40. Haga Y, Sakamoto K, Egami H, et al. Changes in production of interleukin-1 and interleukin-2 associated with obstructive jaundice and biliary drainage in patients with gastrointestinal cancer. *Surgery* 1989;106:842-848.
41. Galdiero F, Carratelli CR, Nuzzo I, et al. Beneficial effects of myristic, stearic or oleic acid as part of liposomes on experimental infection and antitumor effect in a murine model. *Life Sci* 1994;55:499-509.
42. Braunwald J, Nonnenmacher H, Pereira CA, Kirn A. Increased susceptibility to mouse hepatitis virus type 3 (MHV3) infection induced by a hypercholesterolemic diet with increased adsorption of MHV3 to primary hepatocyte cultures. *Res Virol* 1991;142:5-15.
43. US Preventive Services Task Force. *Guide to Clinical Preventive Services: An Assessment of the Effectiveness of 169 Interventions.* Baltimore, MD: Williams & Wilkins; 1989.
44. Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease: predicting risks by levels and ratios. *Ann Intern Med* 1994;121:641-647.

Protease Inhibitors and Rifampin—Serious Drug Interactions

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Protease inhibitors currently are the most potent antiretroviral agents available to treat patients with HIV disease. Three drugs have been approved in this class, including, saquinavir (Invirase), ritonavir (Norvir), and indinavir (Crixivan), and another drug, nelfinavir (Viracept, Agouron Pharmaceuticals) is expected to be available soon from the manufacturer through an expanded access program. All four drugs inhibit HIV protease and thus interfere with viral maturation and replication. However, these protease inhibitors interact with rifamycin derivatives, such as rifampin and rifabutin, which are used to treat and prevent mycobacterial diseases commonly observed in HIV-infected patients.

Rifamycins accelerate the metabolism of protease inhibitors, resulting in a subtherapeutic level of protease inhibitors. In addition, protease inhibitors retard the metabolism of rifamycins, resulting in increased serum levels of rifamycins and the likelihood of drug toxicity. The manufacturers' product labeling for protease inhibitors contraindicates, does not recommend, or discourages the concurrent administration of rifampin and protease inhibitors.

The US Public Health Service recently published interim guidelines that describe a number of approaches for managing patients who are candidates for, or who are undergoing, protease inhibitor therapy when tuberculosis (TB) is diagnosed, until additional data are available and formal guidelines are issued. Because the management of these patients is complex, they recommend an individualized approach undertaken only by, or in consultation with, an expert. Option I involves discontinuing therapy with the protease inhibitor and completing a short (minimum 6 months) course of TB treatment with a regimen containing rifampin. Option II is to use a four-drug TB treatment regimen that includes rifampin for a minimum of 2 months and until bacteriologic response is achieved and susceptibility testing is available. After bacteriologic response and drug susceptibility have been documented, TB treatment may be modified to a 16-month continuation phase with isoniazid and ethambutol. Option III is to continue protease inhibitor therapy with indinavir (800 mg every 8 hours) and administer a four-drug, 9-month TB regimen containing rifabutin (150 mg/day) instead of rifampin. Because options II and III have not been studied in large clinical trials, there are a number of precautions, including the need for careful monitoring for drug toxicity and TB treatment failures.

The CDC's Research and Evaluation Branch, Division of Tuberculosis Elimination, National Center for HIV, STD, and TB Prevention (telephone 404-639-8123) requests inclusion of clinical information in the TB surveillance reports from private practitioners or health department staff who manage HIV-infected patients undergoing protease inhibitor therapy when TB is diagnosed.

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