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Conference Summaries: ICAAC 2001, IDSA 2001, and ASTMH: Part III

CONFERENCE COVERAGE

Editor's Note: *The following summaries represent a selection of papers from those presented at the 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 conferences may have differed. The abstracts can be found online at the URLs given. The 41st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Chicago, Ill, Dec. 16-19, 2001; http://www.icaac.org. The 39th Annual Meeting of the Infectious Diseases Society of America, San Francisco, Calif, Oct. 25-28, 2001; http://www.idsociety.org. The 50th Annual Meeting of the American Society of Tropical Medicine and Hygiene, Atlanta, Ga, Nov. 11-15, 2001; http://www.astmh.org. —* ***Stan Deresinski, MD, FACP***

Streptococcus agalactiae

CDC GUIDELINES FOR PREVENTION OF TRANSMISSION OF GROUP B streptococci from mother to child during pregnancy and delivery include the use of macrolides in penicillin allergic patients. However, 111 of 346 (32%) *S agalactiae* vaginal isolates at 1 US hospital were resistant to macrolides, with 62% of these having the MLSB phenotype. (*ICAAC #326.*)

Streptococcus viridans

Risk factors for viridans streptococcal sepsis in children with malignancies were profound prolonged neutropenia and prophylaxis with trimethoprim/sulfamethoxazole; patients with sepsis due to this group of organisms were at increased risk of developing invasive fungal infection. (*IDSA #77.*)

Penicillin resistance was detected in 7.3% of 191 blood culture isolates of *Streptococcus viridans* from 9 Canadian provinces. Of

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these 191, 39.8% were resistant to erythromycin, 10% to clindamycin, 6% to levofloxacin, 1% to gatifloxacin, and 0.5% to linezolid. None were resistant to telithromycin, moxifloxacin, or moxifloxacin. (*ICAAC #728*.)

Pseudomonas aeruginosa

Antibiotic Resistance. Thirty-nine percent of *P aeruginosa* collected at 97 US community hospitals were resistant to levofloxacin and 34% were resistant to ciprofloxacin. (*ICAAC #79*.)

The mutant prevention concentration (MPC90) of 119 *P aeruginosa* isolates susceptible in vitro to both agents was 4 µg/mL for ciprofloxacin and 16 µg/mL for levofloxacin. 64% of isolates had a levofloxacin MPC that exceeded the usual serum levofloxacin C_{max}; the comparable result for ciprofloxacin was 40%. (*ICAAC #729*.) This suggests that resistance may more readily emerge in *P aeruginosa* in the face of levofloxacin therapy.

Imipenem resistance in *P aeruginosa* due to the loss of OprD was associated with decreased fitness manifested both by reduced growth in vitro and reduced virulence in a murine peritonitis model. (*ICAAC #649*.)

Colistin/Polymyxin B. Nine of 36 (25%) patients infected with *P aeruginosa* resistant to both imipenem and ciprofloxacin and containing the VIM-1 beta-lactamase were bacteremic, while only 3 of 31 infected with *P aeruginosa* not containing this carbapenemase had bloodstream infection. Despite treatment with colistin, 3 of the 9 developed endovascular infection and 1 strain became resistant to this polymyxin antibiotic during therapy. (*ICAAC #1183*.) Five of 12 solid-organ recipients on mechanical ventilation with multidrug resistant *P aeruginosa* pneumonia had improvement with parenteral administration of colistin. (*IDSA #243*.) A review of patients who had received polymyxin B parenterally for multidrug resistant infections found that 7 of 50 (14%) had a doubling of serum creatinine to > 2.0 mg/dL. (*IDSA #553*.) A retrospective study found that 16 of 23 patients with nosocomial infections treated with parenteral colistin for a median 14 days had clinical and bacteriological cure. Four developed increased creatinine, but no patient required dialysis. (*IDSA #105*.)

Antibiotic Combinations. When combined with a beta-lactam (cefepime or piperacillin/tazobactam), gentamicin and levofloxacin each had similar in vitro effects, with synergy against the majority of *P eruginosa* strains. However, more rapid bactericidal activity was achieved with combinations containing gentamicin. Cefepime was more likely to demonstrate synergy with levofloxacin or gentamicin than was piperacillin/tazobactam. No antagonism was observed. (*ICAAC #334*.)

Novel Therapy. The efflux pump inhibitor, MC-04,124, significantly increased the activity of both levofloxacin and azithromycin against *P aeruginosa* and *E coli* expressing the *AcrAB* efflux pump, both in vitro and in mouse infection experiments. (*ICAAC #340*.)

Stenotrophomonas

In vitro studies of 23 clinical isolates of *S maltophilia* found apparent synergy between ticarcillin/clavulanate and aztreonam. (*ICAAC #338*.)

Antibiotics-Miscellaneous Issues

Linezolid. Combinations of linezolid with quinolones were most commonly either antagonistic or indifferent against *S aureus*, *S pneumoniae,* and *E faecalis* in vitro. A similar finding resulted from the com-

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bined administration of linezolid and ciprofloxacin in an experimental mouse. (*ICAAC #330*.)

Examination of data from a randomized trial found that patients with MRSA assigned linezolid who were "dischargeable" had shorter durations of hospitalizations (8 days) than those assigned vancomycin (14 days). This presumably is the consequence of the ability to administer linezolid per os. (*ICAAC #398*.)

A patient with *Nocardia* infection unresponsive to standard therapy had resolution of infection after treatment with linezolid. (*IDSA #173*.)

A number of reports of adverse hematological events in patients receiving linezolid were presented. These included a patient with myelodysplasia and severe fatal pancytopenia, and two patients with both leukopenia and thrombocytopenia. (*IDSA #466, IDSA #467*.) In a retrospective analysis, a decrease in platelet count of > 25% occurred during 12 of 27 courses of linezolid, with all decreases occurring within 2 weeks of initiation of therapy with this drug. The severity of illness of the patients analyzed was, however, a confounding issue. (*IDSA #470.*) A retrospective review at one hospital found that 9 of 19 (47%) who received linezolid for > 5 days had a decrease (30-79%) in platelet count, with 6 of the 9 decreasing to < 100.000/mm^3. All 9 had received linezolid for > 10 days (median, 19.1 days); 37% of patients receiving the drug for > 10 days developed counts below this level. (*IDSA #469*.)

Imipenem. Imipenem was given in high dose (100 mg/kg/d in divided doses) to 145 infected children in an ICU, with resultant 100% time above the MIC of 100% against 8 of 10 pathogens, including some *P aeruginosa*. No toxicity was observed. (*ICAAC #936.*)

Fluoroquinolones & Macrolides. An analysis of 202 reports to the FDA of torsades de pointes associated with macrolide or fluoroquinolone use found that 77% were associated with macrolide use and that concomitant administration of contraindicated drugs was involved in 31% of these cases. Twenty patients died. Approximately one fifth of the 202 patients received other drugs known to prolong the QT interval, cardiac disease was present in approximately one-half and renal disease in one tenth. Seventeen percent had hypokalemia or hypomagnesemia. (*ICAAC #634*.)

Administration of levofloxacin to healthy volunteers in single doses of 500 mg, 1000 mg, and 1500 mg was associated with mean increases in QTc from baseline of, respectively, 1.4, 2.8, and 6.9 msec. Comparable results after twice the usual dose of ciprofloxacin (1500 mg) and moxifloxacin (800 mg) were 2.3 msec and 16.3 msec. (*ICAAC #639a*.)

Four cases of torsades were reported in patients receiving gatifloxacin; each of the 4 either had baseline QTc prolongation or were receiving other drugs known to prolong the QT interval. Three of the 4 had elevated serum creatinine, 2 had hypomagnesemia and 1 hypokalemia. (*ICAAC #632*.)

Moxifloxacin, like other fluoroquinolones, undergoes enteral recirculation. (*ICAAC #40*.) The high intracellular levels of moxifloxacin achieved within macrophages may be the consequence of the fact that moxifloxacin is a poor substrate of the MRP1 and MRD1 transporter efflux pumps. (*ICAAC #2208*.) Coadministration with combination oral contraceptives is associated with a 13% decrease in moxifloxacin C_{max}, a 20% increase in its clearance, and a 15% decrease in it AUC, probably as the result of estrogen induction of Phase II glucuronidation. (*ICAAC #41*.)

Neutropenia and Infection

Prophylaxis. The incidence of bacteremia in EORTC trials of febrile neutropenic patients was higher in 2000 than in 1993 (28% vs 23%) as was the incidence of single-agent Gram-negative bacteremia (12% vs 6.5%). The likelihood of fluoroquinolone resistance was significantly lower in patients not receiving fluoroquinolone prophylaxis; 38% of *E coli* were resistant during the period of high quinolone prophylaxis (1993), while only 20% were resistant during a period of low prophylaxis (2000). (*ICAAC #773*.)

Oral administration of ofloxacin was ineffective as a prophylactic strategy in a small randomized trial in patients with neutropenia. (*ICAAC #781*.)

Empiric Antibacterial Therapy. Comparable results were obtained in febrile neutropenic patients randomized to receive empiric therapy with amikacin plus either piperacillin/tazobactam or cefepime. (*ICAAC #771*.) No significant difference in outcome was observed in a trial in which 562 patients with hematologic malignancies and febrile neutropenia were randomized to receive either cefepime, meropenem or piperacillin/tazobactam plus an aminoglycoside. (*ICAAC #775*.) There was no significant difference in response between treatment arms among 251 patients with malignancy, neutropenia and fever randomized to receive either imipenem (500 mg q.6h.) or cefepime (2 g q.8h.). (*IDSA #106*.)

A metaanalysis of 44 randomized trials of empiric therapy in febrile neutropenia involving 7411 patients found no benefit to the addition of an aminoglycoside to a beta lactam. However, combination therapy was asso-

ciated with a greater frequency of serious adverse events. Ceftazidime or carbapenem monotherapy was superior to combination therapy using a narrower spectrum beta lactam. (*ICAAC #772*.)

In an EORTC trial, neutropenic cancer patients with persistent fever despite 48-60 hours of empiric therapy with piperacillin/tazobactam were randomized to have either vancomycin or placebo added. Patients with FUO, clinically documented infection and piperacillin/tazobactam-susceptible Gram-positive bacteremia were included. There was no benefit to the addition of vancomycin. (*ICAAC #774*.)

Blood Culture Surveillance. A case-control study of blood cultures obtained during antibiotic therapy for febrile neutropenia found that 46 of 320 (14.6%) yielded pathogens while 14 (4.4%) had only contaminants. The most commonly isolated organisms were coagulase negative staphylococci (28.2%), *Klebsiella* (13%), corynebacteria (10.9%), and, at 8.7% each, *Pseudomonas*, *E coli,* and *S aureus*. The presence of a central venous catheter and greater comorbidity were risk factors for breakthrough bacteremia. (*IDSA #78*.)

***P aeruginosa* Infection.** A retrospective review found 46 cases of invasive *P aeruginosa* infection (19 with bacteremia, 11 with bacteremia and pneumonia, and 6 with pneumonia) that occurred a median of 49 days after hematopoietic stem-cell transplantation. The attributable morality was 31.4% despite an average of 16.8 days of treatment with combination therapy. Ten of 28 survivors (35.7%) had a relapse of *P aeruginosa* infection a median of 9 days after stopping antibiotic therapy, and all 10 died. The use of corticosteroids or antithymocyte globulin ATG were associated with a higher risk of relapse. The authors suggest that antibiotics be administered for at least 4 to 6 weeks in the treatment of *P aeruginosa* bacteremia in these patients. (*ICAAC #780*.)

Anthrax

Serial passage of *B anthracis* Sterne in subinhibitory antibiotic concentrations was associated with the selection of clones resistant to ciprofloxacin, alatrofloxacin, gatifloxacin, erythromycin, azithromycin, and clarithromycin. Serial passage in the presence of doxycycline increased the its MIC from 0.025 µg/mL to as high as 0.1 µg/mL. (*ICAAC #UL-6*.)

A nasally administered vaccine consisting of a microparticulate formulation of protective antigen was protective in mice challenged intraperitoneally with *B anthracis*. (*ICAAC #UL-8*.)

Tularemia

Landscaping activities were identified as a risk factor for developing primary pulmonary tularemia during an outbreak in Martha's Vineyard. One patient had "mowed over a rabbit." (*IDSA #29*.)

Lyme Disease

One hundred eighty patients with erythema migrans were randomized to receive one of 3 regimens and followed for 30 months: a single 2-gram IV dose of ceftriaxone followed by doxycycline for 10 days, 10 days of doxycycline, or 20 days of doxycycline alone. Clinical cure rates were, respectively, 87%, 88%, and 87%. One patient developed meningitis 8 days after a 10-day course of doxycycline. Thus, a 10-day course of doxycycline with or without a single dose of ceftriaxone was as efficacious as a 20-day course in patients with early Lyme disease. (*IDSA #5*.)

Miscellaneous

A case of Bezold's abscess, a deep neck abscess occurring as a complication of mastoiditis, is described. (*IDSA #180*.)

Studies in healthy volunteers found that administration of piperacillin/tazobactam 4.5g q6h achieved a 44% T > MIC for MIC values of < 1 6 mg/ml, while 3.375 g q4h achieved 42% T > MIC for MIC values of < 32mg/ml for pathogen simplicated in serious infections. (*ICAAC #950.*)

Vitamin and mineral supplementation in an elderly institutionalized population was not associated with a reduction in infectious episodes in a randomized placebo controlled trial. (*ICAAC #1212*.)

A retrospective analysis described 30 cases of *Bacillus cereus* infection in an Orthopedic-Trauma ward. 23 had had traumatic limb fractures (18 open) and 3 had injury without fracture. (*ICAAC #2284*.)

174 of 179 patients with an RPR > 1:32 had a positive confirmatory test for syphilis; 72% of the men and 36.5% of the women were HIV infected. One third of the total had primary or secondary syphilis. (*IDSA #905*.)

Nineteen of 77 (24.7%) patients with pacemaker related bacteremia who did not have generator infection and who had no detectable vegetation on transesophageal echocardiography were successfully managed without device removal. (*ICAAC #1340*.)

In a prospective randomized placebo-controlled trial, the administration of oral nonabsorbable antibiotics for

1 week prior to cardiac surgery did not affect the incidence of perioperative endotoxemia, cytokine activation during cardiopulmonary bypass, or the occurrence of postperfusion syndrome. (*IDSA #238*.)

Mycobacteria

MOTT

Epidemiology. An outbreak of furunculosis due to *M fortuitum* was associated with contaminated foot baths at a nail salon. (*IDSA #313*.) Both a true outbreak and a pseudo-outbreak of *M fortuitum* occurring in in-patient HIV units were traced to contaminated ice machines. (*IDSA #202, IDSA #201*.) Another pseudo-outbreak, this due to *M simiae*, resulted from a contaminated hospital water supply. (*IDSA #312*.)

Five of 52 (9.6%) of patients who underwent laser-assisted in situ keratomileusis (LASIK) procedures developed keratitis due to *M szulgai*. The surgeon used a saline lavage that was chilled in a tub of ice. An indistinguishable (by PFGE) strain of *M szulgai* was detected in the drain of the source ice machine. The authors warn that ice water should not be used in association with surgical procedures. (*ICAAC #478*.)

A cluster of patients from whom *M lentriflavum* originally misidentified as *M simiae* Complex was described. (*IDSA #333*.)

Treatment. One hundred percent of *M fortuitum* group isolates were susceptible to both ciprofloxacin and gatifloxacin with MIC90s of, respectively, 1 µg/mL and < 0.12 µg/mL. While only 2 of 26 (8%) *M chelonae* isolates had an MIC to ciprofloxacin < 2 µg/mL, the gatifloxacin MIC50 was 1 µg/mL and the MIC90 4 µg/ml. *M abscessus* was generally resistant to both fluoroquinolones. (*ICAAC #723*.)

The MICs of linezolid against *M gordonae*, *M kansasii*, and *M marinum* were, respectively, 0.5, 10 and 2.0 µg/mL, while against *M xenopi* it was 4.0 µg/mL and against *M avium* it was 16 µg/mL. (*IDSA #572*.)

The combination of mefloquine, moxifloxacin and ethambutol was as effective as clarithromycin in a murine model of *M avium* infection. (*ICAAC #1374*.)

The combination of rifampin and amikacin had efficacy in a murine model of *M ulcerans* infection. (*ICAAC #1376*.)

M tuberculosis

Epidemiology. Of 64 infants in a neonatal ICU exposed to a nurse with cavitary pulmonary tuberculosis, and all 51 who were traced were given INH or rifampin preventive therapy. Skin tests were only performed after 6 months, because of potentially misleading results in the first month of life. None of the 51 developed active tuberculosis and all tolerated preventive therapy. (*IDSA #205*.)

A strain of *M tuberculosis* associated with an outbreak in a county jail was subsequently transmitted to people in the community where it has remained prevalent 2 years later. (*IDSA #314*.)

Diagnosis. The sensitivity of a first, first plus second, and first plus second plus third sputum smear for the detection of acid fast bacilli was, respectively, 67%, 72%, and 73%, suggesting that the third smear may be of limited value. (*IDSA #334*.)

Direct testing of sputum for *M tuberculosis* DNA by MTD (Gen-Probe) was specific but highly insensitive, precluding its use for diagnosis and decision making concerning patient isolation. (*IDSA #339*.) It should be noted, however, that an enhanced version of this test (E-MTD) has been reported to have greater accuracy and predictive value than the MTD (*JAMA*. 2000;283:639-645).

Preventive Therapy. A retrospective analysis found that patients given pyrazinamide/rifampin were more likely to complete therapy than those given INH (66% vs 53%), but also more likely to develop significant hepatitis with > 4 × baseline transaminases (13.2% vs 3.8%). (*IDSA #342*.) Eight of 29 (27%) patients prematurely discontinued preventive therapy with pyrazinamide and rifampin, 2 because of gastrointestinal intolerance and 6 because of symptomatic hepatitis. These resolved on discontinuation of the drugs. (*IDSA #340*.) In contrast to these reports, however, the risk of hepatitis (AST > 50 IU) did not differ between recipients of pyrazinamide/rifampin for 2 months and INH for 6 to 12 months (12% vs 10%) in a randomized trial and completion rates were greater for the former regimen (55% vs 22%). (*IDSA #341*.)

Clinical Disease. Nine patients with oral tuberculosis, 3 of whom had normal chest X-rays, were seen at one Spanish center over 10 years. The most common manifestations were ulceration of tongue (4), palate (2), or lip (1). Two patients had granulomatous masses of the gingival. (*ICAAC #2182*.)

In Mexico 20 patients with pyuria and a positive acid fast smear of urine were evaluated. Radiographic abnormalities suggestive of genitourinary tuberculosis were seen in 4 (20%). Three patients had *E coli* urinary tract infection, while mycobacteria were recovered from urine culture in 5: *M tuberculosis* in 2, and *M bovis*, *M fortuitum*, and *M triviale* in one each. PCR for *M tuberculosis* DNA performed on urinary sediment was posi-

tive in the 2 patients with positive cultures for this organism, as well as in an additional 2 with negative cultures. (*IDSA #185*.)

Two of 57 patients treated with infliximab developed severe tuberculosis. (*ICAAC #1372*.) Five patients with either tuberculosis or coccidioidomycosis and CD4 lymphocytopenia without HIV infection had return of CD4 counts to normal with therapy of the granulomatous infection are described. All had normal CD4/CD8 ratios at the time their CD4 cell counts were reduced. (*IDSA #175*.)

The most common manifestations of paradoxical worsening of tuberculosis in 36 HIV infected patients were lymphadenopathy (64%), fever (44%), and worsening pulmonary infiltrates (44%). The median time of onset was 8 weeks after initiation of antituberculous therapy and 2 weeks after initiation of ART. Two patients had tuberculous relapse. (*IDSA #322*.)

Treatment. Molecular analysis of multiple isolates from patients with disseminated tuberculosis found more than one strain in 6% of patients. This suggests the potential need for susceptibility testing of more than one isolate from a patient. (*ICAAC #2183*.)

Linezolid was active in vitro against 40 strains of *M tuberculosis*, including 10 strains resistant to one or more conventional antituberculous drugs. (*IDSA #571*.) In a separate study, the MIC90 of linezolid against 117 strains of *M tuberculosis*, including 44 resistant to at least one first line drug, was 1.0 µg/mL. (*ICAAC #1413*.)

Virus

Herpes Virus

Genital HSV Infection. The median time to a first recurrence in 83 patients with primary genital HSV-1 infection and no evidence of prior HSV-2 infection was 247 days. The overall rate of recurrence was 1.25 per year in the first year and approximately half (0.64) that in the second year, remaining at approximately the second year level in years 3 through 5. During the first year after primary infection, 38% of subjects had no recurrences, 35% had a single recurrence, and 27% had 2 or more. During the second year, 57% had no recurrences, 19% had one, and 24% had 2 or more. The median duration of recurrences was 7 days. (*IDSA #442*.)

In monogamous couples discordant for HSV infection followed for 19 months, 8 of 271 (3%) HSV1-/2- subjects acquired HSV1 infection, as did one of 85 (1%) HSV1-/HSV2+ individuals. In addition, 39 of 271 (14%) HSV1-/2- subjects acquired genital HSV2 infection, compared with 39 of 658 (6%) of HSV1+/HSV2- individuals, suggesting that prior HSV1 infection provides some protection against HSV2 infection. (*IDSA #924*.)

Eighty patients with a history of 4 to 9 yearly recurrences of genital HSV were randomized to receive either episodic or suppressive therapy with valacyclovir. The proportions who, after one year, were recurrence-free were, respectively, 3% and 41%, with a mean number of recurrences of 7.3 and 1.6, mean number of days with pain and lesions of 6.5 and 1.1, and mean number of days between recurrences of 53 and 179. (*ICAAC #UL-17*.)

ICU Patients. HSV was recovered from the throats of 2% of healthy volunteers, 3% of non-ICU patients and 22% of ICU patients. (*ICAAC #1468*.)

Encephalitis. A multivariate analysis of 93 adults with HSV encephalitis found that a SAPS II (Simplified Acute Physiologic Scale II) score > 27 and a delay of > 2 days after hospital admission in the initiation of therapy with acyclovir were independently associated with a poor outcome. (*ICAAC #1973*.)

Hepatitis. The etiology of fulminant hepatic failure requiring liver transplantation in a pregnant patient was found, on examination of the explanted liver, to be HSV-2 infection. The patient had no mucocutaneous manifestations of HSV infection until after transplantation. (*IDSA #443*.)

Cytomegalovirus

Congenital. The demonstration of > 10 copies of CMV DNA by PCR in amniotic fluid in cases of suspected CMV infection correlated with a positive amniotic fluid culture and fetal infection. (*IDSA #305*.)

Symptomatic children with congenital CMV infection who had a high virus burden in urine and/or blood were at increased risk of hearing loss. (*IDSA #8*.) Separately, investigators reported that detectable CMV DNA in serum at the onset of symptomatic congenital CMV infection was associated with a significantly increase risk of thrombocytopenia, hepatitis and hearing loss at baseline and at 6 months. (*IDSA #7*.)

Transplant Patients. Sixteen of 350 liver transplant recipients developed hepatobiliary disease due to CMV at a median interval of 41 days after transplantation (17-240 days). While all had liver tests consistent with moderately severe hepatitis with cholestasis, 10 of the 14 were asymptomatic. Biliary tract leaks and graft loss were frequent complications. (*ICAAC #1891*.)

Allograft rejection was the single most important predictor (RR, 31.3, 95% CI, 6.1-159.8; $P < 0.001$) of late CMV disease among CMV mismatched (D+/R-) solid organ transplant recipients. (*ICAAC #1894*.)

Forty eight bone marrow, liver, or renal transplant

recipients with 2 consecutive positive CMV PCR samples were randomized to receiver either full dose ganciclovir (5 mg/kg IV b.i.d.) or half-dose ganciclovir (5mg/kg q.d.) plus half dose foscarnet (90 mg/kg IV b.i.d.) for 14 days. There was no difference in virological outcomes, but all combination therapy was less well tolerated. (*ICAAC #1118*.)

Assessment of the viral load response to therapy with IV ganciclovir in solid organ transplant recipients with first-episode CMV viremia found that the mean time to resolution of viremia by measurement of CMV DNA was 32 to 45 days, without a significant difference between different risk groups A rise in CMV DNA during therapy, however, was seen in 4 of 6 with ganciclovir resistance but only 4 of 24 (17%) D+/R- patients with ganciclovir susceptible virus and one of 12 (8.3%) D+/R+ with ganciclovir susceptible virus ($P = 0.02$). Thus, an early rise in CMV DNA suggests ganciclovir resistance and the need for alternative therapy. (*IDSA #438*.)

Ganciclovir-resistant CMV was isolated from 3 of 36 (8.3%) lung transplant recipients who received preemptive ganciclovir therapy for CMV infection and one of 8 (12.5%) who received it prophylactically. All isolated contained the UL97 mutation. (*ICAAC #1120*.)

AIDS Patients. Recurrence of CMV viremia in 3 AIDS patients receiving prolonged maintenance therapy for CMV retinitis was associated with failure of HAART in 2 and neutropenia in one. The relapsing CMV was in each case associated with drug resistance mutations. (*ICAAC #1890*.)

One of 14 patients with non-zone 1 CMV retinitis which had been inactive for at least 3 months and who were on stable HAART with a CD4 cell count >50/mm3 suffered a relapse of retinitis after discontinuation of maintenance therapy. The relapse, which responded to reinduction with ganciclovir, occurred at a time when the patient's CD4 cell count was 67/mm^3 and his plasma HIV RNA was < 50 copies/mL. Urine cultures were not useful in predicting relapse. (*ICAAC #1888*.) ■

CME Questions

17. Which of the following is correct?

a. Penicillin resistance in *S agalactae* has not yet been detected.
b. Penicillin resistance in *S viridans* has not yet been detected.
c. Both in vitro and in vivo (animal) evidence indicated that imipenem resistance-associated loss of OprD is associated with reduced bacterial fitness.

18. Which of the following is correct?

a. Colistin administration caused severe nephrotoxicity in > 90% of recipients.
b. The coadministration of combination oral contraceptives with moxifloxacin is associated with an approximately 20% increased clearance of the latter.
c. Vancomycin should be part of empiric antibiotic regimen in all febrile neutropenic patients.
d. Gentamicin shold be part of empiric antibiotic regimen in all febrile neutropenic patients.

19. Which of the following is correct?

a. A 10-day course of doxycycline with or without a single dose of ceftriaxone was as efficacious as a 20-day course in patients with early lyme disease.
b. Linezolid is inactive in vitro against *M tuberculosis*.
c. Ciprofloxacin is active at low concentration in vitro against *Mycobacterium abscessus*.
d. Moxifloxacin is active at low concentration in vitro against *Mycobacterium abscessus*.

In Future Issues:

Preventing Staphylococcal Bacteremia

UPDATES

By Carol A. Kemper, MD, FACP

Pseudomonas Outbreak from Oral Hygiene Product

Source: ProMED-mail post, April 11, 2002. www.promedmail.org.

An increasing number of pseudomonas infections in hospital patients in Norway since August 2001 led to the discovery of a contaminated oral hygiene product, called Dento-o-sept, manufactured by Snogg Industri AS. Dent-o-sept is one of those pre-moistened oral foam swabs that are extensively used in hospitalized patients, especially in the intensive care unit and in ill patients who are unable to brush their teeth. The swabs are commonly saturated with oral mouthwash, glycerine and flavoring, and are not sterile. Pulsed gel electrophoresis identified a strain of pseudomonas contaminating this product, which had subsequently infected patients. Thus far, a total of 78 patients in 9 hospitals in Norway have been infected or colonized with this strain, and public health experts have begun a hospital-wide survey to identify other subjects. Distribution of the product, which has since been quickly halted, is limited to Norway and Denmark. ■

VRE Super-Bug Spreads in Transplant Unit

Source: Herrero IA, et al. *N Engl J Med*. 2002;346:867-869.

This report from the Mayo Clinic in Minnesota describes the transmission of a linezolid-resistant, vancomycin-resistant *Enterococcus faecium* ("Li-VRE") among 7 patients in their liver transplant unit. The isolate was first identified in a liver transplant recipient who received linezolid for 20 days for intra-abdominal infection. He was known to be previously colonized with a linezolid-susceptible VRE.

During routine surveillance of rectal swabs for VRE, the same multi-drug resistant Li-VRE isolate was subsequently detected in the stools of 6 other patients hospitalized on the same unit, none of whom developed clinical infection. All of the isolates carried the vanA gene, as well as a ribosomal mutation (G2576T 23s rDNA) conferring resistance to linezolid (mean MIC, 16 mg/mL). This mutation has also been recently described in a patient with *Staphylococcus aureus*, as well as 2 other isolates of *E faecium* and laboratory-derived mutant strains of *E faecalis*. The Mayo strain was also resistant to penicillin, ampicillin, gentamicin, and streptomycin but fortunately susceptible to quinopristin-dalfopristin (Q/D), as well as 2 newer investigational agents, oritavancin and tigecyclin.

The staff on this unit were previously required to use gloves when entering rooms—all of which were private. After this outbreak, all persons entering rooms were required to wear gloves and gowns. The emergence of Q/D and linezolid resistance in patients during treatment with these agents, as well as the ready transmission of these MDR isolates, especially in high-risk units, is of obvious concern. Clinical laboratories should begin gearing up to perform susceptibility testing of enterococci for Q/D and linezolid, rather than sending isolates out to specialized laboratories for testing, where the delay in receipt of results may be too long. ■

Invasive Aspergillosis: How Likely Is It?

Source: Perfect JR, et al. *Clin Infect Dis*. 2001;33:1824-1833.

This mycoses study group conducted an extensive evaluation of the diagnosis, risk factors, management, and outcome of 1209 patients with *Aspergillus* isolated from various clinical specimens (1477 positive cultures). The majority (81%) of the isolates were obtained from nonsterile sites, such as sputum (n = 733) and bronchioalveolar lavage (n = 344). Based on specific criteria, they focused on 245 cases, 148 of which were consistent with invasive *Aspergillus* (61% were definite and 33% were probable). The remaining 97 cases were believed to be consistent with chronic necrotizing aspergillosis, aspergilloma, or allergic bronchopulmonary aspergillosis.

Based on multivariate analysis, the likelihood of invasive disease in patients with a positive culture varied significantly. More than half of the patients (50-64%) with allogeneic bone marrow transplantation, neutropenia, or hematologic malignancy, and a positive culture from any site had invasive disease. Patients at intermediate risk included those with autologous BMT (28%), malnutrition (27%), corticosteroids (20%), HIV infection (18%), and solid organ transplant (17%). On the other hand, patients less likely to have invasive disease in the presence of a positive culture included those with diabetes (11%), pulmonary disease (9%), solid tumors (8%), and connective tissue disease (0%). Many patients had more than 1 risk factor, which significantly amplified the likelihood of invasive disease in the presence of a positive culture from any site. While the source of the specimens (sterile vs nonsterile site) is obviously important, the predictive value of a positive culture must be evaluated in the context of the underlying disease process. Although these data are interesting, there are many times in the clinical setting where the demand for empirical treatment in patients with a positive culture outweighs any "guesstimates" of the likelihood of disease, especially with the availability of the newer antifungals with reduced toxicity. ■