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ICAAC 2002/IDSA 2002

Editor's Note: *The following summaries represent a selection of papers from among those presented at the 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), held September 27-30, 2002, in San Diego and the 40th annual meeting of the Infectious Disease Society of America (IDSA), held October 24-27, 2002, in Chicago. Antiretroviral therapy is not included. 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 ICAAC abstracts are available on the American Society of Microbiology web site at http://www.asmusa.org. The IDSA abstracts are available at http://www.idsociety.org.

— Stan Deresinski, MD, FACP

Antibacterial Agents

Fluoroquinolones

Coadministration of gatifloxacin or levofloxacin with calcium-fortified orange juice resulted in decreases in fluoroquinolone AUC of, respectively, 14% and 16% (*ICAAC A-1835*, *ICAAC A-1839a*). Depending upon drug dosage and the susceptibility of the target organism, this may be clinically significant.

Moxifloxacin has "balanced" elimination—approximately half is renally eliminated and half is hepatically eliminated. As a consequence, dosage adjustment is not required in the presence of renal insufficiency. In addition, no dosage adjustment of moxifloxacin is required for patients undergoing hemodialysis or continuous ambulatory peritoneal dialysis (*ICAAC A-1383*).

In a study that addressed the potential effect of community antibiotic use on susceptibility patterns in the hospital, it was found that the extent of fluoroquinolone use, especially levofloxacin, within a 10-mile radius of a hospital correlated with the prevalence of ciprofloxacin-resistant *P aeruginosa* in that hospital (*ICAAC K-1088*).

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Levofloxacin has been demonstrated to select methicillin-resistant clones from heteroristant populations of *S aureus* in vitro. Inpatient fluoroquinolone use (mostly levofloxacin) was associated with an increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) (*IDSA 399*). In addition, rapidly increasing use of levofloxacin at a Chicago hospital was associated with an increased incidence of both MRSA and vancomycin-resistant enterococcus infections (*ICAAC K-1087*). Finally, hospital restriction of fluoroquinolone use was associated with a significant decrease in the prevalence of not only ciprofloxacin-resistant *P aeruginosa*, but also of MRSA (*ICAAC K-1349*).

Prolongation of myocardial repolarization appears to be a class effect of fluoroquinolones. A retrospective review found that 4 of 36 patients, who were selected because they had had an EKG before and during levofloxacin therapy, had an increase from baseline in their QTc interval of 30-60 m/sec and 1 had an increase of > 60 m/sec. One patient had ventricular tachycardia with cardiac arrest (*IDSA 611*). It can be assumed, however, that the reason these patients had repeated EKGs is that they had known or suspected cardiac disease.

Since many pharmaceutical agents have also been reported to prolong the QTc interval, it is reasonable to examine the effects seen when 2 such agents are administered simultaneously. Among the patients enrolled in clinical trials evaluating moxifloxacin, 798 receiving moxifloxacin and 702 receiving a comparator took at least 1 drug known to prolong QTc interval. In patients who were followed with ECGs, the mean changes in QTc interval were similar for patients treated with moxifloxacin alone or moxifloxacin plus a QTc-prolonging drug. No significant difference in the frequency of adverse cardiovascular events between moxifloxacin and comparator groups was detected, suggesting that such combination use is safe (*IDSA 211*).

Carbapenems

Administration of meropenem infusions over 3 hours improves the likelihood of maintenance of drug levels above the MIC of susceptible pathogens for at least 40-50% of the dosing interval (*ICAAC A-1388*). This should, theoretically, lead to improved therapeutic outcomes.

Imipenem is a potent inducer of *AmpC*. Ertapenem, on the other hand, failed to induce *AmpC* beta lactamase expression by 20 strains of *P aeruginosa* (*ICAAC C1-1840*). Resistance of this organism to ertapenem requires the presence of both a relevant low frequency chromosomal mutation and either a plasmid encoding an ESBL or an *AmpC* ß-lactamase (*ICAAC C1-1841*).

Linezolid

The maximum median concentration of linezolid in ventricular CSF in 10 patients with "essentially noninflamed" meninges receiving 10 mg/kg IV every 12 hours was 5.4-6.5 µ/mL, representing 54% of plasma levels. The median minimum concentration in CSF was 0.7 µ/mL, 1.3-1.8 times higher than plasma levels (*IDSA 57*).

Adverse effects led to discontinuation of therapy with linezolid in 7 of 21 patients with mycobacterial or nocardial infections who received the drug for 2-26 months (mean 6.4 ± 6.5 months). Two developed peripheral neuropathy (which subsequently resolved in 1), 3 had progressive anemia not responsive to erythropoietin, and 1 had nausea and vomiting. The platelet count of 1 patient dropped below 100,000/mm^3 (*IDSA 609*).

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Linezolid resistance emerged in single isolates each of *S epidermidis* and *S oralis* during therapy with this drug (*ICAAC LB-10*).

Ketolides

Coadministration of ketoconazole and, to a lesser extent, itraconazole, increases exposure to simultaneously administered telithromycin (*ICAAC A-1834*). Coadministration of telithromycin with digoxin increased the bioavailability of the latter by 37% (*ICAAC A-1834*).

Mycobacterial Infections

M tuberculosis

No cases of active tuberculosis were uncovered at the time of detection of a positive PPD among 394 asymptomatic hospital employees with normal physical examinations. Since the results of chest radiography did not affect recommendations of chemoprophylaxis, the authors conclude that "chest radiography is not routinely indicated for asymptomatic hospital employees with positive tuberculin skin tests discovered as part of routine screening" (*IDSA 690*).

Two of 19,035 patients started on INH chemoprophylaxis died with laboratory evidence of hepatoxicity while on therapy. In 1, the liver tests had, however, returned to normal before death, and the other died with extensive metastatic malignant disease (*IDSA 698*). Thus, there were no deaths directly attributable to INH therapy (*IDSA 698*).

INH therapy of latent tuberculosis was well tolerated by 18 patients awaiting liver transplantation (*ICAAC L-677*).

The MIC90s of moxifloxacin and levofloxacin against 51 strains of *M tuberculosis*, 92% of which were resistant to at least 1 first-line antituberculous drug, were, respectively, 2 and 4 µ/mL (*ICAAC E-536*).

MOTT

Of 6 cancer patients from whom *M mucogenicum* was isolated, 5 had positive cultures of blood drawn through a central venous catheter. Therapy involved catheter removal and treatment with clarithromycin and a fluoroquinolone for 2-3 weeks (*IDSA 684*). A retrospective study concluded that allogeneic hematopoietic stem cell recipients are at increased risk of infection with nontuberculous mycobacteria. This is especially true of those with T-cell-depleted transplants and, even more so, those with GVHD. Infecting species included MAC, *M haemophilum*, *M xenopi*, *M abscessus*, and *M fortuitum* (*IDSA 679*, *IDSA 680*, *IDSA 681*).

Both linezolid and the newer fluoroquinolones show promise against nontuberculous mycobacteria. One hundred percent of isolates of *M marinum*, *M szulgae*, *M kansasii*, and *M xenopi* were inhibited by < 8 µg/mL of linezolid, while the MIC90s of *M avium* complex and *M terrae* isolates was > 32 µg/mL (*ICAAC E-535*). Separately, 100% of *M chelonae* isolates were susceptible to linezolid, as were 81% of *M fortuitum*; three of 3 *M abscessus* were also susceptible (*ICAAC E-540*).

One hundred percent of *M fortuitum* and 90% of *M chelonae* isolates were susceptible to moxifloxacin; only 1 of 3 *M abscessus* isolates were susceptible (*ICAAC E-540*). One hundred percent of *M fortuitum* group isolates were susceptible to both ciprofloxacin and levofloxacin with MICs < 1 µg/mL; most *M abscessus* isolates were resistant to both drugs. Seventeen clinical isolates of *M xenopi* were highly susceptible to moxifloxacin (MICs < 0.47 µg/mL) and gatifloxacin (< 0.32 µg/mL), but 10 isolates were resistant to levofloxacin (*IDSA 694*).

A patient with infection due to *M chelonae* resistant to clarithromycin was successfully treated with linezolid for 7 months (plus gatifloxacin for the first 3 months), when it was discontinued due to symptoms of peripheral neuropathy (*IDSA 265*).

Fungal Infections

Candida

In a placebo-controlled, randomized trial, fluconazole (150 mg weekly) was safe and effective in the prevention of vulvovaginal candidiasis in women with recurrent disease, but the protection was lost on discontinuation of azole administration (*ICAAC LB-8*).

In a prospective study of 249 critically ill surgical patients, 26 (10%) developed invasive candidiasis. Examination of the results of twice-weekly surveillance cultures found that rectal, urinary, and endotracheal aspirate colonization were associated with a significantly increased risk of subsequent infection, while oropharyngeal and gastric colonization were not. No patient colonized at fewer than 2 of the critical sites (rectal, urinary, endotracheal aspirate) developed invasive candidiasis (*IDSA 15*).

Three of 3 cases of catheter-related septic thrombosis caused by *Candida* involving peripheral veins were successfully treated with surgery or line removal, while only 3 of 7 with central vein involvement responded to any intervention (*IDSA 408*). While fluconazole was ineffective, caspofungin killed sessile *C albicans* growing as a biofilm. Amphotericin B was intermediate in its

activity (*ICAAC M-468*, *ICAAC M-1512*).

A retrospective analysis found that empiric use of fluconazole in an ICU was associated with an increased incidence of invasive disease due to non-*albicans* species with frequent fluconazole resistance, such as *C glabrata* and *C krusei* (*ICAAC K-1348*).

Caspofungin was superior to amphotericin B in the treatment of invasive candidiasis in a randomized, blinded trial (*IDSA 13*; *N Engl J Med*. 2002;347:2020-2029). Elevated caspofungin MICs did not predict treatment failure in this trial (*ICAAC M-1240*).

Cryptococcus

Fourteen of 31 organ transplant recipients with cryptococcosis had CNS involvement and 7 (50%) of these died (*ICAAC M-885*). A patient developed primary cutaneous cryptococcosis at the site of a puncture wound suffered while in a goat barn (*IDSA 37*).

Six non-AIDS patients with pulmonary cryptococcosis were successfully treated with voriconazole (*ICAAC M-880*). Maintenance antifungal therapy was safely discontinued in a group of selected AIDS patients with cryptococcal meningitis receiving antiretroviral therapy (*ICAAC M-473*).

Rhodotorula

Amphotericin B and posaconazole had the lowest MICs against 10 isolates of *Rhodotorula*. Patients with fungemia due to this organism responded to administration of an amphotericin preparation and removal of central venous catheters (*ICAAC M-900*).

Aspergillus

Only 4 of 15 patients with chronic granulomatous disease and 1 of 6 with Job's syndrome with invasive aspergillosis had detectable galactomannan antigenemia (*IDSA 345*).

Salvage therapy with caspofungin was successful in 50% of 32 patients with pulmonary aspergillosis, 23% of 13 with disseminated infection, and 33% of 6 with single-organ *Aspergillus* infection (*ICAAC M-868*). The combination of amphotericin B and trimethoprim/sulfamethoxazole was antagonistic against most *Aspergillus* isolates tested (*ICAAC M-849*).

Transplant Recipients/Neutropenia

Forty-three (45%) of 96 adult small-bowel transplant recipients experienced 59 episodes of invasive fungal infection; seventy-eight percent were due to *Candida*, 10% to *Aspergillus*, and there was 1 case each of cryptococcal and dematiaceous fungal infection. CMV disease was associated with an increased risk of fungal infection, and in this retrospective analysis, the prophylactic administration of amphotericin B lipid complex appeared to be protective (*ICAAC K-1231*).

A case control study of breakthrough invasive fungal infections in patients with hematological malignancies during itraconazole prophylaxis found that a trough itraconazole concentration > 500 ng/mL at the end of the first week was protective (*ICAAC M-890*). A systematic review of antifungal prophylaxis in cancer patients led to the conclusion that both fluconazole 400 mg qd and itraconazole oral suspension were associated with a reduction in the incidence of invasive fungal infection and mortality when compared to placebo (*ICAAC M-893*).

Micafungin was superior to fluconazole in a randomized, blinded trial of prophylaxis of invasive fungal infections in patients undergoing hematopoietic stem cell transplantation (80% vs 73.5% success rates; 95% CI for the difference, 0.9% to 12%) (*ICAAC M-1238*).

Endemic Mycoses

In a historical reprise, a case of disseminated coccidioidomycosis masquerading as mycosis fungoides was described (*IDSA 381*). (The title of the report of the first case of coccidioidomycosis was "*Un nuevo caso de micosis fungoidea con psorospermias*.")

The overall crude mortality among 36 patients with hematological malignancy who developed coccidioidomycosis (33% disseminated) was 29%. Only 55% of those tested had a positive serological test for coccidioidomycosis (*ICAAC M-886*).

A renal transplant recipient developed cellulitis (as well as colonic ulcers) due to *H capsulatum* (*IDSA 379*).

TNF Antagonists and Fungal Infection

Responses to a questionnaire by infectious disease clinicians participating in the Emerging Infections Network indicated that many had seen cases of both fungal and mycobacterial infections in patients receiving a TNF antagonist; half were also receiving treatment with methotrexate and/or prednisone (*IDSA 414*).

A patient with ulcerative colitis who had received a constant dose of prednisone for 1.5 years developed PCP 8 weeks after his second dose of infliximab (*IDSA 729*).

Two patients with rheumatoid arthritis receiving infliximab developed pulmonary cryptococcosis and 1 developed invasive pulmonary aspergillosis (*IDSA 374*, *IDSA 376*, *IDSA 373*). Fatal disseminated histoplasmosis was reported in a patient with rheumatoid arthritis given etanercept (*IDSA 378*).

Six of 11 allogeneic bone marrow recipients given infliximab for severe graft-vs-host disease developed

invasive fungal infections, while only 4 of 41 who did not receive this monoclonal did so (*ICAAC M-1234*).

Amphotericin B

Administration of amphotericin B by continuous infusion in doses as high as 2 mg/kg/d was reported to be well tolerated (*ICAAC M-889*).

A meta-analysis of studies comparing conventional vs lipid formulations of amphotericin B found that use of the latter was associated with an OR of 0.75 (95% CI 0.55-1.02) for death, 0.36 (0.29-0.45) for nephrotoxicity, and 0.32 (0.16-0.65) for infusion-related toxicity. A subanalysis found that the use of liposomal amphotericin B (AmBisome) was associated with significantly lower mortality (OR 0.66, 95% CI 0.45-0.98) than was conventional amphotericin B (*ICAAC M-888*).

Viral Infections

Hepatitis Viruses

Inclusion of an inactivated hepatitis A vaccine as part of routine childhood immunizations was followed by a > 90% reduction in the incidence of acute hepatitis A infection in all age groups. It is speculated that control of the disease in 2-4 year olds markedly reduced transmission to older unvaccinated individuals (*IDSA 825*).

Because exacerbation of HBV infection is reported to occur in 20-50% of infected individuals following cancer chemotherapy, it was recommended that all chemotherapy recipients be screened for HBV infection (*IDSA 786*).

In an observation that raises concern about reliance on HCV antibody testing in screening organ donors, transplantation of organs and tissue, including of a patellar tendon, from an HCV-antibody-negative but HCV-RNA-positive donor, was associated with apparent transmission of HCV infection (*ICAAC LB-17*).

A case control study involving 450 HCV-infected patients and 757 controls found that hospital stays, GI endoscopy, some dermatological procedures, and cocaine use are risk factors for community-acquired HCV infection in France (*ICAAC V-682*). HCV may also be transmitted from mother to child. Evaluation of 130 HCV+/HIV- mothers and their 151 babies found a rate of vertical HCV transmission of HCV of 2%. All transmissions came from mothers who were viremic at the time of delivery. Higher levels of viremia were associated with increased risk of transmission (*IDSA 789*).

Vaccination against HAV and HBV is recommended for susceptible patients who are chronically infected with HCV. However, while 83% of HCV-infected patients responded to HAV vaccine, only 21% responded to HBV vaccine. Most were vaccinated while they were receiving interferon and ribavirin (*IDSA 800*).

While hepatitis E infection is predominantly acquired in lesser-developed countries, 15 cases apparently acquired in Europe are described (*ICAAC V-240*).

Herpesviruses

HSV. HSV-2 may no longer be the dominant herpesvirus in genital herpes—at least in Nova Scotia where 71% of viral isolates from genital lesions of women younger than 31 years of age were HSV-1; this was true of isolates from 46% of men. Among females, HSV-1 represented 85% of genital isolates from those younger than 16 years but only 4.5% in those older than 60 years. This is likely a reflection of changing sexual habits (*ICAACL-771*).

Sex can be anxiety-provoking when your partner is HSV-2 infected and you are not. In a placebo-controlled, randomized trial involving HSV-2-discordant couples, administration of 500-mg valacyclovir daily to HSV-2-positive source partners for 8 months was associated with a 50% reduction in infection transmission (*ICAAC LB-3*).

In confirmation of previous studies, it was reported that HSV-2 seropositivity was associated with an 80% increased risk of HIV acquisition among men having sex with men (*ICAAC L-773*). Valacyclovir was effective in suppression of anogenital HSV infection in HIV-infected patients in a randomized, blinded, placebo-controlled trial (*IDSA 653*).

HSV-2 is the usual cause of recurrent "aseptic" meningitis in adults. Of 20 patients with meningitis whose CSF contained HSV genome (all but 1 HSV-2), 35% had prior episodes of aseptic meningitis vs 3% of HSV-negative controls with a negative HSV PCR. HSV cases were more likely to have photophobia, nuchal rigidity, and vomiting but less likely to have altered mental status. The median CSF glucose concentration in the HSV cases was 59 mg/dL (58 mg/dL in controls), the protein was 101 mg/dL (45 mg/dL in controls), and WBC was 464/mm^3 (vs 7/mm^3) with 925 lymphocytes (vs 6%) (*IDSA 813*).

HSV can frequently be isolated from respiratory secretions of critically ill patients, but its pathogenicity in that circumstance is usually moot. Of 18 mechanically ventilated patients with HSV tracheobronchitis, two-thirds had bronchospasm. Twenty-eight percent had other sites of active HSV infection. Eighty-eight percent received acyclovir; no patient died as a consequence of HSV infection (*IDSA 812*).

VZV. A surprisingly low frequency of VZV susceptibility was found in US Navy recruits: Only 5.5% lacked antibody to this herpesvirus (*IDSA 820*).

Varicella virus could not be detected in breast milk of 7 women who had received attenuated varicella vaccine (*ICAAC G-141*).

VZV reactivation occurred in 34 (12%) of 285 lung transplant recipients at a median time of 508 days posttransplantation. Sixty-one percent had localized zoster, and 39% had disseminated infection (*ICAAC V-1250*).

Of 10 cases of retinal necrosis, examination of vitreal biopsies by PCR found evidence of HSV in 3 and VZV in 5 (*ICAAC V-932*).

CMV. Valganciclovir (900 mg po o.d.) and ganciclovir (1000 mg po t.i.d.) were comparably effective in the prevention of CMV disease in high-risk (D+/R-) heart, liver, and kidney transplant recipients in a randomized trial when administered from days 10 through 100 posttransplant (*ICAAC LB-4*).

HHV8. Salivary shedding of HHV8 in HIV-infected individuals is highest in those with the highest CD4 counts. This may account for the lack of reduction in HHV8 seroprevalence in gay men in San Francisco. The explanation for this observation is unknown (*IDSA 826*).

Metapneumovirus

Human metapneumovirus caused a febrile respiratory illness in 43 individuals, 41 of whom were children, in Australia (*IDSA 33*). Nasopharyngeal swabs or throat swabs from 11 of 71 patients in Saskatchewan with upper respiratory tract infection in October and January 2001 had evidence of metapneumovirus DNA by PCR. Their age ranged from 6 months to 89 years of age (*ICAAC V-475*). Of 675 respiratory specimens from children hospitalized for respiratory disease, 45 were positive for metapneumovirus, 18% for RSV, 6% for parainfluenza virus, and 3.3% for influenza. Only one-fifth of metapneumovirus infections occurred in children younger than 6 months of age compared to 59% of RSV cases, and they peaked in frequency in March while RSV peaked in January and influenza in February (*IDSA 774*).

In a prospective study of respiratory infections in adults during 2 winters, 4.3% of 984 illnesses were due to human metapneumovirus with peak activity in February. The clinical syndrome in elderly subjects was similar to that due to influenza or RSV. Young adults had nasal congestion, sore throat, cough, and hoarseness (*IDSA 775*).

Parvovirus

Twelve (13%) of 91 HIV-infected children receiving antiretroviral therapy had serological evidence of parvovirus B19 infection and 3 of the 12 had PCR evidence of chronic infection, but none had associated anemia. These results did not significantly differ from those found in a non-HIV-infected control group, indicating that B19 DNA can persist in both HIV-infected and HIV-uninfected children in the absence of related anemia (*ICAAC V-254*).

An 18-year-old woman with parvovirus B19 infection had intraabdominal lymphadenopathy with central necrosis that had resolved 4 weeks later (*IDSA 773*).

Enterovirus

Seventeen percent of 54 cases of neonatal enterovirus infection were judged to be severe, with 44% having myocarditis, 33% encephalitis, and 22% sepsis. The mean age of onset of the severe cases was 1.8 days, compared to 7.5 days for the nonsevere cases. Most of the nonsevere cases had enterovirus detected in their CSF, but pleocytosis was absent in half of these (*IDSA 34*).

Adenovirus

Two patients with acute leukemia in remission who had received hematopoietic stem cell transplants died of adenovirus pneumonia despite administration of cidofovir and IVIG (*IDSA 762*).

Measles

Kawasaki disease should be added to the list of illnesses associated with false-positive IgM antibody tests for measles, a list that includes infection with parvovirus B19, rubella, and HHV6, as well as in patients with rheumatoid factor and those with high levels of IgG measles antibody (*IDSA 770*).

CNS Infections

Two cases of California-La Crosse meningoencephalitis that mimicked HSV encephalitis, including with the presence of focal temporal lesions in one, occurred in Michigan (*IDSA 785*).

When compared to an untreated cohort, 15 patients with St. Louis encephalitis given interferon-α had greater neurologic improvement, and none progressed to quadriplegia, a complication observed in 3 of the 17 controls (*IDSA 823*).

None of 9 children with congenital CMV infection treated with IV ganciclovir developed progressive hearing loss (*IDSA 808*).

Protozoan Infections

A case of *P falciparum* infection in a nurse resulted from a needle stick injury incurred during phlebotomy

of a patient with malaria (*ICAAC P-794*).

Evaluation of IgG avidity testing for the diagnosis of toxoplasmic lymphadenitis found that the presence of low avidity was not reliable in the diagnosis of recent infection. However, a high avidity result was observed only in patients who had developed their adenopathy at least 4 months earlier. Thus, a high avidity result in a patient with recent onset lymphadenopathy suggests a diagnosis other than toxoplasmosis (*IDSA 270*).

Five of 6 solid organ transplant recipients in Spain with visceral leishmaniasis responded to treatment with liposomal amphotericin B, but 3 relapsed (*ICAAC P-786*).

An AIDS patient with CD4 count of 44 cells/UL with babesiosis refractory to other therapies responded favorably to exchange transfusion and administration of atovaquone plus proguanil (*IDSA 728*).

STDs

The prevalence of asymptomatic *Chlamydia trachomatis* infection in male college ROTC cadets in Washington state was 2.5% (*IDSA 657*). The prevalence of urethral *Trichomonas vaginalis* in males presenting to an STD clinic, as determined by PCR examination, was 13%, but its presence was not associated with urethritis in the absence of coexisting gonorrhea or of *Chlamydia* infection (*IDSA 660*).

The prevalence of ciprofloxacin resistance among *N gonorrheae* isolated from STD clinics at each of 4 sites in California (Long Beach, San Francisco, Orange County, San Diego) ranged from 4.1% to 6.4%. Three groups had especially high rates of resistance: Asians (16%), injection drug users (16.7%), and recent consumers of antibiotics (18.8%) (*IDSA 19*).

Thirty-three of 100 male college undergraduates who underwent genital swabbing with emery paper and saline-moistened Dacron swabs and also provided urine specimens had evidence of human papillomavirus infection (*IDSA 655*). Anal cytological examination of 1300 HIV-negative men who have sex with men demonstrated squamous intraepithelial lesions in 29% and high-grade squamous intraepithelial lesions in 5%. The investigators point out that this is a low estimate of the true incidence given the low sensitivity of cytology (*IDSA 654*). ■

CME Questions

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This testing procedure has proven to be an effective learning tool for adults. If you have any questions about the new testing method, please contact Customer Service at 1-800-688-2421.

9. Which one of the following is correct?

a. The dose of moxifloxacin should be adjusted downward in the presence of renal insufficiency.
b. The dose of moxifloxacin should be adjusted downward in patients undergoing peritoneal dialysis.
c. The dose of moxifloxacin should be adjusted downward in patients undergoing continuous ambulatory peritoneal dialysis.
d. Moxifloxacin is active in vitro against both *M tuberculosis* and *M fortuitum*.

10. Which one of the following is correct?

a. Caspofungin was superior to amphotericin B in the treatment of invasive candidiasis in a randomized trial.
b. A trough itraconazole level >100 ng/mL was associated with protection against breakthrough fungal infections during prophylaxis in patients with hematologic malignancies.
c. Hepatitis B vaccine was reliably immunogenic in cohort of patients with chronic HCV infection.
d. Valacyclovir administration did not prevent transmission of HSV-2 infection in discordant couples.

11. Which one of the following is correct?

a. Human metapneumovirus (HMP) can cause an illness resembling that due to respiratory syncytial virus.
b. Metapneumovirus infections are limited to infants.
c. Acquisition of hepatitis E virus infection is limited to lesser developed countries.
d. Genital herpes is rarely caused by HSV-1.

Answers: 9(d); 10(a); 11(a)

In Future Issues:

Therapeutic Drug Monitoring of Vancomycin

UPDATES

By Carol A. Kemper, MD, FACP

FluMist Recommended for FDA Approval

Source: BioWorld Online. December 18, 2002. www.bioworld.com.

An advisory panel has recommended FDA approval of FluMist, the first intranasal influenza vaccine, for people 5-49 years of age. In double-blind, placebo-controlled studies, FluMist, which contains live attenuated influenza A and B virus and is manufactured by MedImmune Inc., was 93% effective in preventing culture-proven influenza infection. Nonetheless, an earlier FDA Advisory Panel, which convened in July 2001, postponed recommendations for approval pending additional safety data.

Newer efficacy data reviewed by the committee demonstrates that the vaccine is sufficiently safe to justify approval, although an increased risk of asthma was observed in children aged 18-35 months. Hence, the recommendation to limit approval to children aged 5 and older—although the ability to administer an intranasal vaccine to younger children would have obvious advantages.

In addition, the panel requested additional vaccine efficacy data for patients aged 50 and older, as well as on shedding of vaccine virus from vaccine recipients. Viral shedding, such as during a sneeze, was found to occur in 80% of recipients and may be observed for up to 21 days following vaccination.

While transmission of vaccine virus was observed in day care attendees, the frequency and clinical significance of this occurrence is not yet known. Experts speculate that the vaccine may cost about $40. ■

Britain Extends Pet Travel to United States

Source: ProMED-mail post, November 19, 20, and 21, 2002; www.promedmail.org.

Great Britain has announced the extension of the popular Pet Travel Scheme to the United States and Canada. This is the first time that cats and dogs from the United States with the appropriate certification will be allowed to enter the United Kingdom without 6 months of quarantine (although some pets may still be quarantined for 2-3 days until their ID and certification can be verified).

Since the Pet Travel Scheme was first introduced in February 2000, more than 75,000 cats and dogs from Europe and other designated countries have traveled to the United Kingdom. The plan is also being extended to several other countries, including New Zealand, Australia, and Japan. In order to qualify for entrance into the United Kingdom, eligible pets must meet all of the requirements, including a recent veterinary exam and certification of good health, current deworming, and microchip ID.

The United Kingdom has understandably been cautious in opening their country to foreign pets. The islands have been largely rabies-free for many years, although the European Bat Lyssavirus 2 was detected there in 2002. The last rabies-like neurologic illness occurred there in 1992, not including imported cases. Recently, an artist and ostensible bat-lover living in Scotland developed a severe neurologic illness, raising red flags in the United Kingdom, but preliminary studies were negative for rabies. ■

Nipah Confirmed in Bangladesh

Source: *Eurosurveillance Weekly*. September 19, 2002.

Investigators now believe that an outbreak of severe encephalitic-like illness that occurred in the remote village of Meherpur, Bangladesh, in April-May 2001 was due to Nipah virus or a closely related viral species. Twenty-eight adults, 9 of whom died, developed an acute, febrile neurologic illness, which was initially believed to be secondary to Japanese Encephalitis virus. Serological studies now point to Nipah as the culprit. A similar outbreak occurred in eastern India near the Bangladeshi border in early 2001. Although Nipah virus may result in subclinical infection, about 50% of the clinically apparent cases may be fatal.

The natural host of Nipah virus is believed to be certain species of the fruit bat, although the large outbreak that occurred in Malaysia in 1998-1999 was thought to be related to occupational exposure to pigs. The route of transmission to animal and humans is not known, but human-to-human transmission has not been documented. This outbreak fuels suspicions that Nipah may become more widespread in the future. ■