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Conference Summaries: ICAAC 2000, IDSA 2000, and ASTMH 2000: Part III

CONFERENCE COVERAGE

Editor's Note: *The following summaries represent a selection of papers dealing with subjects other than HIV infection from those presented at the three meetings listed below. It is important to recognize that many of these summaries are extracted only from the published abstract and it is possible that some of the material presented at the conference may have differed. The abstracts can be found online at the URLs given. The 40th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Toronto, Canada, Sept. 17-20, 2000; http://www.asmusa.org. The 38th Annual Meeting of the Infectious Diseases Society of America (IDSA), New Orleans, La, Sept. 7-10, 2000; http://www.idsociety.org. The 49th Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH), Houston, Tex, Oct. 29-Nov. 2, 2000; http://www.astmh.org. —Stan Deresinski, MD, FACP*

Fungal Infections

New Antifungals

There has been an explosion of new candidate antifungal agents. The largest group are triazoles. At least three of these are far advanced in their clinical development: voriconazole, posaconazole, and ravuconazole. Each has activity against *Aspergillus* spp. in addition to their activity against *Candida* spp.

Voriconazole and fluconazole had equal efficacy and overall tolerability in the treatment of patients (most with AIDS) with *Candida* esophagitis in a randomized trial. "Mild reversible abnormal vision" was reported by 15.5% of voriconazole recipients. The combination of voriconazole and terbinafine was synergistic against clinical isolates of *C. albicans* with reduced susceptibilty to fluconazole and voriconazole. (*ICAAC #706, #930.*)

Voriconazole was administered to 24 hematologic stem cell recipients with invasive fungal infections, most of which were caused by *Aspergillus* spp., who had failed or were intolerant to prior therapy.

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INSIDE

33% had a complete response and 8% a partial response. The most common drug toxicity was blurred vision, which occurred in 12.5%. (*IDSA #41.*)

Voriconazole was administered as salvage therapy to 51 patients with invasive aspergillosis who had failed prior therapy. Twenty patients died—seven in the first week of treatment. Among the adverse effects reported in more than 10% of patients was abnormal vision. (*ICAAC #304.*)

Posaconazole, administered orally either as capsules or in a suspension, and fluconazole appeared equally effective in a randomized trial of oropharyngeal candidiasis in HIV-infected patients. Separately, posaconazole was administered to 51 patients with proven or probable invasive fungal infection refractory (66%) or intolerant (34%) to prior therapy. Tolerance and response rates were good. Eight of 15 patients with invasive aspergillosis responded by four weeks and six of seven who had reached eight weeks of therapy responded. Of patients with invasive fusariosis, three of four responded at four weeks while one of two completing eight weeks of therapy responded. (*ICAAC #1107-1109.*)

Ravuconazole was effective in a murine model of candidiasis and was safe in phase 1 trials. (*ICAAC #838-840.*)

Table

Some Antifungal Agents Under Development

New Azoles

- Voriconazole—Pfizer
- Posaconazole (Sch-56592)—Schering-Plough
- Ravuconazole (BMS 207147)—Eisai Co. Ltd.
- Lanoconazole—Tsumura Co.
- TAK-456—Takeda Chemicals
- TAK-457 (water soluble prodrug of TAK-456)—Takeda Chemicals
- R-120578, R-102557—Sankyo Co, Ltd.
- SS-750—SS Pharmaceutical Co. Ltd.

Steryl ketone (inhibit H^+—ATPase)

- NC1175—Wayne State University

Polyene

- SPK-843—Kaken Pharmaceutical Co., Ltd,
- Nyotran (liposomal nystatin)—Aronex Pharmaceuticals, Inc.

Aazasordarin

- GW-471552, GW-4714558, GW-531920 - Glaxo-Wellcome

Saponin from cayenne pepper

- CAY-1 (USDA/NCI)

Fatty acid synthesis inhibitors (derived from Chlorophora tinctorial (Dorlin Phar, Inc)

Oxidosqualene cyclase inhibitors

- 4-pyrollidonopyridines—AstraZeneca/Microcide Pharmaceuticals

Echinocandins

- Caspofungin (Cancidas™, LMK-0991, L-743-872)—Merck & Co.
- Micafiungin (FK-463)—Fujisawa Pharmaceuticals
- Anidulafungin (V-echinocandin, LY303366)—Eli Lilly/Versicor Inc.

Fungal efflux pump inhibitor

- MC-510,011 - Microcide Pharmaceuticals

Caspofungin is an echinocandin that will be available soon in an IV formulation. It has activity against *Candida* spp., including *C. krusei* and other azole-resistant isolates, as well as *Aspergillus* spp., but not against *Cryptococcus neoformans*. The echinocandins FK463 and V-Echinocandin (LY303366) were each effective in open trials in the treatment of esophageal candidiasis in HIV-infected patients. (*ICAAC #1104, #1106.*)

Liposomal nystatin was administered to 24 patients with invasive aspergillosis (5 definite, 19 probable) who were refractory (21 pts.) or intolerant (3 pts.) to conventional amphotericin B. An objective response was

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VICE PRESIDENT/GROUP PUBLISHER: Donald R. Johnston.

EDITORIAL GROUP HEAD: Glen Harris.

MARKETING PRODUCT MANAGER: Schandale Kornegay.

ASSOCIATE MANAGING EDITOR: Robin Mason.

ASSISTANT MANAGING EDITOR: Neill Larmore.

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observed in six of 19 (31.6%) evaluable patients. One of five patients had a mycological response. Most patients required premedication because of symptoms after the first dose: 20 had chills and two had respiratory distress. Nephrotoxicity led to dose reduction in three patients and treatment was discontinued due to severe rigors and hypotension in two. (*ICAAC #1102.*)

Aspergillus, Zygomecetes/Fusarium, Scedosporium

The epidemiology of aspergillosis was the subject of a number of papers. Of 26 cases of aspergillosis in liver transplant recipients, 20 were of nosocomial origin and six were community acquired. (*ICAAC #484.*) Prolonged intubation and need for dialysis were important risk factors for the development of invasive aspergillosis in liver transplant recipients. (*ICAAC #1332, #1413.*)

Demolition of a hospital building by controlled explosion was associated with an increase in fungal spore count in outdoor air from 16 cfu/m^3 to 70 cfu/m^3 on demolition day, with a return to baseline by days 12-18. HEPA filtered areas showed no aerial spores before or after demolition and no episodes of invasive infection due to a filamentous fungus were seen in the three months following demolition. (*ICAAC #1320.*)

As in other reports, a prospective study found a significant relationship between environmental (air, surfaces) contamination with *Aspergillus* spp. in hematology wards and the incidence of nosocomially acquired invasive aspergillosis. (*ICAAC #2331.*)

Potentially pathogenic *Aspergillus* spp. were found frequently in both hospital air and water in concentrations of 2.3-9.5 CFU/m^3 of air and 1.7-7.4 CFU/L of water. Despite the use of HEPA filtration, bathroom air was the most frequently and heavily colonized indoor site. This observation suggests that the source of the *Aspergillus* in the bathroom air was bathroom water. (*ICAAC #1321.*)

The importance of these observations is indicated by a case report from the same institution. *Aspergillus fumigatus* isolated in a specimen obtained at bronchoscopy from a lymphoma patient with pulmonary aspergillosis had a genotype identical to isolates from the patients room water. Both differed from other isolates obtained contemporaneously from other sites. (*ICAAC #1322.*)

An additional source of *Aspergillus* appears to be tobacco. Ninety-eight different molds were recovered from 64% of 98 cigarettes representing 14 different brands; 75 of the 98 isolates were *Aspergillus* spp. and *A. fumigatus* isolates comprised 37% of the 98. The concentration of molds ranged from 0 to 2×10^2 CFU per gram of tobacco. However, cigarette smoke remained sterile, even when the tobacco contained *Aspergillus*. Molds were also recovered from seven brands of marijuana (the study was done in The Netherlands) in concentrations of 10^4-10^7 CFU per gram, with *Penicillium* spp. predominating. (*ICAAC #2123.*)

Three patients, only one immunocompromised, who regularly snorted crushed narcotic analgesic tablets, developed invasive paranasal sinus infection due to *A. flavus*. (*IDSA #275.*)

The presence of *Aspergillus* in air leads to frequent contamination of culture plates, as well as occasional airway colonization without infection, frequently making interpretation of positive cultures problematic. However, among a group of cardiac allograft recipients, the recovery of *A. fumigatus* from respiratory secretions had a positive predictive value (PPV) for a diagnosis of invasive aspergillosis of 98%. The PPV for recovery of any *Aspergillus* spp. from sputum was 88%. (*ICAAC #483.*)

A PCR assay to detect *Aspergillus* genome in peripheral blood had 100% sensitivity and specificity in a small number of patients. Antigen detection by ELISA (Sanofi) had a sensitivity of 50%, specificity of 97%, positive predictive value of 60%, and negative predictive value of 80%. Prophylactic administration of lipid-associated amphotericin to dialysis requiring liver transplant recipients was associated with an apparent reduced risk of invasive fungal infections relative to historical controls. (*ICAAC #1343, #1416.*)

The not infrequent failures in the treatment of invasive aspergillosis are indicative of the need for new approaches and new drugs or drug combinations. One reason for failure of antifungal therapy may be poor tissue penetration in infection with this angioinvasive fungus. In addition, reduced pH of medium markedly reduced the activity of amphotericin B, but not of fluconazole or voriconazole against *Aspergillus* spp. (*ICAAC #3938.)*

The addition of a single dose of conventional amphotericin B deoxycholate at the start of treatment with liposomal amphotericin B significantly improved the outcome, relative to treatment with liposomal amphotericin B alone, of invasive pulmonary aspergillosis in a murine model . (*ICAAC #1679.*)

In addition to some of the investigational azoles, the echinocandin caspofungin shows some evidence of promise in the treatment of these infections. The caspofungin MIC80 after 24 hours of in vitro incubation was 0.19 mcg/mL for 71 strains of *A. fumigatus*, and was also low for smaller numbers of strains of *A. flavus*, *A. niger*, and *A. terreus*. The MIC80 after 48 hours incubation rose 100-fold or more for each species except *A. niger*, for which the value remained at 0.04 mcg/mL. (*ICAAC #936.*)

Caspofungin was administered to 56 patients with invasive aspergillosis; to 45 who had failed prior therapy

and to 21 who were intolerant to such therapy. 45% received chemotherapy for hematologic malignancy and 25% had received allogeneic bone marrow transplants. The response rate among 54 evaluable patients was 41%. Among patients with infection limited to the lungs, 18 of 40 (45%) responded, while only two of 10 with disseminated infection responded. Treatment was well tolerated, with a discontinuation rate because of adverse events of 5.2%. (*ICAAC #1103.*)

Caspofungin and amphotericin B were synergistic or additive in vitro against nine of 14 *Aspergillus* spp. and four of six *Fusarium* spp. Antagonism was not observed. (*ICAAC #932.*)

Amphotericin B and itraconazole were each synergistic with caspofungin in vitro against *A. fumigatus*. (*ICAAC #931.*)

Itraconazole and terbinafine were synergistic in vitro against *A. fumigatus*, including itraconazole-resistant strains, while antagonism was found between amphotericin B and itraconazole. (*ICAAC #208.*) A cardiac allograft recipient with invasive pulmonary *A. terreus* infection was successfully treated with the combination of itraconazole and terbinafine. (*IDSA #114.*)

A prospective study at eight centers reported 20 organ transplant recipients (18 live, 2 heart) with invasive mold infections over a two-year period. The mortality rate was 74%. Eleven infections were due to *A. fumigatus* and one to *A. terreus*. Two infections were due to zygomycetes (*Mucor*, 1; *Rhizopus*, 1), three to hyalohyphomycetes (*P. boydii*, 2; *Fusarium*, 1), and one each were due to *Cladophialophora bantiani* and *Pyrenochaeta romeroi*, while one was due to an unidentified fungus. (*ICAAC #1327.*)

In vitro susceptibility testing of zygomycetes found that *Rhizopus* spp. were less susceptible to itraconazole, posaconazole, terbinafine, and amphotericin B than were *Mucor* spp. and *Absidia* spp. (*ICAAC #940.*)

Voriconazole and terbinafine were synergistic in vitro against 16 (43%) of 37 strains of zygomycetes, but no synergy was seen with the combination of amphotericin B and terbinafine. Antagonism was not observed with either combination. (*ICAAC #934.*)

Twenty-one patients at the University of Pittsburgh Medical Center with invasive *Fusarium* infection were seen over a 10-year period, with four-fifths seen in the last five years. Two-thirds were seen during summer months. All nine solid organ transplant recipients had pulmonary involvement; one also had peritonitis. Infection in seven trauma patients involved soft tissue in four and bone in three. Five of the patients died; no deaths occurred among the trauma patients. (*IDSA #283.*)

Of 10 solid organ recipients with patients with zygomycosis, six were diabetic and four had chronic renal failure. Infection involved paranasal sinuses in four and lung in four, while three had disseminated infection. Six of the 10 died with five of the deaths directly due to the infection. (*IDSA #285.*)

Seven solid organ recipients developed infection due to *Scedosporium apiospermum*, including one each with sphenoid sinusitis and pulmonary mycetoma, two with pneumonitis, and three with disseminated infection. All but the patient with sinusitis died. (*IDSA #286.*)

Twenty-seven patients with *S. apiospermum* infection and nine with *S. prolificans* infection were treated with voriconazole, most as salvage therapy. All but five trauma patients were immunocompromised. The most common sites of infection were brain (14), lungs (14), bones (9), and skin (8). At the time of the last visit, 17 of 27 (63%) patients infected with *S. apiospermum* and two of seven (28.6%) had a satisfactory outcome. (*IDSA #305.*)

Blastomycosis

Ninety-three cases of blastomycosis were identified in Missouri from 1992 to 1999, for an annual incidence of 0.2 per 100,000. The incidence in southeastern Missouri was five times as high and the incidence in Mississippi county, which lies within this region of the state, was 12 per 100,000; the annual incidence in African-Americans in that county was 43.2 per 100,000. The diagnosis was commonly delayed and the mortality rate was 22%. No environmental, occupational, or socioeconomic risk factors could be identified in a case-control study. (*ICAAC #1693.*)

Two hundred thirteen cases of blastomycosis were identified in Manitoba and northwestern Ontario over 22 years and 150 were reviewed. Two-thirds occurred in rural residents and 45% were "First Nations people." Pulmonary involvement occurred in 92%, with the lungs being the sole identified site of infection in 70%. Skin and/or soft tissue infection occurred in 23%, osteomyelitis in 13%, genitourinary infection in 2%, and CNS infection in 1%. (*IDSA #290.*)

Candida

A ratio of fluconazole dose to the MIC of 25 or more was associated with a more than 90% cure rate in patients with oropharyngeal candidiasis. (*ICAAC #1419.*)

Terbinafine, in doses of 1500 mg or 2000 mg daily, led to cure or improvement in approximately 80% of AIDS patients with oropharyngeal candidiasis who had failed fluconazole therapy. (*ICAAC #1418.*)

Coccidioidomycosis

Twenty patients with chronic coccidioidomycosis (8 with pulmonary, 5 with soft tissue, and 5 with skeletal infection) were treated with posaconazole. Fifteen completed at least 23 weeks of therapy (the duration of treatment was limited to 6 months because of long-term toxicity in animals). Their median disease severity score decreased to 40% of baseline after 11 weeks and to 22% after 24 weeks of therapy. Disease reactivation was observed in three of 10 patients in whom therapy has been discontinued. (*ICAAC #1417.*)

Liposomal amphotericin B given intravenously (IV) was superior to orally-administered fluconazole which was, in turn, superior to conventional amphotericin B (IV) in the treatment of a rabbit model of coccidioidal meningitis. In a novel result, three of eight animals treated with liposomal amphotericin B had no detectable infection in either brain or spinal cord. (*ICAAC #2120.*)

Cryptococcus

A retrospective analysis concluded that lumbar puncture was not necessary in patients with pulmonary cryptococcosis in the absence of significant systemic clinical signs and symptoms or serum cryptococcal antigen titer more than 1:32. (*ICAAC #919.*)

Reversible heteroresistance to fluconazole was detected in five of 107 (4.7%) of clinical isolates of *C. neoformans*. (*ICAAC #1706.*)

Pneumocystis

PCP occurred in 60 of 1241 (4.8%) liver transplant recipients. Prophylaxis may be indicated for those at increased risk of PCP (i.e., those given bolus steroids or antibody preparations for acute rejection). Administration of pentamidine (single IV dose followed by monthly nebulization) was well tolerated and appeared to be effective in the prevention of PCP in 20 solid organ transplant recipients intolerant to trimethoprim/sulfamethoxazole. (*ICAAC #736-737.*)

Antifungal Prophylaxis/Empiric Therapy

Patients with AML or myelodysplastic syndrome undergoing induction chemotherapy were randomized to receive either liposomal amphotericin B or fluconazole + itraconazole for prevention of fungal disease. The liposomal amphotericin B was given in a dose of 3 mg/kg IV three times weekly. Fluconazole was given in a dose of 400 mg po bid and itraconazole in a dose of 200 mg po bid. The incidence of invasive fungal disease was low and similar in both groups. Bilirubin elevation occurred more frequently in amphotericin than in azole recipients. (*ICAAC #701.*)

A systematic review of randomized trials of empirical antifungal therapy in neutropenic patients with persistent pyrexia, despite broad spectrum antibacterial therapy, concluded that azoles, lipid-based formulations of amphotericin B, and amphotericin B deoxycholate each have similar overall efficacy. The use of liposomal amphotericin B may be associated with reduced mortality due to fungal infection; standard amphotericin B deoxycholate is associated with increased risk of infusion reactions and nephrotoxicity. (*ICAAC #702.*)

A minimum trough serum concentration of itraconazole of 500 ng/mL was associated with effective prophylaxis against invasive fungal infections in neutropenic patients. (*ICAAC #700.*)

Geographic Infections

Nematodes

Twenty-one of 72 (29%) Costa Rican children with peripheral blood eosinophilia (≥ 500 cells^3) had evidence of infection with *Angiostrongylis costaricensis*, 29% had toxocariais, and only 5% had intestinal parasitosis with either *Ascaris lumbricoides* or hookworm. Six percent had both toxocariasis and angiostrongyliasis. (*ICAAC #259.*)

Twelve of a group of 23 (52%) U.S. travelers developed eosinophilic meningitis a median of 11 days (range, 6-31 days) after leaving Jamaica where they had spent spring break. Only approximately half tested had peripheral eosinophilia at presentation and only half had eosinophilic pleocytosis at that time. (*IDSA #649.*)

Three outbreaks of schistosomiasis occurred among groups of rafters (1 American, 2 Israeli) on the Omo River in Ethiopia; 25 (73%) of the 43 who underwent screening were found to be infected. Seventeen of the 25 (68%) were symptomatic, most frequently with Katayama fever, which occurred in 58% of the 25. One-third reported cough. Eosinophilia was detected in 83% and elevated serum transaminase in 33%. The diagnosis was made by CDC FAST-ELISA with species-specific immunoblot. (*ASTMH #62.*)

Of 76 consecutive patients with *S. stercoralis* identified in stool in Toronto, 96% had immigrated to Canada a mean of 78 months previously (range, 2-480 months), most commonly from Asia, Africa, South America, and the Caribbean. One-third were asymptomatric, while 42% had GI complaints, and 22% had dermatological complaints. Concurrent infection with additional

helminths was frequent. Eosinophilia (> 400 cells/mm^3) was present in 84% and 95% had a positive CDC serology. Both decreased after treatment with either thiabendazole or albendazole. The ratio of follow-up to initial serology results fell to less than 0.6, thought to be consistent with cure, by six months. (*ASTMH #66.*)

More than 700 cases of cutaneous gnathostomiasis, probably due to *G. spingerum*, have been diagnosed since 1989 in the city of Culiacan, Sinalao, on the northern Pacific coast of Mexico. The seroprevalence of infection in one high-risk community was 20.7%. (*ASTMH #95.*)

Fourteen patients who had been treated with ivermectin, with a median of 3.6 doses each, for onchocerciasis acquired more than 10 years previously during temporary residence in Africa were evaluated. None had evidence of active infection as determined by symptoms, skin snips (microscopy and PCR), Mazzotti test and eosinophil count. Although antibody levels were had diminished, they were still positive. Thus, in the absence of reexposure to onchocerciasis, patients should receive repeated courses of treatment as long as they have symptoms, eosinophilia, or parasitologic evidence of disease, but not simply in response to the presence of antifilarial antibodies. (*ASTMH #61.*)

Ivermectin was effective in a murine model of Toxocara canis infection. (*ASTMH #376.*)

Protozoa

Malaria. One hundred fifty members of the Australian Defense Force were randomized to receive malaria prophylaxis for eight weeks with either docycycline or Malarone (atovaquone/proguanil) on deployment to Papua, New Guinea. Both were well tolerated. Despite a high background risk of malaria, no subject in either group developed malaria. (*ASTMH #16.*)

Weekly administration of tafenoquine, a primaquine analog with a prolonged serum half-life, had safety and efficacy equivalent to that of weekly mefloquine in a semi-immune population in a blinded randomized trial of prophylaxis against *P. falciparum* in Ghana. (*ASTMH #18.*)

Tafenoquine and primaquine were compared in an open comparative trial in the terminal prophylaxis of *P. vivax* malaria in Australian Defense Force personnel deployed to a highly malarious area of Papua, New Guinea (80% *P. falciparum*, 20% *P. vivax*). Personnel receiving doxycycline were given either primaquine for 14 days or tafenoquine for three days. The failure rate after six months follow-up was 3.3% for primaquine recipients and 1.9% for tafenoquine recipients. However, tafenoquine was associated with more frequent and severe adverse events. (*ASTMH #424.*)

Mutations in the *pfcrt* and *pfmdr-1* genes have been linked with choroquine resistance in *P. falciparum*. In a study of isolates in Uganda, it was concluded that one of these mutations, K76T in the *pfcrt* gene, may be necessary, but it is insufficient to confer chloroquine resistance. This is consistent with data from Papua, Indonesia, an area in which the prevalence of chloroquine resistance in *P. falciparum* is 76%. A PCR assay for K76T had a sensitivity of 96% and specificity of 52%, a positive predictive value of 87%, and a negative predictive value of 81%. Similar results were found in Maumere Flores, Indonesia, where detection of the N1042D *Pfmdr* and K76T *Pfcrt* mutations each had 100% sensitivity but low specificity. (*ASTMH #109-111.*)

Thirty-six Javanese transmigrants in Papua, Indonesia, 36 with *P. falciparum* and 29 with *P. vivax* infection, were treated with four Malarone tablets (each contains 1000 mg atovaquone and 400 mg proguanil HCl) daily for three days, followed by 30 mg primaqune base daily for 14 days. The cure rate was 100%. (*ASTMH #17.*)

The presence of HIV coinfection did not appear to affect the response to treatment of acute falciparum malaria in Zambia. (*IDSA #475.*)

Some antimalarials are reported to prolong QT interval. Prolongation of cardiac repolarization, as reflected in the duration of the QT or corected QT (QTc) interval may predispose to the development of malignant polymorphic ventricular arrhythmia, especially torsade pointes. The degree of QTc dispersion is (Qtcmax—Qtcmin) believed to reflect heterogeneity of ventricular repolarization and larger values may also reflect risk of such arrhythmias. An evaluation of the effect of antimalarial drugs on these parameters found that neither QTc interval nor QTc dispersion were affected by either artemether or mefloquine. Quinine moderately prolongs QTc interval without affecting dispersion, while halofantrine significantly increases both. (*ASTMH #449.*)

CSF WBC count was more than 6/mL in approximately 10% of children with cerebral malaria in the absence of other evident cause. In 59 patients with atraumatic LPs, the WBC count ranged from 6 to 63 cells/mL. (*ASTMH #242.*)

Leishmaniasis. Travelers to Costa Rica accounted for 26% of the 195 persons for whom the CDC provided sodiium stibogluconate for treatment of cutaneous leishmaniasis. Preventive measures were frequently not utilized and only a few percent had ever heard of leishmaniasis prior to their diagnosis. (*ASTMH #84.*)

Bednet use was strongly protective against leishmaniasis among residents of Nepal. (*ASTMH #86.*)

An outbreak of visceral leishmaniasis due to *L. dono-*

vani in foxhounds in Dutchess County, New York, led to a serosurvey that found evidence of infection of foxhounds and other hunting dogs in 10 states. Since dogs may serve as a reservoir of infection with this organism, careful surveillance is warranted. (*ASTMH #404.*)

Microsporidiosis. Two hundred immunocompetent Costa Rican children with severe diarrhea for at least 10 days due to *Microsporidium* were randomized to no treatment or to receive albendazole for seven days. At 48 hours, clinical improvement was observed in, respectively, 30% and 95%. The mean duration of diarrhea was 10 days in the "no treatment" group and five days in those given albendazole. (*ICAAC #1468.*)

Babesiosis. More than two dozen cases of transfusion transmitted cases of babesiosis have been reported since 1980. A serosurvey of blood donors in Connecticut found prevalences of antibody positivity of 1.4% in an endemic area and 0.3% in a non-endemic area. Nineteen of 30 seropositive individuals were examined; four of the 19 (21.1%) had PCR evidence of *B. microti* in their blood. There was no correlation between antibody titer and PCR result. (*ASTMH #120.*)

Human babesiosis has recently been identified in Taiwan, Japan, and Switzerland. *B. microti* was detected in *I. ricinus* ticks collected in an area of Switzerland where *B. burgdorferi*, Central European encephalitis virus, and *Ehrlichia* spp. are cotransmitted. (*ASTMH #475.*)

Trypanosomiasis. Of 51 blood donors identified as seropositive for *T. cruzi*, 32 (63%) were PCR postive and three of those were also hemoculture positive. (*ASTMH #145.*)

Cyclosporiasis. In a study of the natural history of cyclosporiasis, three U.S. citizens with *Cyclospora cayetanensis* infection were followed without treatment shed oocyst for 6.5, 7.5, and 8.5 weeks from the time of exposure. Symptoms persisted until oocyst shedding ceased. (*ASTMH #291.*)

Rickettsia & Ehrlichia

Singapore is a modern, hygienic city. Nonetheless, 22 cases of murine typhus were seen over 14 months at one hospital in this Southeast Asian city. (*ICAAC #1986.*)

Of 142 patients presenting to the AFRIMS/Kwai River (Yes, that River Kwai!) Clinical Center, 17% had malaria, at least 8% had leptospirosis, and 3% had a spotted fever rickettsiosis. These were the first acute cases of rickettsial infection from this group identified in Southeast Asia. (*ASTMH #469.*)

In an area of Nova Scotia where the seropositivity rate to *Coxiella burnetii* among parturient women is 4%, an antibody titer of more than 1:32 was associated with an increased risk adverse perinatal outcome. *C. burnetii* could not be detected by culture or PCR from placentas of 153 seropositive women. (*ICAAC #1741.*)

Among 1067 National Guard troops who trained in two-week cycles at Fort Chaffee, Arkansas, from May 17 to June 29, 1997, 162 (15.2%) had serological evidence of one or more tick borne infection. Of 99 with paired serum samples, 36 seroconverted to *R. rickettsii*, five to *E. chaffeensis*, and two to *E. phagocytophilia* (1 converted to both *R. rickettsii* and *E. chafeensis*). Fifty percent of the seroconverters and 24% of those with single-positive serologies reported a clinically compatible illness. While 80% used repellent, only 35% wore impregnated uniforms. (*ASTMH #470.*)

Ehrlichiosis due to either *E. chaffeensis* or *E. ewingii* was diagnosed in 16 HIV-infected patients, 12 (75%) of whom became severely ill. Five (31.3%) died. (*ASTMH #124.*)

In a study providing evidence of the potential for transmission by blood transfusion, *E. phagocytophilia* was inoculated into a unit of adsol-treated packed red blood cells, which was then stored at 4°-6° C. Viable organisms could be isolated from both the cellular and supernate fractions for as long as 27 days. Isolation from the supernatant fluid indicates that leukodepletion of transfusion products may not eliminate the risk of infection. (*ASTMH #471.*)

Four cases of rickettsialpox from Brooklyn, including one in an HIV-infected individual, were described. Clues to diagnosis were a history of exposure to mice and the presence of an eschar. (*ASTMH #472.*)

Ectoparasites of flying squirrels in Florida and Virginia have previously been found to be infected with *R. prowazekii*. Examination of DNA extracted from fleas of flying squirrels captured in Mexico yielded sequences that had 98.3% homology to those of *R. felis*. This organism has previously been found in cat fleas and is a cause of human infection previously identifed in southern California and Mexico. (*ASTMH #474.*)

Bacterial Infection

A total of 1166 laboratory confirmed cases of typhoid fever were reported to CDC between 1994 and 1999—29% from California and 24% from New York. Nine patients (0.8%) died. Of those cases, 855 (73%) were acquired abroad with travel to six countries accounting for 70%—India (30%), Pakistan (13%), Mexico (10%), Bangladesh (6%), Haiti (6%), and the Phillipines (5%). Three-fourths were visiting family; one-fourth of the total cases occurred in children younger than 10 years of age and only 27 patients reported having been vaccinat-

ed. Of infected travelers to a single country for whom the data was available, 48% had spent less than one month and 61% less than six weeks in that country. Thus, even short-term travelers to the Indian subcontinent, children and persons visiting family are especially important targets for vaccination. (*ASTMH #60.*)

Stool cultures of 420 U.S. military personnel who presented with diarrhea during training exercises in Thailand yielded *Campylobacter jejuni/coli* in 33%, nontyphoidal Salmonella in 21% and enteroxigenic *E. coli* in 20%, with no isolates recovered in 32%. Patients infected with *Campylobacter* were more likely than the other agents to have systemic symptoms including fever (72% vs 29%), to have abdominal cramps (87% to 75%), and to have decreased ability to work (81% to 64%). During the years of this study, more than 85% of *C. jejuni* were resistant to fluoroquinolones. Complete symptom resolution by 72 hours for those who received therapy with a fluoroquinolone was 81% for those with *Campylobacter* infection and 94% of those with non-*Campylobacter* infection. (*ASTMH #306.*)

The seroprevalence rates to *Bartonella elizabethae* in injection drug users (IDU) in New York City and Baltimore were, respectively, 46% and 33%, while the rates for *R. akari* at these two sites were 9% and 16%. These data suggest a high rate of rodent exposure among IDU in these two cities since *B. elizabethae* is associated with Norway rats and *R. akari* with house mice. (*ASTMH #512.*)

Viral Infection

A study of patients presenting to Nantucket Cottage hospital with "summer fever," who did not have evidence of tickborne infection, found evidence of seroconversion to Jamestown Canyon virus in 13.3% of 45 subjects from paired sera that were available. This bunyavirus is believed to be maintained in deer and transmitted by *Aedes* mosquitoes. (*ASTMH #704.*)

Intradermal administration of Japanese encephalitis (Biken) vaccine was as immunogenic as the recommended subcutaneous route, but had fewer associated adverse effects, and was less costly. (*ASTMH #225.*)

The prevalence of antibody to hepatitis E virus in North Carolina swine workers was 11%—7% in U.S.-born workers and 28% in those born outside the United States (P = 0.001). Thirty-two percent of workers from Mexico were seropositive. The seropositivity among swine was 34.5% overall but varied from 10-15% at a farm that cohorts the animals to 92% at one that uses "continuous flow" pig production. (*ASTMH #137.*)

The response of Egyptian patients to treatment of hepatitis C with interferon α did not appear to be affected by the presence of coinfection with *S. mansoni*. (*ASTMH #510.*)

Spirochetal Infection

The seroprevalence of *B. burgdorferi* sensu stricto exposure was determined in a representative sample of 9673 of 840,390 U.S. military personnel on active duty. Only 12 (0.75%) were postive by both ELISA and Western Blot. Two of these nine were documented to have undergone seroconversion during military service, for an annual incidence of 5.9 seroconversions per 100,000 person years. (*ASTMH #122.*) ❖

CME Questions

44. Which of the following is correct?

a. All patients with pulmonary cryptococcosis must undergo lumbar puncture.
b. The most common cause of eosinophilia in a cohort of Costa Rican children was angiostrongyliasis.
c. Most patients with strongyloidiasis in Toronto are natives of Canada.
d. Patients who have received a course of ivermectin therapy for onchocerciasis should not receive further ivermectin therapy regardless of symptoms.

45. Which one of the following is correct?

a. Gnathostomiasis has never been acquired in Mexico.
b. Travelers to Costa Rica are not at risk of acquiring cutaneous leishmaniasis.
c. Canine leishmaniasis due to *L. donovani* has been detected in New York state.
d. Untreated cyclosporiasis is associated with rapid (within days) loss of fecal shedding of *C. cayetanensis.*

46. Which of the following is correct?

a. Long-term (> 4-6 weeks) travel, but not shorter term travel to the Indian subcontinent, is a risk factor for infection with *Salmonella typhi*.
b. *Ehrlichia phagocytophila* cannot survive in refrigerated transfusion products for more than six hours.
c. Clues to the diagnosis of rickettsialpox in Brooklyn included a history of mouse exposure and the presence of an eschar.
d. *Campylobacter jejuni/coli* isolates from Thailand remain uniformly susceptible to fluoroquinolone antibiotics.

In Future Issues:

Pharmacology Update: Lopinavir and Ritonavir Capsules and Oral Solution