LITERATURE ALERT

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Fridkin SK, Edwards JR, Courval JM, *et al.*: **The effect of vancomycin and third generation cephalosporins on prevalence of vancomycin-resistant enterococci in 126 U.S. adult intensive care units.** *Ann Intern Med* 2001, **135:**175–183.

Significance: In case-control and cohort studies, proximity to other patients with vancomycin-resistant enterococci (VRE) and exposure to certain antimicrobial agents have been found to be risk factors for VRE colonization and infection. This study set out to determine the independent importance of any association between antimicrobial use and risk factors for nosocomial infection on rates of VRE in intensive care units (ICUs).

Findings: One hundred twenty-six adults in ICUs from 60 US hospitals were evaluated from 1996 to 1999. VRE prevalence varied by ICU type, teaching status, and hospital size. Prevalence of VRE in ICUs was found to be strongly associated with VRE prevalence among inpatient non-ICU areas and outpatient areas within the same hospital, ventilator days per 1000 patient-days, and the rate of parenteral vancomycin use. Rate of vancomycin use and third-generation cephalosporin use were independently associated with VRE prevalence in a weighted linear regression model that controlled for ICU type and rates of VRE among non-ICU inpatient areas. It has become increasingly clear that control of certain classes of antibiotics will be necessary in any program designed to minimize hospital-acquired infections with VRE.

Brenhamou Y, Bochet M, Thibault V, *et al.*: **Safety and efficacy of adefovir dipivoxil in patients co-infected with HIV-1 and lamivudine-resistant hepatitis B virus: an open-label pilot study.** *Lancet* 2001, **358:**718–723.

Significance: Lamivudine inhibits hepatitis B virus (HBV) replication in more than 80% of infected patients, however, 15% to 32% develop lamivudine-resistant HBV within 1 year of therapy. Therefore, new therapies are needed.

Findings: Thirty-five HIV/HBV-coinfected patients were given adefovir dipivoxil (a nucleoside analogue with activity against a broad range of viruses including HIV and HBV) 10 mg once daily for 48 weeks while maintaining their existing anti-HIV regimen. All of these patients had had HBV viral rebound despite ongoing lamivudine therapy and had documented HBV polymerase gene mutations within the YMDD motif. Four patients withdrew. Mean decreases in HBV DNA concentrations in serum were log 3.40 and 4.01 copies/mL at 24 and 48 weeks, respectively. Two patients experienced loss of hepatitis B e antigen. This study supports the activity of adefovir (at low dose) in HBV infection due to lamivudine-resistant virus. Long-term studies will be necessary to confirm safety and clinical efficacy. Additionally, it is time we learned from the lessons of HIV treatment and begin combination therapy for HBV to see if the inevitable resistance seen with monotherapy can be avoided.

Ahmad SR, Singer SJ, Leissa BG: **Congestive heart failure associated with itraconazole.** *Lancet* 2001, **357:**1766–1767.

Significance: Itraconazole is an antifungal agent approved for use in onychomycosis and serious systemic fungal infections. Data from the US Food and Drug Administration's Adverse Event Reporting System suggest that the use of itraconazole is associated with congestive heart failure (CHF).

Findings: The FDA analyzed the 58 postmarketing reports in which patients experienced CHF with itraconazole. The median age was 57 years (range, 15–86 years). The majority of patients were prescribed itraconazole for onychomycosis (50%). The median time to onset of CHF symptoms was 10 days. Doses of itraconazole ranged from 100 to 800 mg/d. Twenty-eight patients were hospitalized and 13 died. Most patients who died had serious underlying conditions and therefore a casual relationship could not be proved. In a canine study, intravenous itraconazole had a dose-dependent negative inotropic effect on the heart, and a study in healthy humans also demonstrated itraconazole-induced transient reductions in left ventricular ejection fraction. No reports of CHF due to other azoles have been reported to the FDA. Because of this rare but potentially serious toxicity, itraconazole labeling has been revised. A black box warning advises against the use of itraconazole in the treatment of onychomycosis in patients with evidence of ventricular dysfunction.