acid-fast organisms are fastidious mycobacteria other than *M. tuberculosis* complex, that they are nonviable *M. tuberculosis*, or that the results are due to laboratory error (false-positive smear, or false-negative culture). The approach in such cases is individualized on the basis of clinical and radiographic findings, as well as the results of rapid molecular diagnostic studies; discussion with the microbiologist performing the cultures is prudent. If clinical suspicion of tuberculosis is high, particularly if there is clinical and radiologic improvement since the start of therapy, then therapy is continued for a minimum of 6 months as for culture-positive pulmonary tuberculosis.

Pregnancy and Breastfeeding

Treatment for tuberculosis is initiated whenever the probability of maternal disease is moderate to high because of the risk of untreated tuberculosis to a pregnant woman and her fetus [342–345]. Although antituberculosis drugs cross the placenta, they do not appear to have teratogenic effects in humans [346–349]. However, the inclusion of PZA in the treatment regimen for pregnant women is controversial in the United States. The FDA previously classified all 4 first-line drugs, INH, RIF, PZA, and EMB, as having equal potential for teratogenicity (all assigned to category C according to the previous FDA letter-based classification system, which is currently being revised [350]). We suggest that clinicians evaluate the risks and benefits of prescribing PZA on a case-by-case basis, allowing the patient to make an informed and educated decision, recognizing that for all first-line drugs, risk cannot be ruled out as there are no adequate and well-controlled studies in humans, but potential benefits warrant use of the drug in pregnant women despite potential risks. It is also important to recognize that PZA has been used extensively in high-burden countries for many years, and is recommended by the WHO for tuberculosis in pregnancy, as part of the standard treatment regimen [98]. Expert opinion is that in pregnant women with tuberculosis and HIV, extrapulmonary or severe tuberculosis, it is more beneficial to include PZA in the treatment regimen than to not include PZA. If a decision is made to exclude PZA from the regimen, a minimum of 9 months of INH, RIF, and EMB is used for most pregnant women with drug-susceptible tuberculosis. Expert consultation should be sought when first-line drugs cannot be used due to adverse effects or antibiotic resistance, when there is extensive disease and/or a risk of noncompliance. Although the fetal effects of many second-line drugs are not well established, small case series of pregnant women treated with second-line drugs (from studies in drug-resistant tuberculosis) suggest that good outcomes are achievable and that termination of the pregnancy is not necessary [351–354]. Overall, the absence of high-quality studies combined with estimates of >200 000 cases of tuberculosis in pregnant women each year highlight the need for additional research in this area [355, 356].

Breastfeeding is encouraged for women who are deemed noninfectious and are being treated with first-line agents. The small concentrations of antituberculosis drugs measured in breast milk have not been reported to produce toxic effects in the nursing infant [77]. Conversely, drugs in breast milk should not be considered to serve as effective treatment for active tuberculosis or latent tuberculosis infection in a nursing infant. Whenever INH is given to a pregnant or nursing woman, supplementary pyridoxine, 25–50 mg/day, is prescribed [42, 43, 357, 358]. According to the AAP, supplementary pyridoxine (1–2 mg/kg/day) is also prescribed to exclusively breastfed infants, even those not receiving INH [77, 289].

Renal Disease

Patients with renal insufficiency or end-stage renal disease (ESRD) are immunocompromised [359]. Tuberculosis patients with chronic renal failure have worse clinical outcomes than those without renal failure, and, thus, experts recommend close monitoring during tuberculosis treatment [360]. The pharmacokinetics of antituberculosis drugs are altered as some are cleared by the kidneys and/or removed via hemodialysis [361, 362]. Therefore, dose adjustment in patients with renal insufficiency or ESRD may be required (Table 3 and Table 12). Decreasing the dose lowers peak serum drug concentrations and can compromise treatment efficacy. Based on expert opinion, the interval between drug doses in patients with a creatinine clearance of <30 mL/minute and those receiving hemodialysis should be increased instead. In patients with borderline renal function, a 24-hour urine collection may be needed to more accurately define the degree of renal insufficiency prior to making regimen changes [242, 363]. Insufficient data exist to guide dosing recommendations for patients with a reduced but >30 mL/min creatinine clearance. In such patients, standard doses are used by experts, but measurement of serum concentrations 2 and 6 hours after timed administration can be used to assist with optimizing drug dosages.

RIF and INH are metabolized by the liver, and conventional dosing can be used in the setting of renal insufficiency. Although PZA is metabolized by the liver, its metabolites (pyrazinoic acid and 5-hydroxy-pyrazinoic acid) may accumulate in patients with renal insufficiency. EMB is approximately 80% cleared by the kidneys and may accumulate in patients with renal insufficiency. Experts suggest a longer interval between doses (ie, thrice weekly) for PZA and EMB [242, 363]. With hemodialysis, PZA and, presumably, its metabolites are cleared to a significant degree, INH and EMB are cleared to some degree, and RIF is not cleared by hemodialysis [361]. The fluoroquinolones are also cleared variably by the kidneys. Levofloxacin undergoes greater renal clearance than moxifloxacin [179]. Postdialysis administration of all antituberculosis medications is preferred to facilitate DOT and to avoid premature clearance of drugs such as PZA. Monitoring serum drug concentrations, along with careful clinical and pharmacological assessment, in patients with ESRD, may be necessary. ESRD patients are often taking other medications that interact with antituberculosis drugs or have comorbid clinical