

excreted primarily through the bile and enters the enterohepatic circulation; <30% of a dose is renally excreted.

As a potent inducer of the hepatic cytochrome P450 system, rifampin can decrease the half-life of some drugs, such as digoxin, warfarin, phenytoin, prednisone, cyclosporine, methadone, oral contraceptives, clarithromycin, azole antifungal agents, quinidine, antiretroviral protease inhibitors, and nonnucleoside reverse transcriptase inhibitors. The Centers for Disease Control and Prevention (CDC) has issued guidelines for the management of drug interactions during treatment of HIV and *M. tuberculosis* co-infection ([www.cdc.gov/tb/](http://www.cdc.gov/tb/)).

**DOSING** The daily dosage of rifampin is 10 mg/kg for adults and 10–20 mg/kg for children, with a maximum of 600 mg/d for both. The drug is given once daily, twice weekly, or three times weekly. No adjustments of dose or frequency are necessary in patients with renal insufficiency.

**RESISTANCE** Resistance to rifampin in *M. tuberculosis*, *M. leprae*, and other organisms is the consequence of spontaneous, mostly missense point mutations in a core region of the bacterial gene coding for the  $\beta$  subunit of RNA polymerase (*rpoB*). RNA polymerase altered in this manner is no longer subject to inhibition by rifampin. Most rapidly and slowly growing NTM harbor intrinsic resistance to rifampin, for which the mechanism has yet to be determined.

**ADVERSE EFFECTS** Adverse events associated with rifampin are infrequent and generally mild. Hepatotoxicity due to rifampin alone is uncommon in the absence of preexisting liver disease and often consists of isolated hyperbilirubinemia rather than aminotransferase elevation. Other adverse reactions include rash, pruritus, gastrointestinal symptoms, and pancytopenia. Rarely, a hypersensitivity reaction may occur with intermittent therapy, manifesting as fever, chills, malaise, rash, and—in some instances—renal and hepatic failure.

**Pyrazinamide** A nicotinamide analog, pyrazinamide is an important bactericidal drug used in the initial phase of TB treatment. Its