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Conference Summaries of ICAAC 1999 and IDSA 1999: Part IV

CONFERENCE COVERAGE

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

Staphylococcus spp.

Staphylococcus aureus remains one of the most commonly encountered pathogens, both in and out of the hospital. A portal of entry was identified in 63% of 153 patients with community-acquired *S. aureus* bacteremia; only five were injection drug users. Approximately three-fourths had underlying chronic illness and one-third had skin/soft tissue infections. Approximately 9.2% had endocarditis and 17.6% had septic arthritis or osteomyelitis. One-fourth died. (ICAAC #1093.)

A study of 217 methicillin-resistant *S. aureus* (MRSA) isolates from 10 hospitals in nine cities on the east coast of the United States from Florida to Massachusetts found that only two clones accounted for 67% of isolates. (ICAAC #1234.)

There have been several recent reports of MRSA infection believed to have been acquired in the community, rather than in hospitals. Several studies reported at these meetings suggest we may need to examine this issue more closely. For instance, most cases of "community-acquired" MRSA in a population of veterans were

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associated with frequent hospital contact suggesting that the true reservoir of these organisms was, in fact, the health care facility and not the community. (*IDSA #158.*) Similar conclusions were reached in a study at the University of Chicago hospitals and in Singapore (*IDSA #165, ICAAC #1705.*) In contrast, however, a study in Dallas found that strains of MRSA isolated from children and thought to be community acquired appeared to be distinct from hospital strains by pulse field gel electrophoresis (PFGE). (*IDSA #597.*)

In contrast to these findings, 62 of 112 (55%) of *S. aureus* isolates from residents of a rural American Indian community in Minnesota were methicillin resistant. Three-fourths of the MRSA infections were community acquired; 76% of the MRSA isolates belonged to one of three closely related PFGE patterns. (*ICAAC #1230.*)

Many of my colleagues outside the specialty of infectious diseases appear to be of the opinion that vancomycin is a more potent agent against all staphylococci, regardless of susceptibilities, than are beta-lactam antibi-

otics. However, in vitro studies indicate that vancomycin is less rapidly bactericidal against susceptible *S. aureus* than are various beta-lactam antibiotics. In apparent clinical confirmation of these results, a prospective observational study of hemodialysis patients with bacteremia due to methicillin-susceptible *S. aureus* found persistent bacteremia at 24 hours in 25% of beta-lactam and 37% of vancomycin recipients ($P > 0.05$). The mean times to defervescence were 1.4 and 3.6 days, respectively ($P < 0.05$). (*ICAAC #1095.*)

One study provided observations that suggest vancomycin may be subject to the inoculum effect and that, as a result, its efficacy may be reduced in the presence of infection with a high density of microorganisms. Twelve patients with prolonged *S. aureus* bacteremia while receiving vancomycin were evaluated. On in vitro testing of the patients' isolates a marked inoculum effect was noted and, at an inoculum of 10^9 , more than 95% of the vancomycin present was rapidly removed from the medium. The dose of vancomycin administered to 11 of the patients was increased to as high as 3 gm q 12h with resultant peak levels of 53 mcg/mL to 123 mcg/mL; all 11 survived whereas the 12th died with persistent bacteremia. One patient developed tinnitus, possibly attributable to vancomycin. (*ICAAC #1774.*)

MRSA infection relapsed in a patient three weeks after discontinuation of an approximately 100-day course of therapy with vancomycin. Although PFGE demonstrated apparent identity of the original strain to the relapsing strain, the latter had acquired heterogeneous vancomycin resistance. (*ICAAC #1238.*)

Vancomycin resistance in *S. aureus* is popping up in new and, perhaps, unexpected places. Seven clinical strains of *S. aureus*, each isolated from a different patient in Guatemala, were highly resistant to vancomycin (MIC 128-256 mcg/mL) by several methods. These strains were also resistant to penicillin, methicillin, cefotaxime, chloramphenicol, and amikacin; four of the seven were susceptible to levofloxacin. (*IDSA #2.*)

Intermediately vancomycin-resistant strains are probably much more commonly encountered than our laboratories are telling us. A survey of 330 responding U.S. laboratories found that 15.4% were using in vitro methods that would not detect *S. aureus* with reduced susceptibility to vancomycin. (*ICAAC #891.*)

The C-8 methoxy group of moxifloxacin appears to be critical to the observed decreased propensity of the development of resistance to this antibiotic in vitro by *S. aureus*. (*IDSA #102.*)

A variety of explanations have been offered for the frequent inability of antibiotic therapy alone to effectively sterilize abscesses—here's another one. Neutrophils

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decreased the density of PBP2 expression by *S. aureus* by approximately one-half while PBP4 increased by 71%, possibly explaining, at least in part, diminished killing of bacteria within an abscess by beta-lactam antibiotics. (IDSA #4.)

Investigators reported a phenotypic change that may be associated with an enhanced risk of catheter-related *S. aureus* bacteremia. The increased cell wall thickness of heterogeneous vancomycin intermediate *S. aureus* is associated with enhanced biofilm formation and adherence to artificial surfaces. (ICAAC #44.)

Enterococcus spp.

The putative virulence factors, hemolysin, gelatinase, and Esp, were not associated with increased 14-day mortality in 231 patients with *E. faecalis* bacteremia. (ICAAC #1551.)

Approximately 44% of *E. faecalis* and 2% of *E. faecium* isolated from chickens purchased from grocery stores in the United States had high-level gentamicin resistance, while no such isolates were detected in chickens purchased in Denmark. Gentamicin is widely used as an antimicrobial growth promoter in the United States, but not in Denmark. (ICAAC #727.)

Quinupristin/dalfopristin has recently been approved for use in humans in the United States (*Med Letter* 1999;41:109-110). Thirty-five of 36 (97%) *E. faecium* isolates from chickens purchased in grocery stores in the United States were resistant to quinupristin/dalfopristin, as were two of 17 (12%) isolates from human feces. This observation is likely related to the use of the streptogramin antibiotic, virginiamycin, as an antimicrobial growth promoter in food animals in the United States since 1974. (ICAAC #726.)

A murine model of gastrointestinal colonization with VRE after gastric inoculation found that the IV administration of either ceftriaxone or vancomycin was associated with high levels of colonization (10^4 VRE/gm stool) that persisted during antibiotic administration. Previous rodent studies had demonstrated that IV administration of vancomycin also produced persistent high-level gastrointestinal colonization with VRE. No such effect was seen with piperacillin/tazobactam administration. (IDSA #464.)

Of 936 cases of enterococcal bacteremia identified in one laboratory over a 13-year period, 15 were caused by *E. gallinarum*, three by *E. casseliflavus*, and one by *E. flavescens/gallinarum*; all are intrinsically vancomycin resistant. There was one case of *E. gallinarum* endocarditis. (ICAAC #1722.)

Of 14 urinary tract isolates of VRE, 10 were susceptible and four were intermediately susceptible to nitrofu-

rantoin. Therapy with this drug was associated with eradication of seven of the 10 susceptible isolates but none of the intermediate ones. (IDSA #230.)

Thirteen of 26 patients receiving quinupristin/dalfopristin, recently approved for use in the United States by the FDA, developed arthralgias and/or myalgias. (IDSA #238.) A patient with enterococcal meningitis (with underlying strongyloidiasis) was successfully treated with linezolid. (IDSA #240.)

Gram-Negative Bacilli

Ten patients with brucellosis were treated with azithromycin 500 mg qd for 21 days plus gentamicin 240 mg qd for the first seven days. Two patients failed treatment and an additional three relapsed within one month of completion of therapy. (ICAAC #1072.)

Antibiotic resistance among gram-negative rods keeps marching on. For instance, carbapenem-resistant *P. aeruginosa* producing a metallo- β -lactamase (VIM-1) has appeared in northern Italy. (ICAAC #1482.)

While 94-96% of 2684 ceftazidime-susceptible Enterobacteriaceae isolates in the United States were also susceptible to levofloxacin, trovafloxacin, and ciprofloxacin, only 78%, 69%, and 66% of ceftazidime-resistant isolates were susceptible to these fluoroquinolones, respectively. (ICAAC #2259.) ESBL production was found in 15 of 25 (60%) of ciprofloxacin vs. only 68 of 427 (16%) ciprofloxacin-susceptible resistant *K. pneumoniae* isolates. (ICAAC #2266.) Eighty-five of 455 (19%) *K. pneumoniae* isolates from seven countries (18% in U.S. isolates) had evidence of ESBL (mostly SHV-derived) production. (ICAAC #1473.) This association between ceftazidime and fluoroquinolone resistance was recently reported in nursing home outbreaks of multidrug-resistant *Klebsiella* and *E. coli* infections (*JAMA* 1999;281:17-23).

Our laboratories may not always be detecting antibiotic resistance. A survey of 330 responding U.S. laboratories found that only 24.2% attempted to identify ESBL-producing Enterobacteriaceae, although 92.5% used adequate screening methods. (ICAAC #891.)

In vitro microdilution MICs were measured for eight beta lactam antibiotics against 86 strains composed of *Klebsiella*, *Escherichia*, *Enterobacter*, *Citrobacter*, *Serratia*, *Morganella*, and *Proteus* spp. containing a variety of extended spectrum beta lactamases (ESBL) and plasmid mediated AmpC beta lactamases at standard and 100-fold higher inocula. Imipenem was, overall, the most potent of the agents tested. Imipenem and cefepime were the most active against organisms producing plasmid mediated AmpC beta lactamase, but

only imipenem was active against all isolates at the higher inoculum. An inoculum effect with ESBL producing strains was seen most consistently with cefotaxime, ceftriaxone, and cefepime, less often with aztreonam and piperacillin/tazobactam, and least with imipenem and ceftiofloxacin. (IDSA #121.)

Eighty-nine percent of 110 clinical isolates of *S. maltophilia* were reported to be susceptible to clinafloxacin at concentrations of less than 2 mcg/mL. (ICAAC #73.) Other studies had susceptibility rates of 77% and 95%. Forty percent were susceptible to ciprofloxacin, 73% to levofloxacin, 69% to gatifloxacin, and 83.1% to moxifloxacin. (ICAAC #2280, #2294.)

Eleven patients received polymyxin B intravenously for a mean duration of 11.7 days for treatment of infection due to multidrug-resistant *P. aeruginosa*. Microbiologic cure was achieved in four of six patients who were treated for at least 10 days. (IDSA #216.)

A series of efflux pump inhibitors enhanced the activities of fluoroquinolones against otherwise resistant strains of *P. aeruginosa* (as well as and of azoles against resistant strains of *Candida*). (ICAAC #1264-1271.)

Miscellaneous Pathogens

Dormitory residence was found to be a significant risk factor in a case-control study of 50 cases of meningococcal disease in college students. Three-fourths of the infections were caused by vaccine-preventable serogroups. (IDSA #63.)

A significant association was found between the interleukin-1 genotype and outcome from meningococcal infection. (ICAAC #496.) Mannose-binding lectin deficiency resulted in increased susceptibility to meningococcal disease in three generations of one family. (ICAAC #2171.) The association of polymorphisms of this gene and susceptibility to infection have been previously reported (*Lancet* 1999;353:1049-1053). 4G/5G promoter polymorphisms in the plasminogen-activator-inhibitor-1 gene have also been associated with the outcome of meningococcal disease (*Lancet* 1999; 354:556-560; *Lancet* 1999;354:561-563).

Sixteen of 44 clinical isolates of meningococcus from nine Portuguese hospitals from 1995-99 were resistant to penicillin (MIC 0.125-0.5 mcg/mL). (ICAAC #2102.)

Contaminated hot dogs and other processed meats were the source of a multistate outbreak of listeriosis. (IDSA #60.) A nosocomial outbreak of listeriosis in Finland was traced to contaminated butter from a single dairy. There were 24 cases with six deaths. (ICAAC #2082.)

Fifty cases of *Rhodococcus* infection in non-AIDS patients were identified over nine years at a cancer cen-

ter. In contrast to the pattern seen in AIDS patients, only one of these 50 had pulmonary infection, with the remainder having bacteremia—94% of whom had central venous catheters. (IDSA #129.)

Four percent of 980 surveyed physicians reported that they had treated or recommended treatment of cardiovascular disease with an antibiotic. This included 2% of family physicians and general practitioners, 4% of infectious disease specialists, 8% of internists, and 12% of cardiologists. (IDSA #574.)

Antibiotic Therapy

Appropriateness. Studies of antibiotic prescribing by emergency room physicians performed by the Emergency ID Net Study Group found that one-third of antibiotics prescribed for respiratory illnesses and one-half prescribed for patients with lacerations were inappropriate. (IDSA #522, 524.)

Antibiotics were administered to 27.6% of 4637 patients with a coded diagnosis of influenza, while amantadine or rimantidine was prescribed for only 6.8%. (IDSA #703.)

Adverse Effects. Review of available information indicates that the phototoxicity of fluoroquinolones is associated with the presence of a halogen at the C-8 position, while severe life-threatening apparently immune-mediated reactions are associated with the presence of a 2,4-difluorophenyl structure. (IDSA #94.)

Both ciprofloxacin and trovafloxacin adversely affected experimental fracture healing in rats. (ICAAC #1766.) Ciprofloxacin and magnesium deficiency each produce identical biochemical alterations in immature canine tendons, consistent with the hypothesis that quinolones cause connective tissue abnormalities by binding to magnesium. (ICAAC #1765.)

Two hundred two inpatients receiving antibiotic therapy were randomized to no intervention or to receive yogurt. Yogurt ingestion was associated with a significant reduction in the incidence and duration of diarrhea. (IDSA #83.)

A retrospective analysis of febrile neutropenic bone marrow transplant patients with a history of penicillin allergy found that the incidence of allergic reactions to imipenem was 33% (2 of 6) among those with documented allergy and only 4.7% (2 of 43) among those in whom there was no documentation. (ICAAC #1088.)

Outpatient Parenteral Antibiotic Therapy. Twenty-four patients receiving outpatient IV antibiotic therapy for a mean of 27.5 days via PICC lines were studied prospectively with ultrasonography performed at the time of symptoms suggestive of thrombosis or at the

time of catheter removal. Five of nine patients (56%) with symptoms (3 had only inability to flush the catheter) and six of 15 (40%) asymptomatic patients had evidence of thrombosis. Ultrasound was more sensitive than venography. (IDSA#505.)

Mycobacteria

Fewer than one-third of patients released from a correctional facility completed a twice-weekly course of directly observed INH preventive therapy against *M. tuberculosis*. Thus, the use of short-course pyrazinamide and rifampin may prove more effective in this group. (IDSA #622.)

Thirty-two percent of all co-primary tuberculosis (TB) cases and 23% of all TB infections detected during contact investigations were associated with smear negative source cases. (IDSA #625.)

The negative predictive value (NPV) of sputum smears of patients isolated in a university hospital for suspected pulmonary TB in an area of low prevalence for this infection was examined. Nine (3.3%) of 274 of the patients had *M. tuberculosis* recovered from their sputum culture. The NPV values of one, two, and three negative sputum smears were, respectively, 98.9%, 99.6%, and 100%. (IDSA #631.)

PCR of specimens eluted from a sputum slide successfully identified *M. tuberculosis* DNA from all 24 culture-positive sputa, including 10 that were microscopy negative. Sequencing of the *rpo B* gene from the PCR product then detected evidence of rifampin resistance in five specimens (2 of which were microscopy negative), all of which were confirmed as resistant by in vitro susceptibility testing. (IDSA #258, ICAAC #857.)

Forty-two percent of pediatric TB isolates in San Diego between 1994 and 1997 were *M. bovis*. A case control study confirmed an association with, among other things, ingestion of raw dairy products. (IDSA #615.)

Three thousand nine Native American and Alaskan Native children were enrolled in a randomized trial of BCG vaccination from 1936 to 1938. Cumulative vaccine efficacy in 1947 was 80%. A record review in 1992 found evidence of continued protection, with a significantly reduced case rate as well as mortality attributed to tuberculosis. (ICAAC #1403.)

A case control study of eight patients with BCGosis after treatment of superficial bladder cancer found that cases were less likely than controls to have a prior history of exposure to tuberculosis or to have received adjuvant interferon alpha therapy. They were more likely, however, to have received intraureteric BCG. (IDSA #618.)

Studies in animal models have found that mefloquine enhanced the activity of ethambutol, azithromycin, and clarithromycin against *Mycobacterium avium* complex infection and that moxifloxacin was active as a single agent. (ICAAC #1207b, 1207e.)

A corticosteroid-dependent patient with multiple lower extremity nodules due to *M. chelonae* was treated with clarithromycin alone. After an initial response, culture-positive recurrence was seen despite continued therapy achieving a peak blood level of 3.5 mcg/mL. The MIC of the new isolate to clarithromycin was more than 32 mcg/mL. (IDSA #249.)

Rapidly growing mycobacteria were isolated from 16 bone marrow transplant unit patients (*M. abscessus* from 9, *M. mucogenicum* from 5, and *M. fortuitum* in 3, with one patient having 2 species). *M. abscessus* and *M. fortuitum* were isolated from ice and tap water. RFLP analyses found 12 patterns in 17 patient isolates with two tap water isolates matching five patient isolates. Continued infections occurred after substituting bottled for tap water for drinking, but none occurred after restricting inpatients to bathing in sterile water. (IDSA #469.)

Thalidomide is the treatment of choice for erythema nodosum leprosum reactions, but its mechanism of action has remained speculative. Examination of peripheral blood mononuclear cells from healthy volunteers after oral administration of thalidomide found evidence of a shift toward a Th1 response. (ICAAC #1599.)

Viral Infections

Respiratory Viruses. Thirty-six of 274 pediatric bone marrow transplant recipients developed a viral respiratory tract infection. The most common etiologic agent was parainfluenza virus-3 (32.5%), followed by adenovirus (17.5%), influenza A (15%), RSV (12.5%), parainfluenza viruses 1 and 4 (each 7.5%), and influenza B (2.5%). Three deaths were attributable to respiratory virus infection. (ICAAC #1899.)

Influenza Viruses. From January through March 1999, all sputum samples received for routine bacterial culture in a community hospital laboratory in Illinois that had moderate to many neutrophils but no predominant bacterial type on gram stain were cultured for influenza A virus using a rapid shell vial technique. Eighty-four of 216 (39%) samples met these criteria; 16 (19%) were positive for influenza A virus after overnight incubation. Only one of the 16 patients had been placed in appropriate isolation at the time the result was reported to the nursing unit. (ICAAC #1689.)

Multivariate analysis of findings from 3815 adults found that, during periods of known influenza circula-

tion, the best predictors of the presence of influenza virus infection were fever plus cough ($P < 0.001$), with a positive predictive value of 81%, sensitivity of 63%, and specificity of 71%. (ICAAC #277.)

Examination of the effect of zanamivir on influenza in 195 high-risk patients randomized to receive drug or placebo in four clinical trials found a 2.5 day reduction in duration of symptoms ($P = 0.114$). (ICAAC #182.) Zanamivir treatment was associated with a significant reduction in antibiotic prescriptions for patients with influenza. (ICAAC #1903.)

A meta-analysis of five clinical trials found that zanamivir administration reduced the duration of symptoms in 220 randomized patients with influenza B virus infection from a mean of 6.0 to 4.5 days ($P = 0.05$). This result was similar to that in the 1352 randomized patients with influenza A virus infection in whom the duration of symptoms was reduced from 6.5 to 5.0 days ($P < 0.001$). (ICAAC #281.)

Sequencing of paired influenza A virus isolates from 39 patients treated with zanamivir found no mutations in the regions associated with substrate or drug binding. (ICAAC #284.)

One hundred seventeen seronegative healthy volunteers were randomized to receive either placebo or oseltamivir beginning 24 hours after intranasal inoculation of influenza B Yamagata/16/88. Oseltamivir administration was associated with an 83% reduction in nasal secretions virus titer, a 75% reduction in the duration of viral excretion, a 46% reduction in median peak viral titer, and a 36% reduction in symptom score. (IDSA #677.)

Zanamivir administration was associated with termination of an outbreak of influenza A virus infection in elderly subjects in a residential home, despite prior failure of amantadine prophylaxis. (ICAAC #283.) The estimated prophylactic efficacy of zanamivir in patients in a continuing care and rehabilitation facility who had been exposed to a health care worker with influenza A infection was 94%. (ICAAC #1701.)

Respiratory Syncytial Virus. Of 165 consecutive elderly (mean age, 82 years) admitted with lower respiratory tract infection, the cause was influenza virus in 46 (27.9%) and RSV in six (3.6%) with mortalities of 13.3% and 16.6%, respectively. (ICAAC #287.)

Fifty of 61 (82%) of hematopoietic stem cell recipients who developed RSV pneumonia had had an RSV upper respiratory tract infection a median of seven days prior to the onset of pneumonia. This suggests that preemptive therapy may be beneficial in this patient group. (ICAAC #1900.)

Adenovirus. Eighty-five patients undergoing bone

marrow transplantation from 1990 through 1998 at one center were found to have evidence of adenovirus infection, affecting 6% of allogeneic bone marrow recipients and only 0.92% of autologous recipients. Thirty-five percent of the allogeneic recipients with adenovirus infection had graft vs. host disease. Nine patients had asymptomatic viruria, 10 had hemorrhagic cystitis, 20 had upper respiratory infection, 15 had pneumonia, 10 had disseminated disease without pneumonia, five had disseminated disease with pneumonia, and 16 had enteritis. The attributable mortality was 21%. (ICAAC #289.)

Detection of adenovirus from two or more sites in children who had undergone hematopoietic stem cell transplantation was associated with organ system injury. Adenovirus infection was responsible for 14% of fatalities. (IDSA #686.)

Hepatitis Viruses

An outbreak of hepatitis A virus (HAV) infections was epidemiologically associated with ingestion of green onions. (IDSA #562.)

In a study of Egyptian children (mean age, 4 years) with acute HAV infection, HAV genome was detected in the serum of those with resolved hepatitis for as long as 126 days after onset. It was also detected in two of 20 with relapsing illness for up to 250 days and in 11 of 24 with persistently elevated ALT for up to 373 days. (IDSA #704.) Studies have also demonstrated fecal excretion of the virus for as long as three months after the onset of illness in some patients (*Hepatology* 1996;24:10-13).

A study of 3302 infants vaccinated within one day of birth and 2353 not so vaccinated found no evidence of an association of hepatitis B vaccination and increased rates of febrile episodes, sepsis evaluations, allergic, or neurologic events. (ICAAC #1631.)

Forty-two nonresponders to standard hepatitis B virus (HBV) vaccination were randomized to receive revaccination with either high-dose (40 mcg) HBV vaccine or with standard dose (10 mcg) vaccine plus 125 mcg GM-CSF at the same site at 0, 1, and 2 months. The success rate in each group was approximately 60% at three months. (ICAAC #1633.) Intradermal administration of HB vaccine (5 mcg in 0.25 mL) induced protective antibody titers and cellular immunity in 94% of health care workers who had been unresponsive to intramuscular vaccination. (ICAAC #678.)

Fifty-eight patients with chronic HBV infection were randomized to receive, for 24 weeks, either lamivudine plus interferon alpha, lamivudine alone, or interferon alpha alone. At the end of therapy, the 94.7% of the recipients of combination therapy and 92.3% of those

receiving lamivudine alone, but only 57.5% recipients of interferon alone, had normalization of serum aminotransferases. The rates of plasma HBV DNA clearance in the three groups were, respectively, 100%, 89.5%, and 60%. Ten of 16 complete or partial responders of interferon alone subsequently relapsed. Combination therapy was well tolerated and highly effective. (*IDSA #6.*)

Although the overall prevalence of hepatitis C virus (HCV) infection in the United States appears to be declining, it is estimated that the number of persons infected for more than 20 years could increase by more than 400% before peaking in 2015. (*IDSA #65.*)

Some HCV infections are cleared, while most become persistent. Among those with persistence, the risk of progression is highly variable. The presence of the class I antigen, HLA-Cw04, is strongly associated with persistence of HCV infection, but not to viral load. (*IDSA #71.*) A recent paper reported the association of several class II antigens and outcome of HCV infection (*Lancet* 1999;354:2119-2224).

TTV, a DNA virus of uncertain pathogenicity, is cleared from serum in some patients receiving interferon alpha treatment for HCV infection. (*ICAAC #93.*) Lamivudine, however, does not affect TTV levels in blood. (*ICAAC #106.*)

Enterovirus

Ten pregnant women with symptomatic enteroviral infection (median gestational age at onset was 35.5 weeks) were identified at one center over a 14-year period. There were no maternal or intrauterine deaths, but five of six infants born to mothers whose symptoms developed within one week of delivery had symptomatic infection with onset at 2 to 6 days of life (median, 3rd day of life). Thrombocytopenia occurred in four of the infants, while hepatitis and myocarditis each occurred in three, and seizures and rash each occurred in two. One child died as the result of myocarditis. (*IDSA #672.*)

An outbreak of enterovirus 71 infection predominantly affecting children younger than 5 years of age in Taiwan in 1998 was associated with more than 75 deaths. Mortality was associated with the development of fulminant brain stem encephalitis extending into the spinal cord. (*ICAAC #1969.*) A bibliography related to this outbreak can be found at <http://www.promedmail.com>.

One hundred thirty-seven of 276 (49.6%) pediatric

patients who were evaluated for possible enteroviral (EV) meningitis had a positive CSF EV-PCR, with the result being available a median of 37.1 hours (range, 4-139 hours) after request. A positive test was associated with reduced further diagnostic testing, reduced antibiotic use, and shortened length of stay. (*IDSA #45.*)

One hundred thirty patients with EV meningitis were randomized to receive either placebo or pleconaril. Pleconaril treatment was associated with shorter duration of headache (2 days less; $P = 0.04$), shorter duration of symptoms of meningitis (2 days less), and quicker return to work or school (by 2 days; $P = 0.045$). (*ICAAC #1904.*) ❖

CME Questions

5. Which of the following is correct?

- Vancomycin is more rapidly bactericidal against *S. aureus* than are beta lactam antibiotics, such as nafcillin.
- An in vitro study reported decreased activity of vancomycin against high, as opposed to lower, inocula of *S. aureus*.
- Fewer than 50% of U.S. hospital laboratories use in vitro methods capable of detecting *S. aureus* strains with reduced susceptibility to vancomycin.
- Nitrofurantoin is highly ineffective (< 25% clearance) in the treatment of urinary tract VRE infection, despite evidence of in vitro susceptibility.

6. Which of the following is correct?

- High-level gentamicin resistance was found in 44% of *E. faecalis* isolates recovered from chickens purchased in grocery stores in the United States.
- Gentamicin is used as a growth promoter in Denmark, but not in the United States.
- High-level gentamicin resistance was found in 44% of *E. faecalis* isolates recovered from chickens purchased in grocery stores in Denmark.
- A microbiological survey of chickens purchased in U.S. grocery stores failed to detect resistance to quinupristin/dalfopristin in any of 36 isolates of *E. faecium*.

7. Which of the following is correct?

- There appears to be linkage between ceftazidime resistance and fluoroquinolone hypersusceptibility among Enterobacteriaceae.
- An analysis of a study of BCG vaccination in Native American and Alaskan native children could find no evidence of protective efficacy.
- Although active against influenza A virus, zanamivir is not active against influenza B.
- Treatment with pleconaril was associated with a shortened duration of symptoms in patients with enteroviral meningitis.

In Future Issues:

ICAAC and IDSA Summaries:
Part V

Had your Clove of Garlic Today?

Source: Jonkers D, et al. *Antimicrob Agents Chemother* 1999;43:3045.

Garlic and onions have long been believed to convey some antimicrobial benefit, supported by limited in vitro data in experiments of aerobic bacteria and cryptococcus. Jonkers and colleagues assessed the antibacterial effect of garlic, alone and in combination with vancomycin, against 14 strains of vancomycin-resistant enterococci (VRE). Not only did garlic exhibit some in vitro bacteriostatic effect by itself, but the MICs of vancomycin for VRE decreased substantially from 32 to 256 mcg/mL without garlic to 0.5 to 16 mcg/mL with garlic (1000-2000 mcg/mL). The combination appeared synergistic for all but one strain of VRE. The concentrations of garlic used were comparable to only one clove on an empty stomach. ■

Influenza A H3N2 Sweeps the Northern Hemisphere

Source: PromedMail. Jan 11, 2000; www.promedmail.org.

As many of you are already keenly aware, this year's flu is particularly nasty, as it sweeps through the Northern Hemisphere. Numerous countries in Europe and North America are reporting record numbers of people with illness and severe staff shortages in clinics and hospitals. Italy, for example, is reporting 2 million flu sufferers, with 250,000 new cases per week for the past three weeks. The culprit is the Influenza H3N2 strain, which was seen in Beijing last year, and is included in this year's vaccine. Many countries, including the United States, did not reach target levels of vaccination, the exception apparently

being China and France.

There is concern that people may be avoiding vaccination because of the heavy direct advertising of the new flu drugs, Tamiflu and Relenza. People should understand that, in cases of uncomplicated flu, these agents can reduce, on average, the duration of symptoms by ~one day, but these drugs are not a cure. Similarly, physicians and ER personnel should be aware that, in cases of more complicated flu, these agents are not a substitute for otherwise necessary medical care, such as observation in the hospital, parenteral fluids, and antibiotics for bacterial complications.

Health departments in many countries are urging that it's not too late to get vaccinated. Health care workers, in particular, should receive vaccine. ■

Transgenic Mice Develop BSE

Source: Scott MR, et al. *Proc Natl Acad Sci U S A* 1999;96:15137-15142.

Investigators at the university of California, San Francisco (including Dr. Stanley Prusiner, who was awarded the 1997 Nobel Prize for his work with prions) and in Edinburgh, Scotland, presented compelling evidence that specially engineered mice injected with brain tissue from either "mad cows" or people diagnosed with new variant Creutzfeldt-Jakob disease (nvCJD) developed a neurological illness similar to bovine spongiform encephalopathy (BSE). Symptoms developed within approximately 250 days of infection, which was inoculated directly into the mouse brain.

Brain tissue from diseased mice was subsequently injected into a second set of mice, resulting in, again, a similar pattern of illness within the same time frame. The mouse prions assumed a "pleated" structure similar to those isolated from patients with nvCJD and

mad cows. In contrast, mice injected with tissue from sheep infected with scrapie developed a different illness with a different prior structure.

While previous evidence linking BSE in cows and nvCJD in people has been largely epidemiological, this is the first direct evidence that the two diseases may be caused by the same prion strain. As the mice in these experiments were directly injected with, rather than being fed, infected tissue, the mechanism of transmission from animals to humans remains a mystery. ■

Frozen Miners' Brains Yield 1918 Flu Virus

Source: PromedMail. Jan 1, 2000; www.promedmail.org.

British scientists have detected BRNA fragments of the 1918 influenza virus from the frozen human remains, including bits of virus found in brain tissue, of several coal miners struck down by the disease and buried in the permafrost in Spitsbergen, Norway, more than 80 years ago. This is the first time that fragments of the deadly 1918 strain have been isolated from brain tissue. If these fragments can be sequenced and pieced together, they may help to explain the basis for this organism's particular virulence. They may also help to determine whether the 1918 influenza virus was the cause of the encephalitis lethargica (von Economo disease) subsequently linked to cases of post-encephalitic parkinsonism, which occurred at approximately the same time. An early effort to isolate virus from the brains of patients with encephalitis lethargica was fruitless, suggesting that the encephalitis may have been unrelated to the viral infection, or was a possible consequence of some other post-infectious inflammatory condition, such as Reye's. ■