

Chapter VIII: Treatment in Special Situations

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A. HIV Infection

Treatment of tuberculosis in patients with HIV infection follows the same principles as treatment of patients without HIV infection. However, there are several important differences between patients with and without HIV infection. These differences include:

- The potential for drug interactions, especially between the rifamycins and antiretroviral agents
- Paradoxical reactions that may be interpreted as a worsening clinical picture
- The potential for the development of acquired resistance to rifamycins when treated with highly intermittent therapy

Management of HIV-related TB is complex and requires expertise in the management of both HIV disease and TB. Because HIV-infected patients often take numerous medications, some of which interact with antituberculosis medications, clinicians are strongly encouraged to consult with experts who treat HIV-related TB. If the patient is receiving treatment for TB and HIV by different clinicians or clinics, frequent and open communication must be maintained to coordinate medical and public health management.

It is especially important to use directly observed therapy (DOT) and other adherence-promoting strategies with patients with HIV-related TB.



The following are contraindicated in HIV-infected patients:

- Isoniazid-rifapentine (INH-RPT) once weekly
- Twice-weekly rifampin (RIF)- or rifabutin (RFB)-based regimens in patients with CD4+ cell counts of less than 100 per microliter ⁱ



Patients with HIV-related TB may experience a temporary exacerbation of symptoms, signs, or radiographic manifestations (paradoxical reactions) of TB while receiving antituberculosis treatment. ⁱⁱ

1. Treatment Recommendations

Recommendations for the treatment of tuberculosis in HIV-infected adults are identical to those without HIV infection: a 6-month regimen consisting of an initial phase of INH, RIF, PZA, and EMB given for 2 months followed by INH and RIF for 4 months when the disease is caused by organisms that are known or presumed to be susceptible to the first-line agents. This regimen may be administered daily or intermittently. Variations in the treatment for HIV-infected individuals include:

- **Intermittent dosing.** There is an increased risk of rifamycin resistance among patients having CD4+ counts of less than 100/ μ l, particularly when receiving intermittent dosing. It is recommended that patients with advanced HIV disease

receive medications daily (5 or 7 days a week) during the induction phase, and daily or thrice (3x) weekly (3-times) during continuation phase, but not twice (2x) weekly. For patients with CD4+ counts of more than 100/ μ l and adherent with antiretroviral therapy, intensive-phase therapy should generally be with daily dosing with selective consideration of thrice (3x) weekly after at least 3 to 4 weeks of daily dosing. Continuation phase in patients should generally be thrice (3x), but twice (2x) weekly can be considered for patients with limited TB disease and higher CD4 counts. Once-weekly rifapentine should not be used for any patient with HIV infection.

- **Treatment length.** Six months should be the minimal length of treatment for adults, even for patients with culture-negative tuberculosis. If cultures are still positive after 2 months of therapy treatment should be prolonged for a total of 9 months. As with HIV-negative adults, treatment for TB of the central nervous system is generally treated for 9 to 12 months and bone and joint TB for 6 to 9 months. The American Academy of Pediatrics recommends a minimum of 9 months of therapy for HIV-infected children.
- **Potential drug toxicities.** Data is inconclusive regarding the frequency of anti-TB drug-related toxicities in patients with HIV infection. U.S. Public Health Service and Infectious Disease Society of America guidelines recommend screening all HIV-infected individuals for hepatitis C virus. Until more data are available, it is prudent to provide more frequent clinical and laboratory monitoring for patients with HIV infection who are being treated for tuberculosis.
- **Antiretroviral therapy.** Most patients with tuberculosis have relatively advanced HIV disease and highly-active antiretroviral therapy (HAART) is indicated. HAART should not be withheld because the patient is being treated for tuberculosis, and based on a number of studies, instituting HAART is recommended for all HIV-infected patients during TB treatment rather than delayed until completion. Nevertheless, it is a challenge to begin both HAART and drug treatment for tuberculosis at the same time. This may involve as many as 8 new drugs with interactions and overlapping toxicities that can be difficult to evaluate. **Treatment for tuberculosis should be initiated first.** Delaying the initiation of HAART until 4-8 weeks after starting anti-TB drug therapy has the potential advantages of being better able to ascribe a specific cause for a drug side effect, decreasing the severity of paradoxical reactions, and decreasing the adherence difficulties for the patient. However, several studies have shown higher mortality among patients with CD4+ counts < 50/ μ l if HAART is delayed beyond 2 weeks of starting TB therapy. Current recommendations in 2013 are to start HAART within 2 weeks when the CD4 count is <50 cells/ μ l and by 8 to 12 weeks for all others. The one possible exception to this recommendation comes from one study of patient with TB meningitis for whom early HAART was associated with worse outcomes.

For patients who are already receiving an HAART regimen, treatment should generally be continued, although the regimen may need to be modified on the basis of the risk of drug interactions. Even though drug interactions are common, a rifamycin, typically rifabutin, should be used as it has fewer interactions than rifampin with the HAART drugs. Not including a rifamycin in the treatment regimen will likely delay sputum conversion, prolong the duration of TB therapy, and possibly result in a poorer outcome.

2. Paradoxical Reactions

A paradoxical reaction is also known as “immune reconstitution syndrome”. On occasion, patients have a temporary exacerbation of symptoms, signs, or chest x-ray manifestations of tuberculosis after beginning anti-TB treatment. This reaction can occur in patients without HIV infection, especially with lymphadenitis, but it is more common among HIV-infected patients. These reactions presumably develop as a consequence of reconstitution of cell-mediated immunity brought about by HAART or by treatment of the tuberculosis itself. Signs of a paradoxical reaction may include:

- High fevers
- Increase in size and inflammation of involved lymph nodes
- New lymphadenopathy
- Expanding central nervous system lesions
- Worsening of pulmonary parenchymal infiltrations
- Increasing pleural effusions.

Such findings should be attributed to a paradoxical reaction only after a thorough evaluation has excluded other possible causes, especially tuberculosis treatment failure. A paradoxical reaction that is not severe should be treated symptomatically without a change in anti-tuberculosis drugs or HAART. Corticosteroids in high doses for 2 weeks with tapering over 2 weeks has appeared useful in managing IRIS reaction although some patient appear to require longer doses. Draining suppurative lymph nodes by needle aspiration has also been used.

B. Pregnancy and Breastfeeding

Untreated tuberculosis represents a far greater hazard to a pregnant woman and her fetus than does treatment of the disease. Infants born to women with untreated tuberculosis may be of lower birth weight than those born to women without tuberculosis and, rarely, the infant may acquire congenital tuberculosis. Treatment of a pregnant woman with suspected tuberculosis should be started if the probability of tuberculosis is moderate to high. The initial treatment should consist of INH, rifampin, and EMB. There is insufficient data to determine the safety of PZA in pregnant women. If PZA is not used in the initial treatment

regimen, then the duration of therapy is 9 months. Pyridoxine at 25 mg/day should be given to pregnant women who are receiving INH.

INH, RIF, and EMB cross the placenta, but none has been shown to have teratogenic effects. Streptomycin (SM), the only anti-TB drug documented to have harmful effects on the human fetus, interferes with development of the ear and may cause congenital deafness. Kanamycin, amikacin, and capreomycin presumably share this toxic potential. 4-aminosalicylic acid (an anti-TB drug commonly referred to as PAS) was used commonly with INH in the past and there was no indication of teratogenicity among babies whose mothers had received these two drugs. There is insufficient data on cycloserine or ethionamide. The fluoroquinolones have been associated with joint abnormalities in young animals and so should be avoided if possible in pregnant women. In general, administration of anti-TB drugs is not an indication for termination of pregnancy. However, in women being treated for drug-resistant tuberculosis, counseling should be done concerning the risk to the fetus of second-line drugs.

Breastfeeding should not be discouraged for women being treated with first-line agents, because the small concentrations of these drugs in breast milk do not produce toxic effects in the nursing infant. Conversely, drugs in breast milk should not be considered to serve as effective treatment for active or latent tuberculosis in a nursing infant. Supplemental pyridoxine is recommended both for the nursing mother and the infant. The use of fluoroquinolones during breastfeeding is not recommended.

C. Children and Adolescents

Children most commonly develop active tuberculosis disease as a complication of the initial infection with *M. tuberculosis* (primary tuberculosis). On chest x-ray, primary tuberculosis is characterized by intrathoracic adenopathy, mid- and lower-lung zone infiltrates, and the absence of cavitation. However, children, particularly adolescents, may develop adult-type tuberculosis (upper lobe infiltration and cavitation associated with sputum production). The lesions of primary tuberculosis have a smaller number of *M. tuberculosis* organisms than those of adult-type pulmonary tuberculosis. Thus treatment failure, relapse, and development of secondary resistance are rare among children.

It is more difficult to isolate *M. tuberculosis* from a child with pulmonary tuberculosis than from an adult. Therefore, it is frequently necessary to rely on the results of culture and susceptibility tests of specimens from the person presumed to be the source of the child's infection to guide the choice of drugs for the child. In children whom drug resistance is suspected or whom no source case isolate is available, attempts to isolate organisms via three early morning gastric aspirations (optimally during hospitalization), bronchoalveolar lavage, or tissue biopsy must be considered.

Because tuberculosis in infants and children younger than 5 years of age is more likely to disseminate, treatment should be started as soon as the diagnosis is suspected.

Asymptomatic children with a positive TST or IGRA and an abnormal chest x-ray (atelectasis, parenchymal infiltrate, or hilar adenopathy) should receive combination chemotherapy for active tuberculosis.

Children are often started on 3 (rather than 4) drugs in the initial phase. This is because the bacillary population is low, and many infants and children cannot tolerate the pill burden required with four oral drugs. This is also due to the difficulty in performing visual acuity tests in young children who are being treated with EMB. In children suspected or known to have been infected with a fully susceptible strain of *M. tuberculosis*, the susceptibility of the presumed infecting strain is not known and the likelihood of failure is low (primary tuberculosis), the initial phase should consist of INH, RIF, and PZA. However, children and adolescents with adult-type pulmonary tuberculosis should be treated with the 4-drug initial phase regimen unless the infecting strain is known to be resistant. Drug-resistant organisms are more likely to be present among children who are foreign-born or whose parents are foreign-born, and EMB can be used safely in a dose of about 15-20 mg/kg per day, even in children too young for routine eye testing. Older children should have monthly eye evaluations of visual acuity and color discrimination while taking EMB. Streptomycin, kanamycin, or amikacin can be used as the fourth drug, when necessary.

 For more information, see *Chapter 4: Anti-Tuberculosis Drugs in Current Use* for the usual doses of daily and twice-weekly treatment in children.

Pyridoxine (Vitamin B₆) is recommended for infants, children, and adolescents who are being treated with INH and who have nutritional deficiencies, HIV infection, or who are breastfeeding.

DOT should be used for all children with tuberculosis. Crushed pills and suspensions are needed because of the lack of pediatric dosage forms of most anti-TB medications. All tablets and capsules may be crushed, mixed together and administered in one syringe as long as they are swallowed within 30 minutes of preparation. Even when drugs are given under DOT, tolerance of the medications must be monitored closely.

Evaluating the response to treatment Because of the difficulties in isolating *M. tuberculosis* in children, bacteriological examinations are less useful in evaluating the response to treatment. Therefore, clinical signs and chest x-rays are of relatively greater importance. However, hilar adenopathy and resultant atelectasis may require 2-3 years to resolve. Thus a persisting abnormality of chest x-ray is not necessarily a criterion for extending treatment. Often a decision to modify the drug regimen must be made on clinical grounds only.

Extrapulmonary tuberculosis Generally children can be treated with the same regimens used for treatment of pulmonary TB disease. Exceptions may be made for disseminated disease for which 4 drugs are recommended in the initial phase of treatment and the recommended duration is 9 to 12 months. Exceptions may also be made for TB meningitis for which 4 drugs are also recommended in the initial phase of treatment and the recommended treatment duration is 9 to 12 months.

HIV The optimal treatment of pulmonary tuberculosis in children and adolescents with HIV infection is unknown. However, the recommendations by the CDC and NIH recommend that initial therapy should include at least 3 drugs for a minimum of 9 months with extension to 12 months for those with central nervous system, disseminated disease or skeletal disease.

D. Extrapulmonary Tuberculosis

The basic principles for treating pulmonary TB also apply to extrapulmonary forms of the disease. The addition of corticosteroids is recommended for patients with TB pericarditis and TB meningitis. Recommendations concerning duration of therapy are as follows:

- Use a six-month course of therapy for TB involving any site. **Exceptions:** For bone or joint TB, use a six- to nine-month regimen. For the meninges, use a nine- to twelve-month regimen.
- Consider prolonging therapy for patients with TB in any site that is slow to respond

Note: Affected lymph nodes may enlarge while patients are receiving appropriate therapy or after treatment has ended without any evidence of bacteriologic relapse. On occasion, new nodes can appear during or after treatment as well.

During an individual's initial encounter with the tubercle bacillus, the primary infection, the mycobacteria are spread via the blood stream and deposited in widely scattered sites throughout the body. An effective immune response can contain these still viable bacilli until some future time when they may reactivate. Tuberculosis can involve virtually any organ or tissue in the body. Non-pulmonary sites tend to be more common among children and persons with impaired immunity. To establish the diagnosis of extrapulmonary tuberculosis, appropriate specimens should be obtained including:

- pleural fluid
- pericardial or peritoneal fluid
- pleural, pericardial, and peritoneal biopsy specimens
- lymph node tissue and
- bone marrow, bone, blood, urine, brain, or cerebrospinal fluid.

As appropriate, each should be obtained for acid-fast bacilli (AFB) staining, mycobacterial culture and drug susceptibility testing. Tissue specimens should also be examined microscopically after routine AFB staining, but the absence of AFB and of granulomas, or even failure to culture *M. tuberculosis*, does not exclude the diagnosis of tuberculosis. Bacteriological evaluation of the response to treatment in extrapulmonary tuberculosis is often limited by the difficulty in obtaining follow-up specimens. Thus, response often must be judged on the basis of clinical and radiological findings.

The basic principles that underlie the treatment of pulmonary TB also apply to extrapulmonary disease. A 6-9 month regimen (2 months of INH, rifampin, PZA, and EMB followed by 4 to 7 months of INH and rifampin) is recommended as initial therapy unless the organisms are known to be or strongly suspected of being resistant to first-line drugs. If PZA cannot be used in the initial phase, the continuation phase must be increased to 7 months. The exception to the recommendation for 6-9 month regimen is tuberculous meningitis, for which 9 to 12 months is recommended. Corticosteroid treatment is a useful adjunct in treating some forms of extrapulmonary tuberculosis, specifically drug-susceptible TB meningitis and pericarditis.

1. Lymph Node Tuberculosis

A 6-month regimen is recommended for initial treatment of all patients with tuberculous lymphadenitis caused by drug-susceptible organisms. Affected lymph nodes may enlarge while patients are receiving appropriate therapy or after the end of treatment without any evidence of bacteriological relapse. On occasion, new nodes can appear during or after treatment as well. Therapeutic lymph node excision is not indicated except in unusual circumstances. For large lymph nodes that appear to be about to drain spontaneously, aspiration or incision and drainage appears to be beneficial. Non-tuberculous mycobacteria are the cause of the majority of cases of lymphatic mycobacterial disease in U.S.-born children in the United States, but foreign-born children are more likely to have tuberculosis.

2. Bone and Joint Tuberculosis

Most bone and joint tuberculosis begins in the growth plates of bones where the blood supply is the richest then spreads into the joint spaces resulting in tuberculosis arthritis. The spine (Pott's disease), hips, and knees are most commonly affected. Regimens of 6- to 9-month duration are believed to be adequate for treatment of bone and joint tuberculosis. Surgery is also beneficial in some circumstances including failure to respond to anti-TB drugs with evidence of ongoing infection, the relief of cord compression in patients with persistence or recurrence of neurologic deficits, and instability of the spine.

3. Pericardial Tuberculosis

A 6-month regimen is recommended for pericardial tuberculosis. In addition, studies have shown quicker clinical resolution and lower mortality rates when corticosteroids are given during the first 11 weeks of anti-TB therapy. For adults the prednisone dose is 60 mg/day (or the equivalent dose of prednisolone) for 4 weeks, followed by 30 mg/day for 4 weeks, 15 mg/day for 2 weeks, and finally 5 mg/day for week 11 (the final week). Surgical treatment to remove part of the pericardium, the so-called "pericardial window", may be useful in management of larger pericardial effusions or those impairing cardiac output due to tamponade. Children should be treated with doses proportionate to their

weight, beginning with about 1 mg/kg body weight and decreasing the dose as described for adults.

4. Pleural Tuberculosis

A 6-month regimen is recommended for treating pleural tuberculosis. Corticosteroid therapy may also play a role in reducing symptoms and improving the chest x-ray more quickly. Tuberculous empyema, a chronic, active infection of the pleural space containing a large number of tubercle bacilli, usually occurs when a cavity ruptures into the pleural space. Treatment consists of drainage and anti-TB drug therapy.

5. Tuberculous Meningitis

Tuberculous meningitis was uniformly fatal prior to effective anti-TB drug therapy. Despite prompt initiation of adequate treatment it is still associated with a high morbidity and mortality. HIV-infected patients appear to be at increased risk for developing tuberculous meningitis, but the clinical features and outcomes are similar for those patients without HIV infection. Patients who present with more severe neurologic impairment such as drowsiness, obtundation, or coma have a greater risk of neurologic sequelae and a higher mortality. Anti-TB drug treatment should be initiated with INH, rifampin, PZA, and EMB in an initial 2-month phase. INH and rifampin, as well as the aminoglycosides, capreomycin, and the fluoroquinolones are available in IV forms for patients who may not be able to take oral medications. After 2 months of 4-drug therapy for meningitis caused by susceptible strains, PZA and EMB may be discontinued and INH and rifampin continued for a minimum of 4 additional months. There are limited comparative data on duration of effective treatment of meningeal TB, and some experts recommend 9-12 total months of treatment. Repeated lumbar punctures should be done to monitor changes in CSF cell count, glucose, and protein, especially in the early course of treatment. Dexamethasone or prednisone is recommended for all patients, particularly those with a decreased level of consciousness.

6. Disseminated Tuberculosis

Disseminated tuberculosis refers to simultaneous involvement of multiple organs. Such disease has commonly been referred to as miliary because of the appearance in the involved tissues of an immense number of small, 1-2 mm, well-defined nodules that look like millet seeds. This miliary pattern has only been seen on chest x-ray (or on other organs at autopsy). A considerable proportion of patients who present with disseminated multi-organ tuberculosis do not have these characteristic findings visible on their chest x-rays. The clinical presentations of disseminated tuberculosis are very diverse, depending on the particular organs involved. Skin testing of persons with disseminated disease is significantly more likely to yield false-negative results than with any other form of tuberculosis. Before drug treatment, disseminated tuberculosis was primarily seen in infants and young children and in the elderly. With HIV/AIDS there are a larger number

of young adults being diagnosed with disseminated disease. Other special risk factors include alcoholism, steroid therapy, pregnancy and post-partum status, cancer, renal failure, and organ transplantation. A 6-month regimen is recommended for adults with tuberculosis and the American Academy of Pediatrics (AAP) recommends 9 months of treatment for children.

7. Genitourinary Tuberculosis

Renal tuberculosis is treated primarily with medical therapy and a 6-month regimen is recommended. If ureteral obstruction occurs, surgical procedures to relieve the obstruction are indicated. Nephrectomy is not usually indicated for uncomplicated renal tuberculosis but is considered if the kidney is poorly functioning, particularly if there is hypertension or continuous flank pain. Tuberculosis of either the female or male genital tract responds well to standard anti-TB drug regimens and surgery is usually needed only for residual large tubo-ovarian abscesses. A positive urine culture for *M. tuberculosis* is fairly common with disseminated tuberculosis, especially in individuals with HIV.

8. Abdominal Tuberculosis

In the United States, abdominal tuberculosis is largely peritoneal and comprises 3-4% of all extrapulmonary tuberculosis. Because there are so few cases it is hard to determine patterns. However, peritoneal tuberculosis appears to be seen most often in young women of child-bearing age, sometimes in association with genital tuberculosis, and in older men commonly in association with chronic alcoholism. A 6-month regimen is recommended for patients with peritoneal or intestinal tuberculosis.

E. Culture-Negative Pulmonary TB in Adults

Failure to isolate *M. tuberculosis* from appropriately collected specimens from persons who, because of clinical or x-ray findings, are suspected of having pulmonary tuberculosis does not exclude a diagnosis of active tuberculosis. In the United States about 17% of the reported new cases of pulmonary tuberculosis have negative cultures. Low bacillary counts, variations in the number of bacilli expelled, and errors in specimen processing all may result in failure to isolate organisms from persons with active tuberculosis. At a minimum, persons suspected of having pulmonary tuberculosis should have three sputa specimens for AFB smear and culture.

Patients whom are thought to have pulmonary tuberculosis, should have treatment initiated with INH, rifampin, PZA, and EMB even when the initial sputum smears are negative. If *M. tuberculosis* is isolated in culture, treatment for active TB disease should be continued.

After the initial phase (first 8 weeks) of therapy is completed, patients with negative cultures but who are still presumed to have pulmonary tuberculosis should have a thorough clinical evaluation and x-ray to determine whether there has been a response that can be attributed

to anti-tuberculosis treatment. If there is either clinical or x-ray improvements and no other cause is identified, treatment should be continued for active tuberculosis. The continuation phase can be shortened to 8 weeks using INH and rifampin. Once-weekly INH and rifapentine may also be used for the last 2 months. This 16- to 18-week regimen should be limited to low-risk patients, e.g., HIV negative, who are without severe weight loss or other symptoms. If PZA was not used in the initial 8 weeks of therapy, completion of therapy with a 16-week continuation phase of INH plus rifampin or rifapentine should be considered.

On occasion, patients who are being evaluated for pulmonary tuberculosis will be found to have positive AFB smears but negative cultures. There are several potential explanations for this including the possibility that the AFB organisms are non-tuberculous and difficult to culture, they are nonviable tubercle bacilli, or they are the result of lab error. If suspicion of tuberculosis is high and the patient has a positive AFB smear, even with negative culture, he or she should be treated as if the culture is positive, using one of the recommended regimens. Several exceptions to this recommendation include patients previously treated successfully for extensive pulmonary TB who may occasionally produce sputum with small numbers of apparently dead bacilli (multiple negative cultures) during the latter phases of treatment or after treatment completions.

F. Radiographic Evidence of Prior TB: Inactive TB

Patients with a positive TST/IGRA who have chest x-ray findings consistent with prior pulmonary tuberculosis (Class 4) and who have not been treated are at increased risk for developing active tuberculosis disease. The x-ray findings consistent with prior tuberculosis are apical fibronodular infiltrations, often with volume loss. Persons with x-ray findings of healed primary tuberculosis (e.g. calcified solitary pulmonary nodules, calcified hilar lymph nodes, and pleural thickening) are a lower risk for tuberculosis (approximately 2-fold) compared with other persons with latent TB infection. Guidelines for treatment of latent TB infection for persons with abnormal chest x-ray consistent with prior tuberculosis are the same regimens recommended for those with normal chest X-rays: 9 months of INH, rifampin (with or without INH) for 4 months, 12 doses of once-weekly INH plus rifapentine, and a 2-month treatment with a regimen that includes at least INH, rifampin, and PZA (e.g., when inactive TB is diagnosed after 2 months of empirical treatment for active TB).

G. Renal Insufficiency and End-stage Renal Disease

Renal insufficiency complicates the management of tuberculosis because some anti-TB medications are cleared by the kidneys (see MMWR 2003, section 8-7, Table 15.) Management may be further complicated by the removal of some tuberculosis medications by hemodialysis. Drug levels and clearance of INH, rifampin, ethionamide, and PAS are not affected by renal dysfunction or hemodialysis. Dosing alterations for EMB, PZA and all of the second-line drugs are needed for patients with renal insufficiency

(creatinine clearance of less than 30 ml/minute) and those on hemodialysis. If doses are decreased, peak serum concentrations may be too low, so increasing the dosing interval is recommended.

In general, anti-TB drugs given immediately after hemodialysis 3 times per week will facilitate DOT and avoid premature removal of the drugs. For patients with extensive disease or HIV infection where early intermittent dosing of INH and rifampin may not be ideal, these can be given daily while the EMB and PZA are thrice-weekly post-dialysis. It is important to measure serum drug concentrations in patients with renal insufficiencies who are taking cycloserine or any of the injectable agents to minimize dose-related toxicity while providing effective doses. For patients receiving more than 2 months of EMB this should also be considered. Patients with renal insufficiency may also have other clinical conditions such as diabetes that affect the absorption of the anti-TB drugs, or they may be taking other medications that interact with these drugs. Because drug removal mechanisms differ between hemodialysis and peritoneal dialysis, it cannot be assumed that all of the recommendations for hemodialysis apply to peritoneal dialysis.

H. Hepatic Disease

The treatment of tuberculosis in patients with unstable or advanced liver disease is difficult for several reasons, and more frequent lab monitoring may be required. First, the likelihood of drug-induced hepatitis may be greater. Second, drug-induced hepatitis on top of a preexisting liver condition can be life-threatening. Finally, fluctuations in the liver function test results, with or without symptoms, make it difficult to monitor for drug-induced hepatitis. Possible regimens for those with liver disease include treatment without INH, without PZA, or with no hepatotoxic drugs.

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