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Conference Summaries of ICAAC 1999 and IDSA 1999: Part III

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 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 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 can be seen in Clin Infect Dis 1999;29:959-1112.*
—Stan Deresinski, MD, FACP

Bacterial Pathogens and Infections

Bacterial Respiratory Tract Infections

Pertussis. The recent switch throughout Canada from the use of whole cell to acellular pertussis vaccines has been followed by a significant reduction in hospital admissions and emergency room visits for febrile seizures and hypotonic-hyporesponsive episodes. (*IDSA #31.*) This is consistent with a controlled trial demonstrating better tolerability of the acellular compared to the whole cell vaccine. (*IDSA #64.*) It has been suggested that the increasing incidence of asthma in children may be related to childhood vaccination. However, an analysis of 116,496 children, including 11,134 with asthma, found no evidence that DTP or MMR vaccines increase the risk of development of asthma. (*ICAAC #230.*)

Antibiotic prophylaxis was prescribed for 198 health care workers (98% female) at a facility linked to a cluster of cases of pertussis. Of the 98 who responded to a subsequent survey, erythromycin was initially prescribed to 83 (84.7%), trimethoprim/sulfamethoxazole (T/S) to eight (8.2%), and azithromycin or clarithromycin to seven

(7.2%). However, 43 (51.8%) changed to an alternative antibiotic because of side effects: 34 to T/S and nine to azithromycin or clarithromycin. Six of those given T/S had to change once again; all changes from this drug combination were due to skin rash. All 21 patients initially or later given azithromycin or clarithromycin completed their course. Side effects due to erythromycin included abdominal cramping (80.7%), nausea (72.3%), diarrhea (54.2%), and vomiting (24.1%). (*IDSA #576.*) These observations indicate that the current recommendation of the use of erythromycin for prophylaxis after pertussis exposure needs reconsideration.

Pharyngitis

A three-day course of azithromycin was as effective as a single dose of benzathine penicillin in the treatment of acute streptococcal pharyngitis in children in Colombia. Rates of eradication of *S. pyogenes* were 84% in each group. (*ICAAC #179.*)

Another study, however, found much lower bacteriological success rates after penicillin treatment. A total of 1131 children with acute pharyngitis culture positive *S. pyogenes* were randomized to receive either a single dose of ceftriaxone (500 mg IM), a single dose of benzathine penicillin, or pencillin VK orally for 10 days. Bacteriological failure was observed in 53% of ceftriaxone, 37% of benzathine penicillin, and 35% of oral penicillin recipients. (*ICAAC #535.*)

Paranasal Sinusitis (Rhinosinusitis)

Approximately 87% of patients with the common cold have CT evidence of maxillary sinus abnormalities (*N Engl J Med* 1994;330:25-30). Although this may be the result of viral infection of sinus mucosa or bacterial superinfection, one group of investigators found that nose blowing, but not sneezing, propels nasal mucus into paranasal sinuses during the common cold. (*ICAAC #1898.*)

Two hundred sixty-five patients with acute rhinosinusitis were randomized to receive either placebo or azithromycin 500 mg qd for three days. Pretreatment nasopharyngeal cultures grew *S. pneumoniae*, *H. influenzae*, or *M. catarrhalis* in 29%. Antibiotic treatment in this predefined subset was associated with a 73% cure rate at seven days vs. 47% in the placebo group (P = 0.007); the duration of illness was shortened by more than two days in the antibiotic recipients. (*ICAAC #781.*) These results are similar to those from a study published several years ago (*Lancet* 1996;347: 1507-1510).

There was no significant difference in cure rates of patients with acute sinusitis (clinical and radiographic diagnosis), whether treated for five days or 10 days with cefuroxime axetil. (*ICAAC #174.*) This is consistent with trial results published several years ago, which found no difference between three and 10 days of treatment of acute maxillary sinusitis with trimethoprim-sulfamethoxazole (*JAMA* 1995;273:1015-1021).

Five hundred thirteen adults with acute sinusitis received, by randomization, trovafloxacin or moxifloxacin for 10 days. Clinical efficacy was, respectively, 88.1% and 89.2%. Twenty percent of trovafloxacin and 5% of moxifloxacin recipients reported dizziness. (*ICAAC #171.*)

Gatifloxacin 400 mg po qd for 10 days was as effective as clarithromycin 500 mg po bid for 14 days in the treatment of acute sinusitis; cure rates were, respectively, 87% and 83% at 7 to 14 days post-treatment. (*ICAAC #169.*) Outcomes of patients with acute sinusitis treated with either gatifloxacin or cefuroxime axetil were also similar. (*ICAAC #170.*)

Acute Exacerbations of Chronic Bronchitis

Patients with acute exacerbations of chronic bronchi-

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tis were randomized to receive either gatifloxacin 400 mg po qd or cefuroxime axetil 250 mg po bid, each for seven to 10 days. Clinical cure was observed in 76 of 85 (89%) gatifloxacin recipients and 62 of 81 (77%) cefuroxime recipients (P = 0.01). Bacterial eradication was more effective among patients infected with *S. pneumoniae* or *H. influenzae* who received gatifloxacin. (*ICAAC #177.*)

Pneumonia

Most often, therapy of community-acquired pneumonia is purely empiric because of the difficulty of making an etiologic diagnosis. While the ultimate answer will be the wider development and availability of molecular techniques of diagnosis, standard microbiological techniques can also be improved upon. Digestion and centrifugation of sputum samples from patients with community-acquired pneumonia significantly increased the yield of potential "typical" respiratory pathogens, particularly *S. pneumoniae*, in culture. (*ICAAC #204.*)

A number of studies confirmed that "atypical" pathogens are a frequent cause of community-acquired pneumonia. Using PCR, culture, and urinary antigen detection, evidence of infection with *M. pneumoniae*, *C. pneumoniae*, or *L. pneumophila* was found in 110 of 431 (25.5%) patients with community-acquired pneumonia. One of these was a sole pathogen in 74 patients (43, 24, and 7, respectively). In three patients, two of these pathogens were identified and in 33 one was identified along with a "typical" bacterial pathogen. (*ICAAC #523.*)

Serological evidence of *M. pneumoniae* infection was found in 11 of 108 (10.2%) patients with community-acquired pneumonia in Zurich who had paired sera for analysis. (*ICAAC #2238.*) Forty-two of 554 (7.6%) patients with community-acquired pneumonia had serological evidence of acute infection with *C. pneumoniae*; 57.8% of these had evidence of being infected with a copathogen. No clinical characteristics distinguished infection with *C. pneumoniae* from infection with other pathogens. (*ICAAC #524.*)

"Legionella-like amoebal pathogens" have previously been implicated as a possible cause of respiratory tract infection (*Emerg Infect Dis* 1996;2:225-230). A serological study in Nova Scotia led to the conclusion that infection with Legionella-like Amoebal Pathogen 4 was approximately as frequent as infection with *L. pneumophila* and that it was commonly a copathogen. (*ICAAC #525.*)

A number of studies found that atypical pathogens are also common causes of community-acquired pneumonia in children and that they may be frequent triggers of asthma. An Italian study found serological evidence of *M. pneumoniae* infection in 33.3% of 507 children 2-14 years of age hospitalized with community-acquired lower respiratory tract infection. Evidence of *C. pneumoniae* infection was found in 14.2% and infection with both in 7.5%. Wheezing was a common feature of infection with either pathogen. (*ICAAC #526.*) Low diffusing capacity in children recovered from pneumonia due to *M. pneumoniae* was associated with delayed treatment or relapse of infection. (*ICAAC #527.*)

Seventy-one children (2-14 years of age) presenting to an emergency department in Milan, as well as 80 healthy controls, underwent serological testing and PCR examination of nasopharyngeal secretions. Evidence of acute infection with *M. pneumoniae* was found in 22.5% of patients and 7.5% of controls (P = 0.01), while acute *C. pneumoniae* infection was found in 15% and 2.5%, respectively. A history of recurrent wheezing was significantly associated with each infection. All 11 infected patients treated with clarithromycin had a complete resolution of wheezing at three months, compared to four of 13 (P = 0.0005) not so treated. (*ICAAC #2234.*)

A diagnosis of legionellosis is infrequently made in children with community-acquired pneumonia. Passive surveillance by the CDC led to the identification of 166 cases of pediatric *Legionella pneumonia* from 1980 through 1997. Known risk factors were present in 41%; 24% were hospital acquired. The median age was 13 years, one-half were female, 7% died. (*IDSA #186.*)

S. pneumoniae remains a frequent cause of pneumonia in all age groups. The recent approval of a pneumococcal conjugate vaccine (*Semin Resp Infect* 1999;14: 285-294) may prove effective in reducing this frequency, but the multiple serotypes of this organism may eventually defeat this hope. Infants who had received a 9-valent pneumococcal conjugate vaccine were significantly less likely to have colonization with vaccine strain pneumococci at subsequent encounters, but there was no reduction in overall pneumococcal carriage rates. (*IDSA #34.*) A second study in children also found a shift to colonization with nonvaccine serotypes not usually seen in this age group. (*IDSA #643.*)

A current major concern about the pneumococcus is the continued evolution of resistance of this organism to multiple antibiotics. Eight ribotypes account for 77% of the penicillin-resistant isolated in the United States in 1997-1998. (*ICAAC #1032.*) Evidence was presented of emergence of a single clone (by PFGE) of penicillin-nonsusceptible *S. pneumoniae* (serotypes 9V and 14) related to the Spanish/French clone with its source in Quebec with spread to Ontario, Alberta, and British Columbia. (*ICAAC #1030.*)

Examination of sterile site isolates from 3429 cases

of invasive pneumococcal disease in the Atlanta metropolitan area revealed that the incidence of erythromycin resistance increased from 16.3% in 1994 to 25.8% in 1998. In 1998, 65.4% of erythromycin-resistant isolates had MICs of more than 16 mcg/mL to this macrolide. Although the frequency of the *erm* gene mediated resistance remained stable at approximately 6.5%, that of the *mef* gene increased from 8.7% of all isolates to 25.8% in 1998. (*IDSA #872.*)

Resistance to the fluoroquinolones is also increasing. Of 80 isolates of *S. pneumoniae* in Canada with MICs of more than 2 mcg/mL to ciprofloxacin, 33 had both *gyrA* and *parC* mutations, 29 had *parC* mutations alone, and two had only *gyrA* mutations. Twenty-six of the 33 with both mutations had ciprofloxacin MICs more than 8 mcg/mL. Further susceptibility testing of these double mutants found that their MIC90s were 16 mcg/mL for levofloxacin and sparfloxacin, 4 mcg/mL for trovafloxacin and gatifloxacin, 2 mcg/mL for moxifloxacin, and 0.25 mcg/mL for gemifloxacin. (*ICAAC #826.*)

Increased fluoroquinolone resistance in *S. pneumoniae* in Hong Kong is associated with mutations in both the *parG* and *parC* genes and appear to be clonal by PFGE while expressing capsular serotypes 19F and 23F. (*ICAAC #818.*) In contrast, clonality was not detected among ciprofloxacin-resistant isolates in Canada. (*ICAAC #821.*)

In the United States, levofloxacin resistance among *S. pneumoniae* isolates increased from 0.1% in 1997-98 to 0.6% in 1998-99. Of 22 resistant isolates from the former time period, six were intermediate and four were resistant to penicillin. (*ICAAC #820.*)

A commonly used approach to empiric therapy of community-acquired pneumonia in hospitalized patients is the administration of a cephalosporin and a macrolide. While the former is ordinarily given intravenously (IV), the necessity of IV administration of the macrolide has remained a matter of debate. In patients with community-acquired pneumonia receiving a second- or third-generation cephalosporin together with a macrolide, the route of administration (IV or PO) of the latter component did not affect the outcome of treatment. In fact, the administration of erythromycin intravenously was associated with a longer duration of hospitalization. (*IDSA #131.*)

The increased resistance of the pneumococcus to commonly used antibiotics has driven the increasing use of newer generation fluoroquinolones in the empiric treatment of community-acquired pneumonia. Patients with moderate to severe community-acquired pneumonia were randomized to treatment with either levofloxacin (500 mg qd) for 7-10 days or ceftriaxone 1-2 g IV qd for 2-3 days plus azithromycin 500 mg IV followed by po for 7-10 days. A total of 154 patients were clinically evaluable. The clinical failure rates were 5% in the levofloxacin group and 8.2% in the ceftriaxone/azithromycin recipients. Thirteen percent of all isolates were resistant to azithromycin while none were resistant to levofloxacin. Nonetheless, the microbiologic eradication rates were, respectively, 94.3% and 93.5%. (*IDSA #141.*)

Four hundred seventy-four patients with community-acquired pneumonia were treated for 10 days with either moxifloxacin 400 mg qd or clarithromycin 500 mg bid by randomization. The most common organisms identified included: *C. pneumoniae* (36%), *M. pneumoniae* (16%), *H. influenzae* (14%), and *S. pneumoniae* (13%). The overall clinical resolution rates for the efficacy-valid population were 95% for both moxifloxacin and clarithromycin (95% CI = -3.7%, 5.3%). Bacteriologic success at follow-up, including end-of-therapy failures, was 96% for both treatment groups (95% CI = -5.8%, 6.2%). In both treatment groups, nausea and diarrhea were the most commonly reported adverse events (8-9%). (*ICAAC #2240.*)

Several studies examined the efficacy of gatifloxacin. "Atypical" pathogens (*M. pneumoniae*, *C. pneumoniae*, *L. pneumophila*) were identified in 187 of 1131 (16.5%) patients with community-acquired pneumonia enrolled in a series of trials comparing gatifloxacin to either clarithromycin, levofloxacin, or ceftriaxone/erythromycin. The cure rate was 97% in gatifloxacin recipients and 92-93% in the comparator recipients. (*IDSA #154.*)

Four hundred thirty-one adults with community-acquired pneumonia were randomized to receive either gatifloxacin 400 mg po qd or clarithromycin 500 mg po bid, each for 7-14 days. The most frequently identified etiologies were, in descending order, *M. pneumoniae*, *S. pneumoniae*, *C. pneumoniae*, and *H. influenzae*. Clinical cure was observed in 95% of gatifloxacin and 93% of clarithromycin recipients. (*ICAAC #2242.*)

Four hundred twenty-seven patients with community-acquired pneumonia were randomized to receive either gatifloxacin 400 mg qd or levofloxacin 500 mg qd, each for 7-14 days. The drugs were initially administered intravenously in some patients. Clinical cure was achieved in 96% of gatifloxacin and 94% of levofloxacin recipients; bacteriological eradication was achieved in 98% and 93%, respectively. (*ICAAC #2243.*)

Patients hospitalized with community-acquired pneumonia were randomized to receive either gatifloxacin 400 mg IV with conversion to oral administration or ceftriaxone 1-2 g IV qd + erythromycin with conversion to clarithromycin 500 mg po bid, each for 7-14 days. Clinical cure occurred in 96 of 99 (97%) gatifloxacin recipi-

ents and in 96 of 106 (93%) ceftriaxone recipients. Both diarrhea and vomiting occurred more frequently in the latter group. (*ICAAC #2241.*)

Legionellosis may be effectively treated with any of several antibiotics. Twenty-five patients with *L. pneumonia* diagnosed by urinary antigen detection were treated with azithromycin 500 mg given qd IV for a mean of four days followed by 500 mg po qd for a mean of eight days. One (4%) patient died. Among 20 evaluable patients, the clinical cure rate was 94% at 10-14 days and 100% at 4-6 weeks. (*IDSA #156.*) The urinary antigen test remained positive for more than two months after the initial diagnosis of *L. pneumonia* in 14 of 42 (33.3%) patients. (*ICAAC #225.*)

Hospital-acquired pneumonia continues to be an important cause of morbidity and mortality. Patients with nosocomial pneumonia, almost half undergoing mechanical ventilation, were randomized to receive either clinafloxacin 200 mg q12 h IV or cefazidime 2 gm IV q8h. Clinical cure was achieved in 81 of 122 (66%) clinafloxacin and 73 of 126 (58%) ceftazidime recipients. (*ICAAC #2247.*)

The diagnosis of pneumonia in critically ill patients is difficult and therapy is often presumptive. Eighty-one ICU patients for whom their physician believed had pneumonia requiring antibiotic therapy but whose "pneumonia score" indicated a low likelihood of this infection were randomized to receive either standard therapy or ciprofloxacin with discontinuation after three days if pneumonia still appeared to be unlikely. Pneumonia was discontinued by days in five of 39 (12.8%) of the standard therapy and 72% of the experimental group (P = 0.001). There was no difference between the groups in mortality or length of ICU stay, but the duration of antibiotic therapy and antimicrobial cost was significantly reduced in the experimental arm. Antimicrobial resistance and/or superinfections developed in 35% of the standard therapy group and in only 15% of the experimental group (P = 0.017). (*ICAAC #710.*)

Bacteremia

A number of groups continue to develop molecular methods for the rapid detection of bacteremia and rapid identification of its cause. An rRNA probe matrix (GenProbe) consisting of a set of DNA probes directed against rRNA of bacteria and fungi was evaluated by testing of medium from BacT/Alert blood culture bottles as soon as a positive signal was achieved, as well as in negative bottles. The assay required a total of 90 minutes. The sensitivity and specificity for species identification of organisms in blood culture bottles were, respectively, 100% and 96.8%. A second study at a different institution reported a sensitivity of 98%, specificity and positive predictive values of 100% each, and a negative predictive value of 98%. (*ICAAC #1557, #1558.*)

Falsely positive blood cultures add significant costs to inpatient care. Positive blood cultures yielding coagulase-negative staphylococci from medical and surgical inpatients were believed to represent contamination in 57%. Neither isolation of *S. epidermidis* nor delayed recovery (after 3 days) were predictive of contamination. Thirty-three percent of positive blood cultures drawn in the emergency room were contaminated. In addition to having the culture obtained in the emergency room, other predictors of contamination were having the culture drawn within 48 hours of admission and recovery of a beta-lactam-susceptible isolate. (*IDSA #204.*) In contrast to the finding above, in another setting, all coagulase-negative staphylococci requiring longer than 24 hours for detection in the Bactec 9240 were thought to be contaminants by clinical criteria. (*IDSA #254.*)

The occurrence of bacteremia may, in some cases, be a clue to the presence of gastrointestinal pathology. This appears to be particularly true in intestinal transplantation recipients. Endoscopy was performed during 107 episodes of bacteremia without an apparent source in children who had undergone intestinal transplantation. Histological evidence of rejection was found in 26 (24%), lymphoproliferative disease in 21 (20%), or both in 17 (16%). Gastrointestinal pathology was predominantly associated with bacteremia due to enteric bacteria; quantitative stool culture correlated with bacteremic isolates 83% of the time. (*IDSA #472.*)

To remove or not to remove the IV catheter—that is the question! Ninety-three episodes of IV catheter-related bacteremia due to gram-negative bacilli, including 23 due to *Pseudomonas aeruginosa*, were reviewed. Attempts to maintain the catheter failed in six of nine (67%) cases of *P. aeruginosa* infection and in 19 of 31 (61%) cases of infection by other gram-negative bacteria. Furthermore, attempted catheter salvage was associated with increased 30-day mortality. (*IDSA #477.*)

Eight patients developed native valve endocarditis a median of 42 days (range, 10-103 days) after cardiac catheterization. All eight had previously abnormal valves. Six infections were due to *S. epidermidis*, and one each to *E. faecalis* and *C. albicans*. (*ICAAC #1681.*)

Urinary Tract Infection

The prevalence of asymptomatic bacteriuria in 636 women with diabetes mellitus was 26% compared to only 6% in nondiabetic controls. Symptomatic urinary tract infection (UTI) occurred, in the next 18 months, in

35 of 127 (28%) with and 72 of 289 (19%) without asymptomatic bacteriuria (P = 0.03). There was no association between HbA1c level and the presence of asymptomatic bacteriuria. Mean serum creatinine increased 5.4% in women with asymptomatic infection and only 1.2% in those without (P = 0.057). (*ICAAC #604, 607.*)

Diabetic women with asymptomatic bacteriuria were randomized to receive placebo or treatment with either trimethoprim/sulfamethoxazole or ciprofloxacin for 14 days and were then followed for 36 months. After the initial six weeks, patients were followed every three months and those in the treatment group received antibiotics whenever they were found to have bacteriuria. Symptomatic pyelonephritis occurred in 27 of 52 (51.9%) placebo recipients and one of 57 treated patients, and placebo recipients were more likely to be hospitalized because of pyelonephritis. There was no significant difference in change in renal function between the groups. (*ICAAC #609.*)

Only 60.9% of *E. coli* urinary isolates from throughout the United States were susceptible to ampicillin; 72.4% were susceptible to cephalothin, 82% to trimethoprim/sulfamethoxaxole, and 97.7% were to ciprofloxacin. There was little difference in susceptibility rates between outpatient and inpatient isolates. (*ICAAC #611.*)

Recently published Infectious Disease Society of America guidelines recommend 7-14 days of treatment of otherwise healthy young women with acute uncomplicated pyelonephritis (*Clin Infect Dis* 1999;29:745-758). Three hundred four women with acute pyelonephritis received ceftriaxone 1g IV qd until afebrile, followed by cefixime 400 mg po qd. The patients were randomized to receive a total duration of antibiotic therapy of either seven or 14 days; there was no difference in outcomes between the groups. (*ICAAC #613.*)

Transrectal echography was of little value in the diagnosis of acute prostatitis. (*ICAAC #608.*)

Enteric Infections

Cholera continues to afflict large parts of the world. Fifty-one cases of infection due to *V. cholerae* 01 were reported to the CDC between January 1995 and July 1999. Latin America, Asia, and the United States appeared to each be the source of approximately one-third of the cases. Nine of the 16 patients who had acquired their infection in the United States had eaten seafood, two had eaten contaminated sliced cantaloupe, with the suspected source unknown in the other five. There were no fatalities. (*IDSA #29.*)

Gulf of Mexico oysters continue to be a source of *Vibrio parahaemolyticus* infection despite increasing precautions. Bacteriological monitoring at harvest sites in Galveston Bay did not prevent the occurrence of a large multistate outbreak of oyster-associated *V. parahaemolyticus* infections. (*IDSA #38.*)

For you vegetarians, 47 cases of infection due to *Yersinia pseudotuberculosis* were traced to consumption of iceberg lettuce in Finland, while an outbreak of *Salmonella baildon* infection in California was linked to ingestion of raw tomatoes. (*ICAAC #2216, #2215.*)

In an event that was nothing to cheer about, an outbreak of Shiga-toxin producing *E. coli* 0111:H8 infection occurred in attendees at a cheerleading camp. (*IDSA #727.*) Elsewhere, a large outbreak of *E. coli* 0157:H7 resulted from contamination of well water. (*IDSA #728.*)

One hundred three children with typhoid fever in Egypt were randomized to seven days of treatment with either azithromycin (10 mg/kg/d po) or ceftriaxone (75 mg/kg/d IM). One microbiological failure occurred in each group; four relapses, all in ceftriaxone recipients, occurred. (*IDSA #135.*)

Recent receipt of fluoroquinolones for other reasons was a significant risk factor for infection with a fluoroquinolone-resistant *Salmonella* serotype Schwarzengrund during a nursing home outbreak. (*IDSA #61.*)

Examination of unformed stools for fecal leukocytes was 14% sensitive and 90% specific in samples positive for *C. difficile* toxin, but 52% sensitive and 88% specific in samples from which a bacterial pathogen was recovered in culture. When evaluated with regard to geographic source of the specimen, examination of fecal leukocytes was useful in outpatients, but not in inpatients—a finding consistent with the fact that *C. difficile* is largely a hospital pathogen, while other bacterial pathogens are almost exclusively outpatient pathogens. (*IDSA #259.*) Three new commercial chromatographic assays have significantly improved sensitivity compared to previously available latex agglutination or ELISA assays in the detection of the *C. difficile* toxin or antigen in stool. (*ICAAC #228.*)

Intra-abdominal Infection

Four hundred twenty-two patients with intra-abdominal infection were randomized to receive either piperacillin/tazobactam (4 g/500 mg) or imipenem/cilastatin (1 g/1 g)—each given q 8 h. The efficacy rates in evaluable patients were almost identical—72% and 73%, respectively. (*IDSA #143.*) In a separate randomized trial involving more than 200 patients with intra-abdominal infections, piperacillin/tazobactam (4 g/0.5 g q 8 h) was as effective as imipenem. (*ICAAC #520.*)

As many as 30% of biliary stents may fail because of lumenal occlusion. An analysis of 30 stents found that

occlusion was due to the accumulation of extensive biofilm, consisting of bacteria embedded in an amorphous matrix together with crystallized bile salts. The bacteria appeared to be of duodenal origin with predominance of enterococci and coagulase-negative staphylococci. (*ICAAC #1675.*)

Skin and Soft Tissue Infections

Curettage specimens were obtained using a scalpel from infected superficial foot ulcers (< 15 mm in depth) from 835 diabetic outpatients. Examination of gram stains of the specimens revealed the presence of bacteria and subsequent culture results yielded organisms consistent with those seen microscopically in more than 95% of cases. However, additional organisms were commonly recovered. The presence of bacteria on gram stain was associated with a reduced response to antimicrobial therapy. (*IDSA #145.*)

Eighty cases of subareolar infection of the nonlactating breast were treated nonsurgically with antibiotics. An abscess was detected by sonography in 57.5% and bacteria were recovered from needle aspirates in 65% of these—most often staphylocci, anaerobes, and *Proteus mirabilis*. Antibiotics were administered for a median duration of eight weeks. The recurrence rate after at least two years of follow-up was 20% and after at least four years was 40%. (*IDSA #136.*)

Orthopedic Infections

Forty-eight patients with prosthetic joints and 25 with other orthopedic prosthetic devices who had *S. aureus* bacteremia were prospectively evaluated to determine the risk of prosthetic device infection. The device infection was presumed to be hematogenous in origin if the bacteremia occurred in the absence of direct joint inoculation at least one year after surgery. Twelve of the 25 with devices other than joints had infection of their prostheses, but only one was hematogenous in origin. In contrast, 19 of those with prosthetic joints had infection of the device and 11 of these were hematogenous in origin. Thus, while the risk of hematogenous seeding of nonjoint devices was only 7%, that of joint prostheses (after exclusion of primary device infections) was 28%. In addition, knee prostheses appeared to be at greater risk of hematogenous seeding than were hip prostheses (50% vs 20%). (*IDSA #149.*)

Seventeen prosthetic joint infections (12 knees and 5 hips) in 16 patients due to penicillin-susceptible streptococci occurring more than 30 days after surgery were treated with debridement and systemic antibiotics without removal of the prosthesis. None of the prostheses was loose. IV antibiotics were administered for a median duration of 28 days and five patients received chronic suppressive antibiotics orally. Relapse occurred in two cases, both involving prosthetic hips; the overall five-year survival free of relapse was 88%. (*IDSA #480.*) ❖

CME Questions

1. **Which of the following statements is correct?**
   a. Among patients treated for acute sinusitis, the incidence of dizziness was greater in trovafloxacin than in moxifloxacin recipients.
   b. *Mycoplasma pneumoniae* infection is rare among children.
   c. *Chlamydia pneumoniae* infection is rare among children.
   d. *Legionella pneumophila* is a common cause of respiratory tract infection in children.

2. **Which of the following statements is correct?**
   a. Erythromycin is well tolerated among health care workers receiving it as prophylaxis against pertussis.
   b. Evidence indicates that both DTP and MMR administration are associated with an increased subsequent risk of asthma.
   c. The use of an acellular pertussis vaccine in Canada was associated with an increased risk of admission for febrile seizures.
   d. Nose blowing, but not sneezing, propels nasal mucus into paranasal sinuses during the common cold.

3. **Which of the following statements is correct?**
   a. Wheezing is commonly associated with childhood infection with either *M. pneumoniae* or *C. pneumoniae.*
   b. IV administration of a macrolide antibiotic is superior to PO in patients with community-acquired pneumonia also receiving a cephalosporin.
   c. Azithromycin is ineffective in the treatment of legionella infection.
   d. Treatment of women with acute uncomplicated pyelonephritis with ceftriaxone/cefixime was improved by antibiotic administration for 14 days, rather than seven days.

4. **Further development of adefovir dipivoxil for HIV has been terminated due to:**
   a. adverse effects in many patients.
   b. clinical trials suggesting that in combination with other antiretroviral agents, it contributed to a reduction in HIV viral load.
   c. an FDA advisory committee recommendation against the accelerated approval for the drug for the treatment of HIV.
   d. All of the above

In Future Issues:

ICAAC and IDSA Summaries:
Part IV

UPDATES

By Carol A. Kemper, MD, FACP

Adefovir Dipivoxil no Longer Available for HIV

Source: Gilead Sciences correspondence and press release: Dec. 3, 1999.

Following an fda advisory committee meeting on Nov. 1, 1999, at which the committee recommended against the accelerated approval for adefovir dipivoxil 60 mg daily for the treatment of HIV, Gilead Sciences has decided to terminate its program for further development of this agent for HIV in the United States. Clinical trials suggested that adefovir dipivoxil, in combination with other antiretroviral agents, contributed to a reduction in HIV viral load. And, the once daily dosing schedule was attractive, and the resistance profile appeared unique with little evidence of cross-resistance to other nucleoside reverse transcriptase inhibitors. Unfortunately, the development of adverse effects in many patients precluded its long-term use. Potentially the most serious side effects were renal, occurring in up to 40% of patients following six months of administration of the higher 120-mg dose, including proximal tubular defects with glucosuria, hypophosphatemia, metabolic acidosis, Fanconi's syndrome, renal insufficiency, and, renal failure. While the 60 mg daily dose appeared less toxic, the committee nevertheless raised questions regarding the long-term safety of this agent in HIV-infected patients.

Rather than pursue additional clinical trials with this agent, the company indicated that it felt its efforts and resources were better spent on other promising drugs in the pipeline. As a result, all HIV-related clinical trials involving adefovir dipivoxil in the United States have been terminated, and the final date for enrollment in the expanded access study in the United States was December 10, 1999. The company is continuing to develop adefovir dipivoxil for hepatitis B virus infection. ■

Failure of Ivermectin in Crusted Scabies

Source: Walton SF, et al. *Clin Infect Dis* 1999;29:1226-1230.

Crusted scabies, sometimes referred to as Norwegian scabies, is due to hyperinfection of the human mite, *Sarcoptes scabei*, most commonly seen in patients with impaired immunity, such as those with HIV, but may also be seen in small hyperendemic areas, such as groups of aboriginals in northern Australia. While topical scabicides are often ineffective in crusted scabies, ivermectin in doses up to three doses 14 days apart has resulted in apparent cures. But relapses, weeks to months later, are not uncommon.

Walton and colleagues performed genetic analyses over a period of four years on mites obtained from four patients with multiple recurrences of infection despite apparent responses to ivermectin plus topical 5% permethrin cream and topical keratolytic therapy. Sequential population of mites in at least two of four patients were genetically similar, suggesting that patients were more likely to develop infection with the same organism—either from a common source or as the result of ivermectin failure. One patient experienced multiple recurrences despite receiving 16 doses of ivermectin (1057 mites were collected from this patient over 2 years alone!). Specimens taken from 12 of his family members were negative for infection, further suggesting that his relapses were due to incomplete eradication of the organism. Mites from patients 3 and 4, who were sisters, appeared to have greater genetic diversity, although the possibility that patient 3 was reinfected by her sister could not be excluded. There was no evidence of emergent resistance to ivermectin following relapse.

Ivermectin failure and reinfection from inadequately treated contacts remains a problem for patients with crusted scabies, pointing out the need for more rigorous treatment of both patients and contacts for this particularly challenging disease. ■

Name-based Reporting for HIV

Source: Osmond DH, et al. *Ann Intern Med* 1999;131:775-779.

This interesting survey challenges the concept that name-based surveillance of HIV infection will result in improved partner notification and more timely access to health care for infected contacts. The Multistate Evaluation of Surveillance for HIV Study Group surveyed 1913 people with AIDS who tested positive for HIV in five states with name-based surveillance. Surprisingly, just as many sexual and needle contacts were notified by HIV-infected persons who were tested anonymously as those identified through the confidential testing sites and tracked through the health department (3.85 vs 3.80 partners). Furthermore, both types of contacts sought medical care with a similar frequency and within a similar time-frame. In general, about two-thirds of infected contacts began medical care within two months irrespective of the means of notification. About 6% of patients had not sought medical care within three years of receiving a positive HIV test.

Most patients who delayed seeking care indicated that they either felt well or were not yet ready to deal with their HIV. Other common reasons for delaying care was uncertainty about where to go and concerns regarding the affordability of care. Only 8.6% of patients expressed concern that they would be identified to the health department. Contrary to current thought, named-based surveillance reporting for HIV may not increase identification of infected contacts nor does it appear to facilitate their access to medical care. Improved counseling at anonymous test sites with better information about health care options is needed. ■