized placebo-controlled study of 629 U.S. patients with acute febrile respiratory illness, 374 (60%) of whom had influenza virus infection, GS4104 shortened the duration of symptoms due to influenza virus by a median of 1.4 days (2.9 vs 4.3 days; P = 0.0001). The severity of illness and incidence of secondary complications, predominantly sinusitis and bronchitis, were also reduced. *(Friday, Abstract LB-4.)* A second study performed in Canada, Europe, and China found similar results. *(Friday, Abstract LB-5.)*

Both zanamivir and GS4104 were reported to be effective in the prophylaxis of influenza virus infection. In a study of 1559 non-immunized adults, zanamivir administration was compared to placebo. Each was administered for six weeks during a period of local influenza activity. GS4104 administration was associated with a 74% protection rate against illness due to influenza. *(Friday, Abstract LB-6.)* Daily inhalation of zanamivir for four weeks was associated with an 84% reduction of febrile influenza virus infection and a 67% reduction in laboratory-confirmed influenza infection, when compared to placebo. *(Friday, Abstract LB-7.)*

The effectiveness of influenza vaccination of children attending day care centers was evaluated in a study in which hepatitis A vaccine was used as a placebo. Influenza vaccination was associated with a significant reduction in respiratory illness in household members, with the greatest effect on siblings ages 5-17 years, among whom there was a 55% reduction in respiratory illnesses and a 78% reduction in febrile respiratory illnesses. There was also a reduction in the number of school days missed, number of physician visits, and antibiotic prescriptions. *(Friday, Abstract LB-8.)*

Respiratory Syncytial Virus

In a placebo-controlled, randomized blinded study, no benefit from ribavirin administration to previously healthy infants undergoing mechanical ventilation because of RSV bronchiolitis could be demonstrated. *(Abstract H-60.)*

There is increasing recognition of the role of RSV as an important cause of respiratory infections in adults. A prospective observation of 134 adults with severe COPD or CHF over two winter seasons found that three of 12 hospitalizations were associated with RSV infection. *(Abstract H-70.)*

Herpes Viruses

HSV. Famciclovir (500 mg tid for 7 days) was equivalent, in a blinded, randomized trial, to acyclovir (800 mg 5 times daily for 7 days) in the treatment of a total of 454 patients with ophthalmic branch herpes zoster. *(Friday, Abstract LB-3.)*

Our understanding of clinical aspects of herpes simplex encephalitis is becoming increasingly complex, with the recognition of unusual presentations as well as the danger of relapse. Five (13.5%) of 37 patients with prior herpes simplex encephalitis had a total of nine apparent relapses during a median period follow-up of 8.7 years. However, HSV DNA could not be demonstrated in any of the 19 CSF samples obtained during the apparent relapse. *(Abstract H-13.)*

Recurrent neurological disease due to HSV takes a variety of forms. Retrospective analysis of 28 consecutive patients with meningomyelitis and/or radiculitis due to HSV-2 followed for at least one year found that 18 (64%) had neurological recurrence. *(Abstract H-15.)*

HSV is an important cause of Bell's palsy. Approximately one-half of 225 patients with Bell's palsy had neurological symptoms not related to the facial nerve, including blurred vision, memory loss, limb paresthesias, incoordination, and ataxia, indicative of diffuse HSV-1 neurological reactivation. The investigators conclude that Bell's palsy should be considered an "HSV reactivation polyganglionitis." *(Abstract H-17.)*

The occurrence of acyclovir-associated neurotoxicity in patients with end stage renal disease correlated with the accumulation in serum of 9-carboxymethoxymethylguanine (CMMG), the concentration of which is reduced 50% by a single hemodialysis session. *(Abstract A-83.)*

Varicella-Zoster

The evidence of the value and efficacy of varicella vaccination in susceptible individuals continues to grow. The cumulative antibody persistence rate four years after a single dose of the Merck varicella vaccine is 99.8%, and five-year follow-up indicates it provides 89.2% protection following household exposure. When varicella did occur in vaccine recipients, it was mild, with patients developing only 16-34 lesions. *(Abstract H-19.)*

Life-threatening streptococcal infections have been reported as a complication of varicella infection in children. In a population-based surveillance study, the incidence of invasive infection due to *S. pyogenes* in the month following chickenpox was 5.2/100,000 compared to 0.09/100,000 in those without chickenpox. Despite the fact that it is an uncommon complication of chickenpox, it is estimated that 15% of all invasive *S. pyogenes* infections in children could be prevented by routine VZV vaccination. *(Abstract L-95.)*

CMV

Intraoperative hypothermia is an independent risk factor for CMV infection in liver transplant recipients. *(Abstract H-102.)*

Erythroviruses

An erythrovirus (V9) with more than 14% genomic divergence from parvovirus B19 was detected in the serum of a child with aplastic anemia who had negative PCR and IgM serology for B19. Using a broadly reactive PCR for human erythroviruses, a positive result was obtained in the serum of 18 of 43 patients with either sickle cell anemia and aplastic crisis, HIV infection with chronic anemia, or acute anemia with weak B19 PCR positivity. Five of the 18 positives were due to the presence of V9, while the remainder were due to B19. The pathogenicity and taxonomic status of V9 remain to be determined. *(Friday, Abstract LB-1.)*

'Transfusion-Transmitted Virus'

Transfusion-transmitted virus (TTV) is a recently identified novel DNA virus that appears to be parenterally transmissible, but whose role as an agent of human disease remains undetermined (*Lancet* 1998;352:191, 195; *Infect Dis Alert* 1998;17:185). TTV DNA was detected in the serum of 22 (95.6%) of 23 infants born to TTV-positive mothers; in contrast, only one (2.3%) of 43 infants born to HCV-infected mothers became HCV positive. TTV DNA was detected in breast milk of 17 (73.9%) of the TTV infected mothers. However, all 17 TTV-positive infants tested in the first week of life were already infected, indicating that the high rate of vertical transmission was the result of infection during pregnancy. None of the 22 TTV infected children had biochemical evidence of hepatitis. *(Friday, Abstract LB-2.)*

Hepatitis B

Hair loss after hepatitis B vaccination has been reported. However, a case-control study failed to find evidence of a statistically significant increased risk of alopecia after HBV vaccination in children. *(Abstract H-131.)*

Rubeola

Measles inclusion body encephalitis due to vaccine strain virus occurred in a previously healthy 21-month-old infant 8.5 months after vaccination. *(Abstract H-134.)*

Tick-borne Infections

Serological screening of healthy blood donors in Westchester County, New York, found that 15.7% were seropositive for antibodies to the agent of human granulocyte ehrlichiosis and 29.7% had antibody to *Borrelia burgdorferi*. *(Abstract D-81.)*

Plasma is superior to serum as a culture source for recovery of *B. burgdorferi* in patients with early stage Lyme disease. *(Abstract D-3.)*

Antimicrobials

Antibiotic use. The yearly number of prescriptions for systemic antibiotics in the United States between 1992 and 1996 fluctuated between 266,752,000 and 291,215,000. (There were only approximately 240,000,000 Americans in the 1990 census; what is going on here?). *(Abstract O-22.)*

Adverse effects. A retrospective review of records of 5293 consecutive pediatric outpatients found that the incidence of oral antibiotic associated rash (9% overall) was highest with cefaclor (12.3% of recipients), followed by sulfonamides (8.5%), penicillins (7.4%), and other cephalosporins (2.7%). *(Abstract MN-1.)* The high rate of allergic reactions, including serum sickness, to cefaclor has been repeatedly described (*J Clin Epidemiol* 1992;45:1177). The reasons for the tremendous use of this antibiotic in the United States remain a mystery to me, given the rate of reactions and its rather poor performance against infections caused by beta-lactamase producing *Haemophilus influenzae*.

The dizziness associated with trovafloxacin administration can be significantly reduced by dosing with food or at bedtime. *(Abstract A-86.)*

Nephrotoxicity has been previously reported to occur with greater frequency when once daily aminoglycoside is administered during usual sleeping hours (12-7:30 a.m.) than during other times of the day (*Clin Pharmacol Ther* 1997;62:106-111). This occurs despite comparable peak and trough serum concentrations. A similar result was reported from a retrospective study of 65 patients. *(Abstract A-87.)*

In an attempt to evaluate the clinical relevance of antibiotic-induced endotoxin release from gram-negative bacilli, 66 patients with acute septicemic melioidosis were randomized to treatment with either imipenem or ceftazidime. Plasma endotoxin levels were significantly higher following the initial dose of ceftazidime than after imipenem ($P < 0.0005$). Furthermore, the mean time to defervescence was 124 hours in the ceftazidime group and only 77 hours in those treated with imipenem ($P = 0.01$). However, survival rates were almost identical (67.6% vs 66.3%, respectively). *(Abstract MN-34.)*

Drug interactions. Quinupristin and dalfopristin are primarily metabolized by the CYP3A4 pathway. Coadministration of this combination with nifedipine resulted in a median increase in AUC of the latter of 44%. The inhibition of nifedipine metabolism was, however, wildly variable with a range of AUC decrease of 1-169%, indicating a need for extreme caution in the use of these drugs together. *(Abstract A-77.)*

Coadministration of the leukotriene receptor antagonist, zafirlukast, does not affect the pharmacokinetics of clarithromycin or 14-OH clarithromycin. *(Abstract A-79.)*

Linezolid is a weak competitive inhibitor of human monoamine oxidase, but related adverse effects have not been observed in clinical trials to date. *(Abstract A-85.)*

Omeprazole, which is known to inhibit the NorA efflux pump, enhanced the bactericidal activity of ciprofloxacin but not norfloxacin, against *Staphylococcus aureus*. *(Abstract A-39.)* ❖

CME Questions

25. Which one of the following was found to be associated with an increased risk of nosocomial pneumonia by Cook and colleagues?

a. Nasoenteral alimentation
b. Witnessed aspiration
c. Antibiotic therapy
d. Use of ranitidine

26. Which of the following is *incorrect*?

a. Amantadine use is associated with a higher incidence of neurological side effects than is rimantidine use in elderly nursing home patients.
b. Influenza virus vaccination of children in day care is associated with a decreased incidence of respiratory illness in their household members.
c. The Merck-Sharp & Dohme varicella vaccine loses its efficacy within five years of its administration to children.
d. Children with chickenpox appear to be protected from simultaneous invasive infection due to *Streptococcus pyogenes*.

27. Which of the following is correct?

a. The etiologic agent of babesiosis is transmitted by the bite of Anopheles mosquitoes.
b. Babesiosis in the United States is most highly prevalent in the Pacific northwest.
c. Human babesial infection may be asymptomatic.
d. Relapse of babesiosis always occurs within three months of infection.

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In Future Issues:

ICAAC Summaries Part III

UPDATES

By Carol A. Kemper, MD

E. gingivalis and Periodontal Disease in AIDS

Source: Lucht E, et al. *Clin Infect Dis* 1998;27:471-473.

Severe periodontal disease is a frequent occurrence in patients with HIV infection. While earlier studies suggest that many of these patients have significant alterations in their viral and fungal but not their bacterial oral microflora, the possible role of protozoal infection in gingival disease has not been previously explored. Lucht and associates examined the prevalence of various protozoa in salivary and dental plaque specimens in 45 patients with HIV and 15 HIV-negative controls. Peridontal disease was present in 13 of 45 (29%) HIV-positive patients compared with two of 15 (13%) HIV-negative controls.

Entamoeba gingivalis was the only protozoa found in the oral cavities of HIV-infected patients, where it was present in 10 (77%) of those with peridontal disease. Only one of the HIV-negative controls and none of the HIV-positive patients, without evidence of gingivitis, had *E. gingivalis* present in plaque specimens. No other protozoa were identified, including *Cryptosporidium* or *Microsporidium* species, or *Pneumocystis carinii*.

While good dental cleaning combined with topical solutions of 10% povidone-iodine solution and chlorhexidine mouth rinses are effective for many of these cases, oral metronidazole has been useful in cases of severe acute necrotic gingival disease—which may be, in part, explained by the known susceptibility of *E. gingivalis* to metronidazole. Metronidazole is a safe and effective therapy for HIV-infected patients with severe gingival disease. ■

An Odd Case of Cat Scratch Disease?

Source: Margileth AM, Baehren DF. *Clin Infect Dis* 1998;27:353-357.

This unusual case report describes a previously healthy 35-year-old male physician who presented with two months of fatigue and left shoulder pain. He was diagnosed with an inflammatory brachioplexy and treated with dexamethasone for one week. Two weeks later, he presented with a tender pectoral mass confirmed by MRI. He was diagnosed with myositis, and treated with prednisone for nearly three weeks during which time the mass continued to expand. Follow-up CT scanning confirmed the presence of a large abscess in the upper chest wall extending into the axilla, which spontaneously ruptured a few hours later before it could be surgically drained. A culture of the drainage yielded two colonies of *Streptococcus pneumoniae*. He rapidly improved with drainage and one week of cephalosporin therapy. Skin testing for cat scratch disease using a *Bartonella henselae* antigen was positive, but IFA and EIA serological studies for *B. henselae* and *Bartonella quintana* were negative.

More than two years after his initial presentation, the patient's stored sera was retested using newer IFA tests to seven different *Bartonella* species. Only one titer was positive to *B. clarridgeiae* (Heller R, et al. *J Clin Microbiol* 1997; 35:1327-1331). Additional follow-up specimens from the patient confirmed the persistence of IgG antibody to *B. clarridgeiae* (titer, 1:256) On further questioning, the patient had three cats, originally stray, which had often scratched him. Blood samples from the cats were obtained, one of which was culture-positive for *B. clarridgeiae*.

Although the cat's infection was identified more than two years after the patient's initial presentation, Margileth and Baehren point out that infection can persist in cats for up to two years. Although the patient's frequent exposure could have resulted in infection due to any number of *Bartonella* strains, the circumstances here suggest that the physician's original infection, although highly unusual for cat scratch disease, may have been due to *B. clarridgeiae*—quite possibly the second documented human infection due to this organism. ■

I've Heard of 'Horse Pills!'

Source: Ringger NC, et al. *Equine Vet J* 1996;28:476-479.

Ringger and associates examined whether serum and CSF levels of ceftriaxone might be adequate for the treatment of bacterial meningitis in horses. Five healthy horses were administered a single IV bolus of ceftriaxone (50 mg/kg body weight). Peak serum levels of 145 microg/mL were achieved within 15 minutes, and a mean CSF concentration of 0.6 ± 0.14 microg/mL was obtained 3 hours later. The apparent volume of distribution was 331 mL/kg.

While this serum concentration compares favorably with those achieved in humans following a 2 g IV dose, the volume of distribution in horses is almost twice that of humans, and the CSF levels are lower. The other major difference being, of course, that most horses weigh about 400 kg. At this weight, a dose of 20 g. of ceftriaxone (about $600 worth) is necessary to achieve adequate equine CSF levels. ■