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Conference Summaries of ICAAC 1999 and IDSA 1999: Part V

CONFERENCE COVERAGE

Editor's Note: The following summaries represent a selection of papers presented at the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), held Sept. 26-29, 1999, in San Francisco and at the 37th Annual Meeting of the Infectious Disease Society of America (IDSA), held Nov. 18-21, 1999, in Philadelphia. 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 conferences may have differed. The ICAAC abstracts are available on the American Society of Microbiology Web site at: <http://www.asmusa.org>. The IDSA abstracts can be seen in *Clin Infect Dis* 1999;29:959-1112. —Stan Deresinski, MD, FACP

Herpes Viruses

Herpes Simplex Virus (HSV). An analysis of patients enrolled in an unsuccessful genital HSV vaccine trial uncovered 155 new HSV-2 and 19 new HSV-1 infections among 2393 HSV-2 seronegative subjects, 885 of whom were also HSV-2 seronegative. The rates of new HSV-2 and HSV-1 infections among seronegative infections were 5.1 and 1.7 per 100 person-years, respectively. Of the new HSV-2 infections, 37% were symptomatic and 15% of these developed genital lesions on follow-up. Women were more likely than men to acquire HSV-2 infection and were more likely to be symptomatic. While preexisting HSV-1 infection was not protective against HSV-2 infection, it increased the likelihood of asymptomatic seroconversion by a factor of 2.6. Twelve of 19 new HSV-1 infections were asymptomatic. These sexually active subjects were as likely to have genital as oral acquisition of HSV-1. HSV-2 was clinically misdiagnosed in 20% of symptomatic cases. (ICAAC #1405.)

Five hundred thirty-one monogamous HSV-2 discordant cou-

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ples were followed for 18 months; 37 (7%) individuals (30 women, 7 men) acquired HSV-2 infection. While the overall rate of acquisition was 5.2 per 100 person-years, the risk markedly decreased from 9.1 during the first 150 days of the study to 1.4 per 100 person-years after 450 days. Consistent condom use was associated with a reduced risk of transmission, while frequent sexual activity was associated with an increased risk. Prior HSV-1 seropositivity was not protective. (*ICAAC #1406.*)

HSV was detected in genital cultures obtained at the time of delivery in 122 of 31,810 women (0.4%) and neonatal HSV infection occurred in offspring of nine (7%) of those shedding virus. Based on serological studies, 20 (17%) of the mothers were shedding due to first episode disease and 86 (83%) due to viral reactivation. Three of the 20 first episodes were primary HSV-1 infections, all of which were transmitted; three were primary HSV-2 infections, one of which was transmitted. The remaining 14 were due to non-

primary HSV-2 infections and four (29%) were transmitted. Neonatal HSV infection occurred in five (0.2%) offspring of the 31,694 culture-negative mothers one each of primary HSV-1 and HSV-2 and three recurrent HSV-2. PCR analysis of three of the five culture-negative specimens from transmitting mothers detected HSV DNA. Thus, given an HSV-2 seroprevalence of 28%, the risk of neonatal transmission among women with reactivation HSV-2 is approximately one in 4000. (*ICAAC #1317.*)

A case of an illness resembling Fitz-Hugh-Curtis syndrome caused by HSV was described. The patient had just completed a five-day course of prednisone given because of hives. She had active genital herpes and laparoscopy revealed multiple small vesicular lesions on the surface of the liver; examination of a biopsy specimen revealed herpetic hepatitis and culture was positive. (*IDSA #611.*)

Cytomegalovirus. Asymptomatic cytomegalovirus (CMV) infection occurred in 0.9% of 1000 normal newborns as determined by detection of viral DNA in urine. Cord blood IgM antibody was negative in all nine, although it was positive in both infants with symptomatic infection identified during the same period of observation. (*IDSA #687.*)

CMV DNA was detected in the blood and/or tracheal secretions of 16 of 40 (40%) prospectively monitored nonimmunosuppressed surgical ICU patients. Two patients developed CMV pneumonia and died with progressive multiple organ failure. (*ICAAC #1949.*)

Detection of CMV pp65 antigenemia has become a widely used method for detection of CMV infection in immunocompromised hosts. However, a case of high-level CMV viremia despite antiviral prophylaxis who had repeatedly negative assays for pp65 antigenemia is described, bringing into question the sensitivity of the assay in this setting. (*ICAAC #1333a.*)

Approximately 30% of allogeneic bone marrow or stem cell recipients given ganciclovir for presumptive CMV infection have rising pp65 antigenemia. Analysis of a cohort of patients indicates that rising antigenemia is not an indicator of phenotypic drug resistance and does not portend an increased risk of CMV disease. (*ICAAC #1410.*)

Two hundred thirteen allogeneic stem cell recipients with presumptive CMV infection were randomized to receive either ganciclovir or foscarnet. CMV disease developed in five patients in each group. Severe neutropenia (< 500 cells/mm³) developed in 11% of ganciclovir and 4% of foscarnet recipients (P = 0.04), while impaired renal function occurred in 2% and 5% (P = 0.4), respectively. (*ICAAC #1409.*)

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Varicella-Zoster Virus. From 1988-1995, there were approximately 11,000 hospital admissions due to varicella annually in the United States, with 65.9% in children younger than 15 years of age. Approximately 14.4% had a listed diagnosis indicating immunocompromise. The most common complications were soft tissue infection (20.3%), viral pneumonia (20.0%), fluid/electrolyte disturbance (19.5%), and bacterial pneumonia (9.9%). (IDSA #571.)

A study of 230,000 children, 53% of whom had been vaccinated against varicella, found that vaccination at ages 12 to 24 months reduced the risk of varicella by 86%. There was as yet, however, no evidence of herd immunity. (ICAAC #1622.)

Seroconversion (by FAMA) was observed in all 56 susceptible health care workers to whom varicella vaccine was administered. Three-fourths seroconverted by commercial ELISA. There was no evidence of decline in antibody level over the next several years. Two cases of modified varicella without subsequent spread to patients were observed, one at four years and one at five years post-vaccination. (IDSA #32.)

Varicella vaccination of susceptibles within 72 hours of contact with cases of chickenpox had an efficacy of 80.7% in preventing disease. Illness was mild (< 50 lesions) in seven of 11 vaccinated susceptibles who became infected while the other four had typical chickenpox. (IDSA #647.)

Nipah Virus

A case control study confirmed the association of contact with pigs and the development of Nipah virus infection in the recent Malaysian outbreak. (IDSA #721.)

West Nile Virus

The ages of the first five cases identified during the New York City outbreak of West Nile virus encephalitis ranged from 58 years to 80 years; four were male. All had abnormal CSF; four of the five had pleocytosis with lymphocyte predominance. CSF WBC ranged from 0 cells/mm³ to 100 cells/mm³ (mean, 48.4 cells/mm³) and protein from 51 mg/dL to 129 mg/dL (mean, 84.4 mg/dL), while glucose was normal. (IDSA #723.)

Mycoses

Yeasts

Candida spp. Sixty-one percent of 100 stool samples from 100 healthy volunteers yielded *Candida* on

culture, with two-thirds being *C. albicans*. (ICAAC #971.) Cultures of stool samples from healthy volunteers who had not received antifungal or antibacterial agents in the previous six weeks yielded fungal isolates in 118 of 228 (51.8%); only a single species was detected in 88% of those. Yeast accounted for 90.7% of isolates, with *C. albicans* accounting for 62.7%. There were only three isolates of *C. glabrata*, the second most common species isolated from hospitalized patients. Of 31 families with fungi isolated from at least two members, the same species was found in 67.5%. (ICAAC #967.)

A molecular epidemiologic study of gastrointestinal carriage of *C. albicans* found that in most colonized individuals, only a single strain was present, although women commonly harbored 2-23 closely related clones. There was no evidence of intrafamily strain exchange—each individual harbored a unique strain. (IDSA #285.)

Asymptomatic Israeli women were found to have a 44.5% rate of vaginal carriage of non-*albicans Candida*, one-half of which were *C. glabrata*. (IDSA #274.)

A prospective study of 4276 SICU admissions over 18 months found that the overall risk of death attributable to *Candida* bloodstream infection was 7.7%. The relative risk of death among patients older than 65 years of age with this infection was 10.5 (95% CI 5.0-22.3). Receipt of an antifungal drug was associated with a reduced risk of mortality (RR = 0.4; 95% CI 0.3-0.5). (IDSA #289.)

Eleven of 12 cases of fungemia due to *C. lusitania*, representing 1.3% of all cases of candidemia seen at one cancer hospital in an 11-year period, occurred in patients with hematological malignancies; nine of the 12 were neutropenic and all had central venous catheters and had received antibacterial agents. Four patients died. (ICAAC #957.)

A case control study of 54 patients with *Candida* peritonitis found associations with a perforated viscus, ascites, emergent surgery, prolonged central venous catheterization, TPN, and prolonged exposure to antibacterial agents. Sixty-nine percent had more than one *Candida* species isolated and 65% had bacteria also isolated from intra-abdominal cultures. Eleven of 12 (92%) patients who did not receive antifungal therapy recovered. (IDSA #309.)

Cryptococcus neoformans. A serological study in the Bronx found evidence of multiple antibodies to antigens of *C. neoformans* in 53 of 82 (65%) children older than 2 years of age, indicating early exposure to this organism. (IDSA #283.) *C. neoformans* isolated from a patient and from the feces of his pet cockatoo appeared to be

identical when tested by multiple methods, including RFLP. (IDSA #298.)

A survey of clinical isolates of *C. neoformans* from Atlanta, San Francisco, Houston, and Alabama found that resistance to fluconazole remained uncommon and had not changed in the previous decade. There was also no significant change in susceptibility to itraconazole and to 5-flucytosine. (IDSA #395.)

Mouse studies identified cryptococcal capsule size as the single most important virulence factor. (IDSA #271.)

Saccharomyces cerevisiae. *Saccharomyces cerevisiae* was found to be a nosocomial colonizer in 20 of 42 patients with hematologic malignancy at one center in Finland. No invasive infections were detected. All the isolates were resistant to fluconazole and itraconazole but susceptible to amphotericin B. (ICAAC #1906.)

Blastoschizomyces capitatus. Four neutropenic patients receiving empiric therapy with liposomal amphotericin B developed invasive infection with *Blastoschizomyces capitatus*; three died. Of a total of 11 isolates of this organism from 11 patients, 78% were resistant in vitro to amphotericin B and 67% to itraconazole. All were susceptible to flucytosine, fluconazole, and ketoconazole, as well as voriconazole. (ICAAC #973.) Four additional isolates of this organism were reported to be inhibited, but not killed, by clinically achievable serum concentrations of amphotericin B. (ICAAC #962.)

Histoplasma capsulatum. An outbreak of histoplasmosis affected at least 43 individuals who had visited a tourist cave in Costa Rica. *H. capsulatum* was isolated from bat guano in the cave. (IDSA #294.)

Filamentous Fungi: *Aspergillus* spp. and *Zygomycetes.* Fourteen transplant patients (10 bone marrow, 2 lung, 1 liver, 1 kidney) developed fungal brain abscess over a two-year period at a single center. This complication occurred in 10.6% of bone marrow transplant patients and in 1.8%, 0.5%, and 0.17% of, respectively, lung, liver, and kidney recipients. The median time to onset of symptoms was 90 days in the bone marrow transplant recipients and 467 days in the others. At presentation, 70% had fever and change in mental status, while only 20% complained of headache; a mean of three lesions were detected. Pathogens included *Aspergillus* spp., *Xylohypha bantiana*, *Microascus cinereus*, and *Mucor* spp. Infection was often associated with rejection in bone marrow recipients, as well as with GVHD. Ninety-three percent of patients died. (IDSA #264.)

A retrospective analysis using stored serum speci-

mens from liver transplant recipients found that a commercially available sandwich-ELISA test for *Aspergillus* galactomannan had a sensitivity of 62.5% in the diagnosis of invasive aspergillosis. The specificity, negative, and positive predictive values of the test were, respectively, 94%, 91.4%, and 71.4%. (IDSA #278.)

Fifty-five of 591 (9.3%) cardiac allograft recipients at one center developed aspergillosis from 1980 to 1998. Fever was present in 58.6%. Twenty-nine had invasive pulmonary disease, 21 had nodular disease (72.3%), and five had diffuse infiltrates (17.2%). Three-fourths of cases occurred within 90 days (median, 46 days); none were neutropenic, but 86.2% received corticosteroids, 44.8% had organ rejection, and 31% had CMV coinfection. The mortality rate among the patients with invasive pulmonary disease was 24%. (IDSA #269.)

One thousand four hundred twenty-one cultures positive for *Aspergillus* from 1024 patients at 24 centers were evaluated. Forty-three percent of the cultures were believed to represent colonization, 18% contamination, and 17% unknown, while 22% were associated with infection. Among the last group, 60% had invasive infection, 6% chronic necrotizing aspergillosis, 17% aspergilloma, and 17% allergic bronchopulmonary aspergillosis. In addition, 55% had received corticosteroids, 38% had a hematologic malignancy, 32% had underlying pulmonary disease, 27% had neutropenia, 20% had stem cell transplantation, and 20% were malnourished. *A. fumigatus* was responsible for 68% of cases of invasive disease, this was followed by *A. flavus* (13%), *A. niger* (6%), *A. terreus* (3%), and *A. nidulans* (1%). Of the patients with invasive disease, 60% were dead at three months, with death directly attributed to aspergillosis in 19%. Fourteen percent of those who were only colonized with this fungus were dead at three months. Three-month mortality was 48% in patients treated with amphotericin B and 28% in those given itraconazole. (IDSA #299.)

Only 11 of 36 (30%) patients with malignancy with a positive blood culture for *Aspergillus* were believed to have true definite or probable "aspergillemia" with the rest being either indeterminate (28%) or contaminants (42%). Recovery of species other than *A. fumigatus*, especially *A. terreus*, was more likely to represent true infection than was recovery of *A. fumigatus*. (IDSA #292.)

Three new cases of native valve *Aspergillus* endocarditis were reported and discussed along with 36 cases from the literature. Forty percent were receiving

corticosteroids or had an underlying malignancy; 76% had embolic phenomena. Eighteen of the 24 speciated isolates were *A. fumigatus* and six were *A. flavus*. Two patients (5%) had a positive blood culture. The diagnosis was made antemortem in 21 (54%) patients; none of 10 treated only medically survived, while three of 11 who also had valve surgery survived. (IDSA #308.)

Sixty-five of 122 (54%) patients with invasive aspergillosis who had failed other antifungal therapy responded to therapy with amphotericin B lipid complex (ABLC). (IDSA #293.)

Seven of 11 patients with zygomycosis who had failed prior antifungal therapy and six of seven receiving their initial antifungal therapy responded to liposomal amphotericin B. (IDSA #229.)

The six previously described cases of gastrointestinal basidiobolomycosis due to the zygomycete, *Basidiobolus ranarum*, in Arizona were discussed in greater detail (MMWR Morb Mortal Wkly Rep 1999;48:710-713). All underwent surgical resections followed by therapy with itraconazole for a median of 5.5 months; none died. Five of the six had preoperative eosinophilia. A case control study found that cases had lived in Arizona longer than controls. Univariate analysis found an association between the use of H2 antagonists and infection. (IDSA #295.)

The addition of trovafloxacin to fluconazole treatment improved survival in a murine model of pulmonary zygomycosis due to *Rhizopus oryzae*. The administration of a single dose of amphotericin B followed by therapy with trovafloxacin plus fluconazole resulted in 90% survival (no survivors in untreated controls). Itraconazole was largely ineffective in combination with trovafloxacin. (IDSA #305.)

Mycetoma. Eight of 10 Senegalese patients with mycetoma due to *Madurella mycetomatis* treated with terbinafine 1000 mg po qd improved within the first four weeks. Seven of these had received 24 weeks of treatment and improvement was present in five. (ICAAC #1082.)

Antifungal Prophylaxis and Therapy

Effective antifungal prophylaxis with itraconazole in neutropenic patients was associated with maintenance of a trough serum concentration of more than 500 ng/mL. (ICAAC #1417.) The introduction of antifungal prophylaxis with orally administered itraconazole in cardiac transplant recipients was associated with a decrease in incidence of invasive aspergillosis from 9.6% to 2% in sequential time periods, as well as a 50%

decrease in cyclosporin dosage requirement. One breakthrough infection with *Scedosporium prolificans*, resistant to itraconazole, occurred. (ICAAC #1416.) Terbinafine and itraconazole acted synergistically in vitro at achievable serum concentrations against 18 isolates of *S. prolificans*. (ICAAC #149.)

Seventy-one liver transplant recipients were randomized to receive either placebo or itraconazole beginning with a loading dose prior to transplantation and continuing for a mean of 13 ± 10 days. Itraconazole prophylaxis was well tolerated and was associated with a reduced incidence of fungal infection requiring systemic therapy (4% vs 24%). (ICAAC #1649, #1650.)

Sixty-seven patients were randomized to receive amphotericin B intermittently over four hours or continuously over 24 hours each day. The mean total daily doses in these groups were, respectively, 0.91 and 0.97 mg/kg and the mean durations of therapy were 11.5 and 14 days. Infusion-associated chills or fever, as well as the need for drug discontinuation, occurred significantly more frequently in the four-hour than the 24-hour infusion group. Nephrotoxicity was also less in the 24-hour group. (ICAAC #1423.)

Patients with invasive infection with aspergillosis (13), zygomycosis (5), or fusariosis (3) received 7.5-15 mg/kg/d of liposomal amphotericin B; all doses were well tolerated. Successful outcomes were achieved in 68% by intent-to-treat analysis and in 75% of evaluable patients. (ICAAC #1640.)

Itraconazole and terbinafine were each active in vitro against 26 isolates of *Penicillium marnefei*. (ICAAC #1520.)

Oral administration of amphotericin B contained within supramolecular assemblies folded in a spiral configuration based on phosphatidyl serine and divalent cation called cochleates resulted in significant gastrointestinal absorption of the polyene antifungal. (ICAAC #1940.)

Parasitic Disease

Forty-two cases of malaria, 93% due to *Plasmodium falciparum* and 62% in recent West African immigrants, were diagnosed at Harlem Hospital from 1993 to 1999. Despite the fact that 79% gave a previous history of malaria, the diagnosis was initially missed in one-fourth. There were no fatalities. (IDSA #266.)

An 89-year-old diabetic male receiving prednisone for temporal arteritis presented with radiographic evidence suggestive of ischemic bowel disease. Many *Strongyloides stercoralis* larvae were found in his

stool. After treatment with ivermectin, his symptoms resolved and CT scan showed resolution of pneumato-sis intestinalis as well as gas which had been present in mesenteric and portal veins. (IDSA #213.)

An outbreak of cryptosporidiosis in students in Wash-ington, D.C., was linked to a meal in a college dining hall. (ICAAC #2225.)

Of 1036 children in a poor area of Managua with watery diarrhea absent blood or mucus, 9.6% were found to have *Cyclospora cayetaensis* infection. Other organisms found were *Giardia* in 40.9%, *Ascaris* in 14.0%, *Entamoeba histolytica* in 10.1%, and *Cryp-tosporidium* in 5.0%. (ICAAC #2214.)

Twelve apparently immunocompetent patients with visceral leishmaniasis acquired in the Mediterranean region were treated with cholesterol dispersion amphotericin B in a dose of 2 mg/k/d for seven days. Cure was achieved in all 12. (ICAAC #1855.)

Two patients from Cape Verde presenting with abdominal pain and found to have evidence of fascioliasis were successfully treated with single doses of tri-clabendazole. (IDSA #219.)

Hospital Epidemiology

Beware of the patient transferred from another hospi-tal. A multivariate analysis of nosocomial infection risk identified three significant factors: hospital stay longer than seven days, having undergone at least one invasive procedure, and having undergone hospital transfer. (ICAAC #1694.)

A comparison of nail colonization in 20 wearers of artificial nails and 20 controls found that a potential pathogen was isolated from 73% of the former and only 32% of the latter ($P < 0.001$). *S. aureus*, gram-negative bacilli, and yeast were each recovered significantly more frequently from the former than the latter group. (ICAAC #1696.) Artificial nails (as well as increased age) were a significant risk factor for hand carriage of an epidemic strain of *Pseudomonas aeruginosa* in health care workers. (IDSA #21.)

The risk of mediastinitis correlated with preopera-tive fasting blood glucose level in diabetics undergoing cardiac surgery. (IDSA #22.) A case control study of 67 patients with surgical site infections after median ster-notomy found that only alcoholism and insulin require-ment were significant risk factors. (IDSA #479.)

A prospective study found that MRSA infection occurred in seven of eight (87.5%) of MRSA carriers and in only three of 25 (12%) of MSSA carriers. (ICAAC #513.) 1440 patients undergoing cardiac surgery had mupirocin ointment applied intranasally

twice daily for five days. When compared to a histori-cal control group, there was no decrease in the total rate of sternal wound infections (1.4% in each group), but, while 50% of infections among controls were caused by *S. aureus*, none during mupirocin use were ($P = 0.00469$). (ICAAC #512.) In contrast, eradication of nasal carriage of *S. aureus* was not associated with a decreased risk of surgical site infections due to *S. aureus* in orthopedic procedures involving artificial implants. (ICAAC #514.)

Six of 18 (33.3%) of inpatients and outpatients with recurrences of *C. difficile*-associated diarrhea in Sacramento were infected with new strains as deter-mined by DNA analysis. (ICAAC #739.) A similar study in Madrid found that recurrences in HIV-infected patients were due to infection by a new strain of *C. difficile* in 32%. (ICAAC #740.) A significant associa-tion between increasing nursing workload and simul-taneous outbreaks of VRE and *C. difficile* was found. (ICAAC #2085.)

Stool colonization with vancomycin-resistant *E. fae-cium* was identified in three of 52 (6%) of households with members who were hospital employees with patient contact and in none of 40 without patient contact. Molecular typing demonstrated evidence of intrahouse-hold transmission of the organism. (ICAAC #744.)

Only 29.5% of 1157 health care workers reported having received influenza vaccination within the previ-ous 12 months. (ICAAC #752.)

Two transplant ICU patients cared for in the same space as a patient with an abdominal wound infection due to *A. fumigatus* developed infection due to an *A. fumigatus* of the same subtype by RFLP analysis. Increased numbers of *A. fumigatus* were found on settle plates near the patient; these numbers increased further after a dressing change. These results are compatible with the occurrence of person-to-person transmission of *A. fumigatus* as the result of aerosolization of spores from the abdominal wound and its dressings. (IDSA #19.)

Air sampling studies suggested that aerosolization of *Aspergillus* spp. spores occurs during showering and that this may represent a potential source of patient exposure. (ICAAC #1908.)

An increase in cases of invasive aspergillosis, in association with an increased recovery of spores from air samples, occurred contemporaneously with a major construction project taking place on the floor immediately below the bone marrow transplant unit. (ICAAC #757.)

Seventy-two water samples were taken and 20 water-related surfaces sampled over three months in a pedi-

atric bone marrow transplantation unit in Oslo. Twenty-five percent of water-related surfaces and 100% of water samples yielded filamentous fungi, with *A. fumigatus* being recovered from 10% of the former and 60% of the latter samples, albeit in low density (2.5 CFU/500 mL). (ICAAC #1909.)

Fungal cultures of non-heat-sterilizable food distributed to neutropenic patients found potential pathogens in most, including 15% of grapefruit juice, 25% of banana, and 66% of apricot samples. Of tea and pepper samples, 100% were culture positive. Most samples of these foods yielded *A. fumigatus*; other organisms recovered included *A. flavus*, *A. niger*, *Mucoraceae*, and *Trichoderma* spp. (ICAAC #972.)

M. xenopi was isolated from 40.6% of faucets, 33.3% of showers, and 80% of hot water tanks in a drug dependency unit in which an outbreak of colonization occurred. (ICAAC #753.)

Three patients contracted malaria due to *P. falciparum* while hospitalized on an infectious disease ward on which three additional patients with travel-acquired falciparum malaria also resided. DNA typing demonstrated apparent identity between the organisms involved in each of the three nosocomial cases and one of the travel-related cases. Classical epidemiological investigation had suggested that blood from that travel case had contaminated IV fluids administered to the three patients with hospital-acquired infection. (ICAAC #2081.)

Febrile Neutropenia/Infection in Transplantation

Piperacillin/tazobactam was more effective than gentamicin plus ceftriaxone in the empiric treatment of febrile neutropenia. (ICAAC #1090.) Cefpirome vs. piperacillin/tazobactam were equivalent, while meropenem was superior to ceftazidime (ICAAC #1089, #1091.) No benefit from the addition of amikacin to piperacillin/tazobactam was observed in a randomized clinical trial. (ICAAC #1092.)

Of 96 liver transplant patients with documented infection, only 65 (68%) were febrile, while 26 (27%) were eutermic and five (5%) were hypothermic. Mortality rates at 30 days for each of the three groups were, respectively, 20%, 23%, and 100% ($P = 0.0006$). Four of the five hypothermic patients had pneumonia. (ICAAC #1691.) ❖

CME Questions

8. Which of the following is correct?

- Pre-existing HSV-1 infection is protective against subsequent HSV-2 infection.
- Prior HSV-1 infection is associated with a reduced risk of symptomatic primary HSV-2 infection.
- Consistent condom use was not protective against transmission of HSV-2 infection in HSV-2 discordant couples.
- The risk of neonatal transmission of HSV-2 at delivery among women with reactivation of HSV-2 infection is approximately one in four.

9. Which of the following is correct?

- In allogeneic stem cell recipients with presumptive CMV infection randomized to receive either foscarnet or ganciclovir, no significant difference in occurrence of CMV disease was found between the two treatment groups.
- In allogeneic stem cell recipients with presumptive CMV infection randomized to receive either foscarnet or ganciclovir, severe neutropenia occurred more frequently in those assigned foscarnet.
- Varicella vaccination at ages 12-24 months was associated with only a 23% reduction in the risk of varicella infection.
- Of 56 health care workers who received varicella vaccine, only 33% seroconverted and these had subsequent rapid antibody decline.

10. Which of the following is correct?

- Nipah virus infection is associated with exposure to camels.
- Neutrophilic predominant cerebrospinal fluid pleocytosis was the rule in New York patients with encephalitis due to West Nile virus.
- Candida albicans* is rarely isolated from the stool of normal healthy volunteers.
- Evidence from the Bronx indicates that the majority of children older than 2 years of age have been exposed to *Cryptococcus neoformans*.

Readers are Invited. . .

Readers are invited to submit questions or comments on materials seen in or relevant to *Infectious Disease Alert*. Send your questions to: Neill Larmore—Reader Questions, *Infectious Disease Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. You can also reach the editors and customer service personnel for *Infectious Disease Alert* via the Internet by sending e-mail to neill.larmore@medec.com. We look forward to hearing from you. ❖

In Future Issues:

Controlling the Ever-Present Methicillin-Resistant
Staphylococcus aureus

German Student Dies of Lassa Fever

Source: PromedMail, Jan 12-15th, 2000; www.promedmail.org.

A 23-year-old female student in southern Germany died 13 days after becoming ill with what proved to be Lassa fever. The young woman had participated in a student program in Ghana and the Cote d'Ivoire in November and December 1999, and then traveled through the region with a friend for a few weeks. She became ill with flu-like symptoms on about January 2, and returned via Air Portugal through Lisbon and Frankfurt on January 6 and 7. She was admitted to the hospital in a small town in southern Germany, where she was treated for malaria without improvement. On January 11, she was transferred to a hospital in Wuerzburg where she was placed in an intensive care isolation room. Within hours, the diagnosis was confirmed by RT-PCR. Despite the initiation of ribavirin, she developed progressive multi-organ system failure and, finally, uncontrollable hemorrhage.

Sequencing of this woman's virus demonstrated 82% homology with the Josiah strain and 65% with the Nigeria strain. The Josiah strain has been previously seen in Sierra Leone, Liberia, Guinea, and Nigeria; this case confirms its presence in adjacent territory.

Lassa is an RNA arena virus, similar to hantavirus, which is transmitted to humans from food contaminated with the urine and feces of the West African *Mastomys* rat, which lives in the huts and homes of villagers. Similar to Ebola, the greatest risk for human-to-human transmission is via contact with infected blood, saliva, vomitus, and urine. Health care workers are therefore at particular risk. In Africa, human infection from contaminated medical equipment and syringes may be significant. Studies show that ~9% of the population in Sierra Leone has antibodies to Lassa, although up to 40% in some regions

may show evidence of past infection.

The incubation period is typically 7-12 days, beginning with flu-like symptoms (fever, headache, myalgia, and GI symptoms). It is fatal in up to 40% of cases, although this figure may be higher in nonimmune populations.

Portuguese health authorities have been attempting to contact all 74 passengers aboard the flight from Africa to Lisbon, and German authorities have been closely monitoring about 15 friends and family members, as well as 37 employees where she was first hospitalized for any signs or symptoms of disease. Thus far, no secondary cases have been identified. Given our increasing "globalization" of microbes, physicians and emergency room personnel should be trained to recognize and manage febrile viral illnesses, such as Lassa, in returning travelers, especially those without evidence of malaria. ■

INH in Resistant MTb

Source: Cynamon MH, et al. *Antimicrob Agents Chemother* 1999;43:2922-2924.

The utility of inh in the treatment of INH-resistant *Mycobacterium tuberculosis* (MTb) remains controversial. Various dosages of INH were fed by gavage to CD-1 mice infected with either an INH-sensitive or -resistant strain of MTb (INH MIC, 2 mcg/mL). The resistant strain had a point mutation in the *KatG* protein. After four weeks, colony counts in lung and spleen were compared with that of untreated controls. Similar antimycobacterial responses were noted for both the INH-sensitive and -resistant groups of mice, irrespective of the dosage received. Although the lack of a dose response relationship in this study suggests that dosages greater than the standard 300 mg/day would not be more effective, INH may provide antimycobacterial activity in MTb isolates with low-level INH resistance. These findings should be confirmed in

strains with mutations other than *KatG*, continued administration of INH to patients with low-level INH resistance may be of value. ■

Hydroxyurea and Herpes

Source: Neyts J, et al. *Antimicrob Agents Chemother* 1999;43:2885-2892.

Hydroxyurea (hu) has been found to be synergistic with the nucleoside reverse transcriptase inhibitors, such as ddI and d4T, against HIV, as well as to potentiate the anti-HIV activity of the nucleoside phosphonate analogues, adefovir adenine (PMEA) and tenofovir adenine (PMPA). The mechanism of action is not entirely clear, but is believed to be due to, in part, to competitive inhibition of cellular ribonucleotide reductase, the enzyme that converts ribonucleotides to deoxyribonucleotides (dNTP). This competitive interaction may result in a reduction in our normal pools of intracellular dNTP, thus favoring the use of nucleoside analogues.

It turns out that HU may have a similar effect on nucleoside analogs used for the treatment of herpes-1 and -2 virus infections. The anti-HSV activities of acyclovir, ganciclovir, penciclovir, lobucavir, and H2G were markedly increased in vitro in the presence of HU. In the presence of HU, the inhibitory concentrations for these agents against TK-deficient HSV-1 virus decreased markedly from concentrations not attainable in plasma (20 to > 100 mcg/mL) to 1 to 5 mcg/mL. In single-cycle viral yield reduction assays, viral replication was reduced by 60-90%. HU appeared to have an even greater effect on the activity of these agents against HSV-2.

Patients receiving HU for the treatment of HIV may be gaining dual benefit with enhanced activity of their anti-HSV drugs. One wonders whether HU could also enhance the activity of other agents, like famciclovir and adefovir dipivoxil, against other herpes viruses or even HBV. ■