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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

Bacterial Infections

Bloodstream Infections/Endocarditis

Cardiac valves electively removed from 2 patients without symptoms of infection were found to have thickened cusps, macroscopic vegetations, and microscopic inflammation. Electron microscopy revealed long, slender organisms, and PCR analysis yielded evidence of *Tropheryma whippleii* genome (*ICAAC L-766*).

Nineteen (73%) of 26 cases of *S viridans* bacteremia (at least 2 blood cultures positive) were community acquired; one hundred percent of the community cases and only 56% of the nosocomial cases were judged to represent true bacteremia. The source was identified in 20 patients: 4 had endocarditis, with 4 originating in the lower respiratory tract, 2 from the oropharynx, 4 from soft tissue, 3 from the GI tract, 2 from an AV hemodialysis graft, and 1 from the urinary tract (*IDSA 119*).

The major predictor of mortality in a retrospective analysis of 220 injection drug users with native valve endocarditis was the presence of a vegetation > 2 cm in size (*ICAAC L-762*). The predictors of mortality in 162 noninjection drug users with native valve endo-

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carditis were infection with *S aureus* and age older than 60 years (*ICAAC L-763*).

In 11 patients with bacteremic pacemaker infection in whom replacement was felt to be contraindicated and who were given prolonged antibiotic therapy, only 1 (with *S epidermidis*) died of infection. Three with *P aeruginosa*, 2 with *S aureus*, and 5 others with *S epidermidis* infection survived during a mean of > 6 months of antibiotic therapy (*ICAAC K-586*).

A prospective study of 834 arterial catheters used for hemodynamic monitoring found that 13% became colonized and 1.3% were the apparent source of bloodstream infection, representing 3.7 infections per 1000 arterial line-days, a frequency similar to that seen with central venous catheters (*ICAAC K-81*).

The use of full sterile barrier precautions was not associated with a reduced risk of arterial catheter colonization or catheter-site infections in a randomized trial when compared to a standard-of-care group in which only hand washing, sterile gloves, and skin disinfection were used (*ICAAC K-670*).

Musculoskeletal Infections

Culture of sonicates of explanted knee prostheses had 100% sensitivity and specificity for the diagnosis of prosthetic joint infection in a small study (*IDSA 279*).

In 13 of 15 cases of *Clostridium* spp. infection associated with musculoskeletal allograft transplantation, the graft had been processed by a single company that treated tissues with a nonsporicidal antimicrobial solution (*IDSA 409*).

Five children with a foot injury due to an embedded toothpick (or, as the authors suggest, "footpick") presented with evidence of local infection, having failed previous antibiotic therapy. As expected, the toothpick could not be detected by plain radiography, but was visualized on 1 of 3 ultrasound examinations and by CT and MRI in 1 each. Two children had metatarsal osteomyelitis. A variety of organisms were recovered in culture. All 5 responded to surgical removal of fragments and prolonged antibiotic therapy (*IDSA 632*).

Intra-abdominal Infections

A comparison of cases of spontaneous bacterial peritonitis in patients with end-stage liver disease during 2 consecutive 5-year periods beginning in 1991 found that the incidence of infection with multiply resistant bacteria increased from 8% to 39%, and the incidence of fungal peritonitis increased from 4% to 19%. The mortality rate in patients with multiply resistant bacterial infection was 57% compared to only 17% in those with susceptible bacteria (*ICAAC K-1230*).

CNS Infections

Eight of 17 cases of neuroretinitis due to *Bartonella henselae* were severe, and 5 of these did not have significant improvement at 1 month. All had incomplete visual recovery at last visit (*IDSA 238*).

Early adjunctive dexamethasone therapy improved outcome in adults with bacterial meningitis (*ICAAC L-1596*; *N Engl J Med*. 2002;347:1549-1556).

Seventeen (7%) of 233 cases of community-acquired meningitis in adults seen by a group of Parisian investigators were due to Gram-negative bacilli. The Gram stain was positive in 15. All but 1 patient had predisposing illness. Four of the 17 had strongyloidiasis, and this was disseminated in 2 (*ICAAC L-1972*).

Urinary Tract Infections

Screening for and treatment of asymptomatic urinary

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VICE PRESIDENT/GROUP PUBLISHER: Brenda Mooney.

EDITORIAL GROUP HEAD: Glen Harris.

MARKETING PRODUCT MANAGER: Schandale Kornegay.

MANAGING EDITOR: Robin Mason.

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THOMSON
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Please call **Robin Mason,** Managing Editor, at (404) 262-5517, or e-mail to robin.mason@ahcpub.com, or **Christie Messina,** Senior Copy Editor, at (404) 262-5416, or e-mail to christie.messina@ahcpub.com between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

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tract infections in women with diabetes mellitus did not reduce subsequent related morbidity (time to and incidence of symptomatic infection, pyelonephritis, and UTI hospitalization) (*ICAAC L-1796*).

In a placebo-controlled, randomized trial, daily nitrofurantoin was significantly better than the use of a vaginal estradiol pessary in the prevention of recurrent urinary tract infection in postmenopausal women (*ICAAC L-1798*).

Bacteriologic data from recent clinical trials have demonstrated a shift toward recovery of Gram-positive pathogens in cases of chronic prostatitis. However, a lack of concordance between clinical cure and bacterial eradication was detected in these same clinical trials (*IDSA 144, IDSA 145*).

Upper Respiratory Infections

An outbreak of pharyngitis due to *Arcanobacterium haemolyticum* occurred in young adults in Halifax (*ICAAC L-1962*).

Two outbreaks of pertussis were reported. In Illinois, investigation of the index case, a 62-year-old man, uncovered 65 cases of patients meeting CDC clinical criteria, whose median age was 32 years (*IDSA 133*). In Arkansas, 97 cases were identified in a rural community, representing an attack rate of 50 per 1000. The clinical case definition was met by 17.6% of household contacts of identified cases (*IDSA 132*). A 5-day course of azithromycin was as effective and better tolerated than a 10-day course of erythromycin in the treatment of pertussis in a randomized, open trial in children (*IDSA 169*).

The use of a rapid diagnostic test for influenza virus infection in an emergency department was associated with significant reductions in laboratory testing and antibiotic use (*ICAAC V-246*). Treatment of children with influenza virus infection with oseltamivir was associated with a reduced incidence of influenza infection in pediatric household contacts (*ICAAC V-244*).

Enteric Pathogens

There was a decline in major bacterial food-borne illnesses in the United States from 1996 to 2001, including a 49% decrease in those due *Yersinia*, 35% in *Listeria*, 27% in *Campylobacter*, 21% in *E coli* 0157, and 15% in *Salmonella*. The incidence of cryptosporidiosis decreased by 33% from 1997 to 2001 (*IDSA 9*). An outbreak of cryptosporidiosis involving at least 358 cases resulted from exposure to recreational contamination at a water park (*IDSA 705*).

Outbreaks of *Salmonella* related to ingestion of eggs and cantaloupe, an outbreak of shigellosis related to tomatoes, and an outbreak of *E coli* 0157:H7 linked to homemade butter were described (*IDSA 285, IDSA 286, IDSA 292, IDSA 297*). Females had greater morbidity from *Salmonella* infections than men (*IDSA 284*). An outbreak of yersiniosis in infants was associated with the preparation of chitterlings in the home, and an outbreak of listeriosis was associated with pasteurized cheese (*IDSA 316, IDSA 322*). An outbreak of ciguatera poisoning involving at least 20 individuals in an extended family was the result of eating fish that had been frozen and shipped from Fiji (*IDSA 325*).

An outbreak of *E coli* 0157:NM infections was associated with attending a dance in a barn used to show farm animals at a county fair. Genetically indistinguishable *E coli* 0157:NM isolates were recovered from patients and from sawdust, bleachers, handrails, walls, and rafters of the barn (*IDSA 10*).

The prevalence of nontyphoidal *Salmonella* resistant to ceftriaxone isolated in the United States increased from 0.1% in 1996 to 1.3% in 2000; most were not associated with international travel. Only 0.1% were resistant to ciprofloxacin, and all 9 resistant isolates were associated with international travel (*IDSA 289, IDSA 290*). A strain of *S newport* (Newport9+) resistant to third-generation cephalosporins and accounting for 25% of nontyphoid *Salmonella* isolates in 2001 was identified at 17 US sites (*IDSA 21*). Decreasing susceptibility of *S typhi* to nalidixic acid in the United States was associated with increased MIC, but not resistance, to ciprofloxacin. This portends the future emergence of ciprofloxacin-resistant *S typhi* (*IDSA 289*).

In 2001, 18% of 259 *Campylobacter jejuni* from 9 states were resistant to ciprofloxacin (*IDSA 315*). Seventy-three percent of 160 clinical isolates of *C jejuni* at 1 hospital in Madrid were resistant to ciprofloxacin (*ICAAC C2-1281*).

Thirty-five (58%) of 60 hospitalized patients with unexplained leukocytosis (WBC > 15,000/mm^3) but only 3 (13%; $P < 0.001$) of 23 controls had a positive stool EIA test for *C difficile* toxin. Symptoms of colitis were often subtle or absent—or overlooked by the primary physician (*IDSA 300*). A symptom complex in patients with fulminant *C difficile* disease consisting of worsening ascites and hypoalbuminemia with progressive leukocytosis and systemic toxicity leading to hemodynamic collapse was described (*IDSA 303*).

Approximately 3% of cases of diarrhea in travelers to Mombasa, Guadalajara, and Montego Bay were due to norovirus at each location (*ICAAC L-1969*).

Gram-Negative Bacillary Infections

No difference was found in the risk of isolation of *Enterobacter* spp. resistant to third-generation

cephalosporins from patients treated with either piperacillin/tazobactam or a third-generation cephalosporin. Fluoroquinolone, but not aminoglycoside, use was associated with apparent protection (*ICAAC K-1351*).

A retrospective study of 2950 patients from whom *P aeruginosa* had been isolated found that ß-lactam resistance emerged in 28% of those treated with a ß-lactam, 38% of those with a ß-lactam plus an aminoglycoside, and 19% of those treated with a ß-lactam plus ciprofloxacin. After adjustment, there was a trend (OR 0.63, $P = 0.7$) toward lesser emergence of resistance in association with administration of a ß-lactam plus ciprofloxacin than with ß-lactam plus aminoglycoside (*ICAAC K-1943*).

One hundred percent of 691 *P aeruginosa* isolates, including 209 resistant to imipenem, were susceptible to polymyxin B. Polymyxin exhibited concentration-dependent bactericidal activity that was enhanced by azithromycin (*IDSA 96*).

A study at a hospital in Madrid found that one-fifth of extended spectrum beta-lactamase (ESBL)-containing *Enterobacteriaceae* were community acquired (*ICAAC K-1947*).

An outbreak of Pontiac fever due to *Legionella anisa* occurred after exposure to ornamental water in a restaurant (*IDSA 827*).

Haemophilus spp.

Nationwide *Haemophilus influenzae* B vaccination of infants in The Netherlands was followed by a significant increase in cases of invasive non-B *H influenze* infections in vaccinated children (*ICAAC G-1223*). In the year after the introduction of Hib immunization in Salvador, Brazil, the incidence of *H influenzae* type B meningitis decreased by 69% to 0.81 cases per 100,000 person-years, but the incidence of type A meningitis increased 8-fold to 0.16 cases per 100,000 person-years (*IDSA 133*).

ESBLs in *Hemophilus*! Two unique isolates of *H parainfluenzae* carried an ESBL conferring resistance to ceftriaxone, cefotaxime, and cefpodoxime (*ICAAC C2-645*).

In a frightening development, 36% of 101 *H influenzae* isolates examined at New York Hospital in Queens were resistant to levofloxacin; most isolates were from patients who had been in long-term care facilities (*ICAAC C2-647*).

Meningococcus

Approximately one-fourth of residents of 1 district of Burkina Faso, a country within the African meningitis belt, had nasopharyngeal carriage of *N meningitidis* W-135 belonging to the same clone that caused the 2000 Hajj pilgrimage-associated outbreak (*ICAAC LB-18*).

Four of 435 children with meningococcal infection developed a reactive pericarditis 6-18 days after the onset of illness and at a time when the infection had been controlled with antibiotic therapy. The pericarditis was treated with salicylates and corticosteroids (*IDSA 629*).

Staphylococcus

Epidemiology and Prevention. Sneezing (histamine-induced) by nasal carriers of *S aureus* was associated with the airborne dispersal of 8 colony-forming units (CFU) per sneeze and this dispersal was further increased in the presence of rhinovirus infection (*ICAAC K-457*). Sneezing associated with experimental rhinovirus infection also led to increased dispersal of coagulase-negative staphylococci from nasal carriers of this organism (*ICAAC K-458*).

S aureus isolates from simultaneous nasal and wound cultures in patients with community-acquired soft tissue infections were frequently genetically indistinguishable (*ICAAC K-94*).

A total of 1627 patients with nasal *S aureus* colonization admitted to nonsurgical services were randomized to receive nasal mupirocin or placebo. While the use of mupirocin was associated with a significant delay in the time to *S aureus* infection, the overall rates of infection did not significantly differ between treatment arms (*ICAAC K-461*).

MRSA. The use of both levofloxacin (OR 3.4) and ciprofloxacin (OR 2.5) was associated with an increased risk of recovery of methicillin-resistant *S aureus* (MRSA), but not of methicillin-susceptible *S aureus* (MSSA) (*ICAAC K-105*).

The relative virulence of MRSA and MSSA has been a matter of discussion. In 1 study, postoperative mediastinitis caused by MRSA, but not MSSA, was associated with increased mortality relative to matched controls (*ICAAC-579*).

Evidence of an increasing prevalence of MRSA acquisition in the community continues to grow. While the annual number of nosocomial pediatric MRSA infections in southern Texas has remained constant over the last 11 years, there has been an exponential increase in community-acquired MRSA infections in children (*IDSA 618*).

In a study in southeastern New England, almost one-half of pediatric MRSA infections, most involving skin and soft tissue, appeared to be community acquired. Community-acquired isolates were less likely to be mul-

tidrug resistant (*IDSA 617*). Several lines of evidence indicate that MRSA in the community differ from hospital strains. In San Francisco, MRSA of community origin are largely clonally distinct from hospital-associated strains (*IDSA 23*). Methicillin resistance was highly associated with the presence of the Panton-Valentine leukocidin during a community outbreak of MRSA infections in Alaska (*IDSA 126*).

The proportion of MRSA that were community acquired was 5% in Georgia, 1% in Maryland, and 11% in Minnesota. When compared to patients with nosocomial MRSA, those with community MRSA were younger and more likely to have skin and soft tissue infection (*IDSA 121*). Forty (34%) of 118 community-acquired *S aureus* isolates at a Detroit hospital were MRSA; more than 50% of the patients with MRSA had had no previous hospital contact, and their isolates were genetically distinct from hospital isolates (*IDSA 123*).

In a note of caution, however, a study in Louisville found that many pediatric infections believed to be community acquired actually derived from recent direct contact with the health care system (*IDSA 620*).

VRSA. The first infection with vancomycin-resistant *S aureus* (VRSA) was preceded by vancomycin-resistant *Enterococcus faecium* (VREF) colonization, recurrent MRSA infections, and repeated exposures to vancomycin (*LB-6*). The VRSA isolate, which also carried the *mecA* gene associated with methicillin resistance, contained a *vanA* gene identical to that of the *vanA* gene from a VREF isolated from the same catheter tip, suggesting in vivo transfer of this resistance gene cassette (*ICAAC LB-7*).

Bacteremia/Endocarditis. You are asked to see a patient who had a single positive blood culture that yielded *S aureus*. Is this likely to represent a real infection or is it a contaminant? One group reported that 85% of patients with a single positive blood culture yielding *S aureus* were considered to be truly bacteremic with this organism (*ICAAC K-84*).

In a cohort of patients with *S aureus* bacteremia, community acquisition of infection and persisting bacteremia on therapy were significant predictors of a secondary focus of infection, and sustained bacteremia was associated with a 6-fold increased risk of death (*ICAAC K-462*).

In an analysis of 98 injection drug users with *S aureus* endocarditis (two-thirds right-sided), the presence of 2 or more complications and initiation of therapy with vancomycin, rather than a ß-lactam, were associated with an increased risk of death. Vancomycin therapy was also associated with a slower clinical response and a longer duration of bacteremia (*ICAAC L-765*).

The combination of linezolid and vancomycin was less effective than vancomycin alone in a rabbit model of MRSA endocarditis (*ICAAC B-276*).

Fourteen (8.6%) cases of native valve endocarditis were due to coagulase-negative staphylococci; ten had a predisposing factor such as the presence of an intravascular device, and 11 had preexisting valve disease (*ICAAC L-768*).

A woman in Canada presented with multiple embolic stokes resulting from intracardiac echinococcosis (*IDSA 730*).

Antibiotic Therapy. Of 69 MRSA that were erythromycin-resistant but clindamycin-susceptible by broth microdilution testing, 58 (84%) had inducible resistance to clindamycin, and all 23 tested contained the *ermA* (5) or *ermB* (18) gene (*IDSA 92*). Similarly, 35 (30%) of 73 *S aureus* and 5 (63%) of 8 *S pneumoniae* isolates classified as erythromycin-resistant but clindamycin-susceptible had inducible *erm* genes expressing MLSB resistance. Thus, in the absence of testing for inducible resistance, clindamycin may not be a good choice for treatment of infections due to erythromycin-resistant *S aureus* and *S pneumoniae* (*IDSA 91*).

Vancomycin is a poor choice for treatment of MSSA infections. A retrospective analysis found that initial treatment with vancomycin was an independent predictor of related mortality ($P = 0.012$) in patients with bacteremia due to methicillin susceptible *S aureus*. When compared to beta-lactam therapy, vancomycin therapy was associated with a slower clinical response and longer duration of bacteremia (*IDSA 579*).

In vitro antagonism between linezolid and both gentamicin and vancomycin against MRSA was reported. Linezolid, however, prevented the emergence of rifampin-resistant isolates when combined with this drug (*ICAAC E-1132*).

Enterococcus

The introduction of linezolid was associated with a subsequent decrease in susceptibility of vancomycin-resistant *E faecium* to this oxazolidinone from 100% to 80% at a Houston hospital (*ICAAC E-1134*).

Of 2278 patients with endocarditis from 7 sites in 5 countries, 166 (7.3%) were due to *Enterococcus*. Compared to endocarditis due to other organisms, enterococcal endocarditis was associated with an increased risk of systemic embolization and heart failure. Patients with enterococcal endocarditis were older and more likely to have infection of a prosthetic valve but had equivalent mortality (18% vs 20%) (*ICAAC L-764*).

A review of 25 cases of enterococcal meningitis found that 20 had a CSF shunt, 7 had CSF leakage, and 7 had recent neurosurgery. The infection was mixed in

13 (*ICAAC K-1954*). A case of *E faecium* meningitis in a patient with lymphoma was successfully treated with linezolid, 600 mg IV q 12 h for 4 weeks (*IDSA 221*).

S pneumoniae

In addition to a significant decrease in the incidence of invasive pneumococcal disease in young children since the introduction of the 7-valent pneumococcal conjugate vaccine, a significant decrement in older children and adults, consistent with a herd effect, was reported (*IDSA 31, IDSA 32*). Administration of the conjugate pneumococcal vaccines to renal transplant recipients was associated with a 50% response rate, while a response to the polysaccharide vaccine was observed in only 23% ($P = 0.032$) in a randomized trial (*ICAAC G-1073*). A 3-year study of the efficacy of pneumococcal polysaccharide vaccine in almost 50,000 subjects found that vaccination was not associated with a decrease in the risks of all-cause community-acquired pneumonia or death but was associated with a 54% reduction in the risk of pneumococcal bacteremia (*ICAAC G-840*).

Sixty-three percent of 496 invasive pneumococcal isolates from Asian countries were resistant to erythromycin, mostly related to the presence of the *ermB* gene (*ICAAC C2-1622*). Although nationwide only 0.8% of approximately 10,000 *S pneumoniae* isolates were resistant to levofloxacin, 4.6% and 4.8% of those from Massachusetts and Colorado, respectively, were resistant to this fluoroquinolone. In Salem, Mass, 21.8% were resistant (*ICAAC C2-650*).

A Monte Carlo analysis using clinical PK data found that the probability of achieving a free (nonprotein-bound) drug AUC0-24/MIC > 33.7, a value associated with increased likelihood of bacterial eradication, against ciprofloxacin-resistant *S pneumoniae* isolates was 61% for moxifloxacin, 58% for gatifloxacin, 38% for levofloxacin 750 mg qd, and 10% levofloxacin 500 mg qd (*IDSA 66*). A similar analysis with 4940 unselected pneumococcal isolates found that the likelihood of achieving a free drug AUC0-24/MIC > 33.7 was 99% for moxifloxacin, 97% for levofloxacin 750 mg IV qd, and 87% for levofloxacin 500 mg qd. The probabilities of achieving a target mutant prevention exposure with an AUC0-24/MIC > 135 were 99% for moxifloxacin, 25% for levofloxacin 750 mg, and 1.5% for levofloxacin 500 mg qd (*IDSA 67*).

The presence of the IL-10 polymorphism, IL10G, which is associated with increased IL-10 secretion in vivo, was associated with a more complicated course of pneumococcal infection (*ICAAC B-953*).

Neutropenia

Resistance to fluoroquinolones emerged in *viridans* group streptococci in the majority of patients with hematological malignancy given fluoroquinolone prophylaxis (*ICAAC C2-648*). Levofloxacin prophylaxis in neutropenic cancer patients was associated with the emergence of *viridans* streptococci resistant to levofloxacin and with reduced susceptibility to moxifloxacin and gatifloxacin (*IDSA 19*).

The incidence of *S viridans* bacteremia in adult allogeneic hematopoietic stem cell recipients was 9%, and the attributable mortality (death with shock and respiratory distress without other explanation) was 19%. In these patients, who received ticarcillin/clavulanate plus amikacin as empiric therapy, there was no association between penicillin resistance and mortality (*ICAAC K-1228*).

The most commonly identified cause of diarrhea in hematopoietic stem cell recipients was *C difficile* (19%), followed by adenovirus (6%). The combination of stool culture, examination for ova and parasites, and testing for rotavirus had a yield of only 0.5% (1 case of giardiasis) (*ICAAC K-1229*). Twenty-four (18%) of 135 hematopoietic stem cell recipients with diarrhea who were tested for stool rotavirus had a positive test; twenty-two of the 24 were adults. Many had additional reasons to have diarrhea, including *C difficile*, chemotherapy, and GVHD (*IDSA 760*).

Shock

Twenty-eight-day mortality among 124 patients with severe sepsis randomized to receive, for 5 days, placebo or platelet-activating factor at doses of either 1 mg or 5 mg was, respectively, 44%, 21%, and 28%. The difference between the 1-mg dose of the factor and the placebo was statistically significant ($P = 0.026$) (*IDSA 209*).

A case of recurrent toxic shock-like syndrome related to repeated exposure to diclofenac is described (*IDSA 244*).

Nosocomial Infections

In a randomized trial, selective gut decontamination with oropharyngeal and GI tobramycin, polymyxin E, and amphotericin B was associated with a reduction in mortality in critically ill patients (*ICAAC K-1091*).

A cut-off point of > 10^6 CFU/mL on endotracheal aspirate cultures correlated well with invasive techniques in the diagnosis of ventilator-associated pneumonia in patients who had not received previous antimicrobial therapy (*ICAAC K-1360*).

Ceftazidime plus gentamicin was superior to ciprofloxacin monotherapy in a small, randomized trial in patients with severe late onset (> 4 days after ICU admission) pneumonia (*ICAAC K-1361*).

Forty-six (77%) of 60 patients who had undergone coronary artery bypass grafting (CABG) who had *S aureus* bacteremia had postoperative *S aureus* mediastinitis. The investigators conclude that "*S aureus* bacteremia after CABG strongly suggests … mediastinitis until proven otherwise" (*ICAAC K-1807*).

Health Care Epidemiology and Antibiotic Stewardship

Households were randomized to use either plain or antimicrobial (with 0.2% triclosan) soap. After the end of 1 year, there was a significant decrease in bacterial colony counts on the hands of both groups, but no difference between groups. Users of both types of soap had comparable decreases in Gram-negative rods and *S aureus* but an increase in coagulase-negative staphylococci. There were no differences between plain and antimicrobial soap. Thus, improved hygiene has an impact on hand microbial flora in the home over time, but there was no difference in efficacy of the 2 soaps in this regard (*IDSA 424, IDSA 425*).

A contaminated disinfectant proved to be the source of an outbreak of external ear infections due to *P aeruginosa* infections. Seven (13%) of those who had piercing of upper ear cartilage were affected in contrast to none of 65 with lobe piercings. All had auricular chondritis, 5 required surgery, and 4 were left with residual deformity (*IDSA 148*).

Having a child (6 months to 5 years of age) who receives out-of-home care in a setting with at least 5 other children present is associated with a high burden of respiratory and GI illness in family members. On average, 3.7 respiratory illnesses and 1 gastrointestinal illness per patient-year were introduced into households (*IDSA 319*).

An outbreak of bloodstream infections due to *Alcaligenes xylosidans* in an outpatient oncology office was statistically associated with the use of multidose heparin and saline vials used in flushing venous access catheters (*IDSA 415*).

Outbreaks of invasive *S pyogenes* infections occurred in 2 nursing homes (*IDSA 113, IDSA 114*).

A prospective, observational study found that leaving peripheral venous catheters in place for up to 4 days is safe and reduces costs (*ICAAC K-663*).

The use of Polysporin ointment was associated with a reduced frequency of hemodialysis catheter-related infections when compared to a placebo in a randomized, blinded trial (*ICAAC K-669*).

A patient receiving chronic total nutrition, who had had 14 catheter-related bacteremias over 6 years and who had in place her fourth Hickman catheter, had no further infections for 35 months after she used a 25% alcohol lock solution for 1 hour daily (*ICAAC K-671*).

Open hospital antibiotic formularies were associated with a trend toward lower rates of bacterial resistance than were closed formularies in a 34-hospital study (*ICAAC K-1352*).

A stochastic mathematical model of the transmission of drug-susceptible and -resistant colonizing bacteria found that the simultaneous use of different antimicrobial classes for different patients ("mixing") was superior to antimicrobial cycling (*ICAAC K-1345*).

Only 44% of members of a military community presenting to medical facilities who had antibiotics detected in their urine admitted to having consumed antibiotics (*IDSA 104*). ■

CME Questions

6. Which of the following is correct?

a. Arterial catheters are associated with a risk of bloodstream infection only one-tenth of that with central venous catheters.
b. Toothpick injuries of the foot invariably respond to antibiotic therapy alone.
c. Early adjunctive dexamethasone therapy improved outcome in adults with bacterial meningitis.

7. Which of the following is correct?

a. Nitrofurantoin was superior to the use of a vaginal estradiol pessary in prevention of urinary tract infection in postmenopausal women.
b. A 5-day course of azithromycin was inferior to a 10-day course of erythromycin in the treatment of pertussis.
c. Resistance to ciprofloxacin has not been reported to occur in *Campylobacter jejuni*.
d. Resistance to levofloxacin has not been reported in *Haemophilus influenzae*.

8. Which of the following is correct?

a. Community-acquired MRSA have all been clonally related to nosocomial MRSA.
b. Vancomycin is superior to beta-lactam therapy in the treatment of infection due to methicillin-susceptible *S aureus*.
c. *S pneumoniae* are uniformly susceptible to levofloxacin in all US locations.
d. n a randomized trial, there was no significant difference in reduction in the microbial flora of the hand when plain soap and triclosan-containing soap were compared in a household stud.

Answers: 6(C); 7(A); 8(D)

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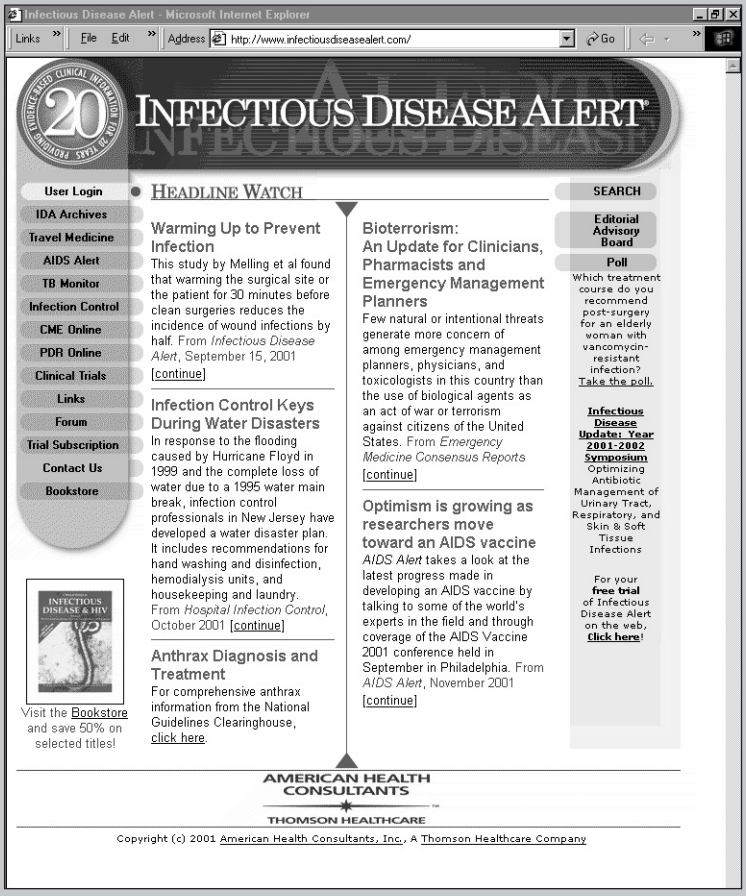

PHARMACOLOGY WATCH

FDA Issues 'Black Box' Warning Based on WHI Study

The FDA has mandated a "Black Box" warning for all estrogen and estrogen/progestin products for use by postmenopausal women. The new warnings are based on analysis of data from the Women's Health Initiative (WHI) study that was published July 2002. The box warning emphasizes that these drugs have been associated with increased risks for heart disease, heart attacks, strokes, and breast cancer and that they are not approved for heart disease prevention. Wyeth Pharmaceuticals, the manufacturer of Premarin, Prempro, and Premphase, products that were used in the WHI study, are also required to change their indications to: treatment of severe vasomotor symptoms, vulvar and vaginal atrophy associated with menopause, prevention of postmenopausal osteoporosis, and should only be used when the benefit clearly outweighs the risk. The labeling will also be required to include consideration of other therapies for the atrophy and osteoporosis indications, and to recommend use of the lowest dose for the shortest duration possible. While Wyeth's products are the focus of this initial press release and FDA action, all estrogen products will be subject to new labeling. The FDA is also recommending future research to answer questions regarding the risks of lower-dose estrogen products and if other types of estrogens and progestins are associated with lower risk of CVD and breast cancer. The complete press release can be viewed at www.fda.gov.

ALLHAT: Thiazide for Hypertension Treatment

Thiazide diuretics should be considered first-line therapy for hypertension, according to the authors of the ALLHAT study published in December. In a finding that surprised nearly everyone (especially the sponsors of the study) in patients with hypertension and at least one other cardiovascular risk factor, the diuretic chlorthalidone was associated with better cardiovascular outcomes at less cost and with equal tolerability compared to a calcium channel blocker or an ACE inhibitor. ALLHAT enrolled more than 33,000 patients from 623 centers in the United States, Canada, and the US Virgin Islands. Patients were randomized to the calcium channel blocker amlodipine, the angiotensin-converting enzyme inhibitor lisinopril, or chlorthalidone. Mean follow-up was 4.9 years with the primary outcome being combined fatal CHD or nonfatal MI. Secondary outcomes included all-cause mortality, stroke, combined CHD, and combined cardiovascular disease (CVD). The 6-year rate of the primary outcome and all-cause mortality was virtually identical for all 3 drugs. Chlorthalidone was superior to amlodipine in preventing heart failure (10.2% vs 7.7%, RR, 1.38, 95% CI, 1.25-1.52) and was superior to lisinopril for lowering blood pressure and in 6-year rates of combined cardiovascular disease including stroke (6.3% vs 5.6%) and heart failure (8.7% vs 7.7%). With improved cardiovas-

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. Telephone: (404) 262-5517. E-mail: robin.mason@ahcpub.com. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

cular outcomes, lower cost, and equal tolerability, the study concludes that thiazide-type diuretics are superior in preventing one or more forms of CVD and that they should be the preferred agent in antihypertensive therapy, and should be included in all multidrug regimens (*JAMA*. 2002;288:2981-2997). An accompanying editorial calls ALLHAT "one of the most important trials of antihypertensive therapy" and suggests that national guidelines should be changed to emphasize use of thiazide diuretics as initial therapy (*JAMA*. 2002;288:3039-3042).

Candesartan Effective Against Migraines

The angiotensin II receptor blocker candesartan is effective in preventing migraine headaches, according to a new study. Norwegian researchers looked at 60 patients age 18-65 with 2-6 migraines per month. Patients were randomized in a double-blind placebo-controlled crossover study with the main outcome being number of days with headache. Secondary outcomes included use of pain medications and triptans, hours with headache, headache severity, and days lost from work. During the 12-week study, the mean number of days with headache was 18.5 with placebo vs 13.6 with candesartan (P = .001) in the intention to treat analysis (n = 57). Patients were considered a candesartan responder if they noted a reduction of 50% or more of days with headache (18 of 57 patients, 31.6%) or days with migraine (23 of 57 patients, 40.4%). Although this represented a minority of patients, those who did respond benefited from effective migraine prophylaxis. Candesartan's tolerability profile was comparable with placebo (*JAMA*. 2003;289:65-69).

Cough! No Cold Relief from Echinacea

Echinacea offers no benefit in treating the common cold according to a study from the University of Wisconsin. A total of 148 college students with recent onset colds were randomized to an encapsulated mixture of unrefined Echinacea (*E purpurea* herb and root and *E angustifolia* root) 6 times a day on the first day of illness and 3 times a day on the subsequent days up to a total of 10 days. The main outcome was the severity and duration of self-reported symptoms of URI. No statistically significant differences were detected between Echinacea and placebo groups for any of the measured outcomes, which included trajectories of severity over time or mean cold duration. No significant side effects were noted with Echinacea. The study concludes that no detectable benefit or harm could be found with Echinacea treatment for the common cold (*Ann Intern Med*. 2002;137:939-946).

COX-2 Inhibitors and GI Benefits Could Be Overrated

Could the GI benefits of COX-2 inhibitors be overrated? A new study suggests that the COX-2 inhibitor celecoxib is no safer than a combination of diclofenac plus omeprazole with regard to ulcer risk in patients with a history of peptic ulcer disease and arthritis. Researchers from Hong Kong recruited patients with arthritis and NSAID-related bleeding ulcers. After their ulcers had healed, 287 patients who were negative for *Helicobacter pylori*, were randomly assigned to receive celecoxib 200 mg twice a day plus placebo, or diclofenac 75 mg twice a day plus 20 mg of omeprazole for 6 months. Recurrent bleeding ulcer occurred in 7 patients receiving celecoxib and 9 receiving diclofenac/omeprazole (4.9% vs 6.4%). Renal adverse events including hypertension, peripheral edema, and renal failure occurred in 24.3% of patients receiving celecoxib and 30.8% of those receiving diclofenac/omeprazole. The authors suggest that neither regimen offered effective protection against recurrent ulcer complications or renal adverse effects (*N Engl J Med*. 2002;347:2104- 2110).

FDA Actions

Pfizer's new anti-migraine drug, eletriptan (Relpax) has been approved by the FDA for marketing. The drug that is available in 20-mg and 40-mg tablets has been shown to be effective in aborting migraine headaches within 2 hours. The company is marketing a 80-mg tablet in Europe, but the FDA refused to approve the higher dose due to an increase in adverse events.

Montelukast (Singulair), Merck's leukotriene inhibitor, has been approved by the FDA for the treatment of seasonal allergic rhinitis. The drug has been on the market since 1998 for the treatment of asthma in adults and children. This new indication is the first for a leukotriene inhibitor, and creates a new, nonantihistamine treatment modality for this indication. Montelukast was approved for symptoms of seasonal allergic rhinitis in adults and children aged 2 years and older. It is available in 10 mg strength for adults, and a chewable 4 mg or 5 mg strength for children. ■