a life-threatening condition. The decision to initiate combination chemotherapy for tuberculosis is based on multiple factors including clinical, radiographic, laboratory, patient, and public health factors (Figure 1). Clinical judgment and index of suspicion also play a critical role in deciding to initiate treatment. In addition to smear microscopy and mycobacterial culture, CDC recommends the use of a rapid molecular test on at least one specimen from each patient with signs and symptoms of pulmonary tuberculosis for whom a diagnosis of tuberculosis is being considered but has not been established, and for whom the test result would alter case management or tuberculosis control activities [147]. Use of molecular tests directly on clinical samples has been shown to shorten time to diagnosis, and some tests have the additional ability to provide information on drug susceptibility [147, 148].

In the presence of a clinical syndrome compatible with tuberculosis, a positive AFB smear provides strong inferential evidence for the diagnosis of tuberculosis. If the diagnosis is confirmed by isolation of *M. tuberculosis* or a positive rapid molecular test, or is strongly inferred from clinical or radiographic improvement consistent with a response to tuberculosis treatment, the regimen is continued to complete a standard course of therapy. In patients with a positive AFB smear, but a negative rapid molecular test (including an assessment for polymerase chain reaction inhibitors, reported to be present in 2%–5% of respiratory specimens tested by nucleic acid amplification tests [149, 150]), it is unlikely that the positive smear is due to *M. tuberculosis*, particularly when molecular testing of a second smear-positive specimen is also negative [147]. If empiric treatment is started, cultures throughout are negative, and there is no response to treatment, yet the interferon-γ release assay (IGRA) or purified protein derivative (PPD)–tuberculin skin test (TST) is positive, consideration is given to treatment of latent tuberculosis infection using the following options: (1) stop treatment if RIF and PZA were included in the initial empiric 4-drug therapy, administered for at least 2 months [151]; (2) continue treatment with RIF, with or without INH, for a total of 4 months; (3) give 12 weekly doses of INH/RPT by DOT [152]; or (4) continue treatment with INH for a total of 9 months [83, 153, 154]. In patients in whom there is a low suspicion for active tuberculosis (not initially treated), if cultures remain negative, the IGRA or PPD-TST is positive (≥5 mm), and the abnormal chest radiograph is unchanged after 2 months (ATS/CDC class 4), treatment for latent tuberculosis infection is indicated [155]. If not previously treated, these patients are at increased risk for development of active tuberculosis with case rates 2.5–19 times higher than those of persons infected by *M. tuberculosis* with normal chest radiographs [156–159]. These patients are high-priority candidates for treatment of latent tuberculosis infection.

If clinical suspicion for active tuberculosis is low, the options are to begin treatment with combination chemotherapy or to defer treatment until additional data have been obtained to clarify the situation (usually within 2 months). An advantage of the early use of combination chemotherapy is that once active disease is excluded by negative cultures and lack of clinical or radiographic response to treatment, the patient will have completed 2 months of combination treatment that can be applied to the total duration of treatment for latent tuberculosis infection. Even when the suspicion for active tuberculosis is low, treatment for latent tuberculosis infection with a single drug is *not* initiated until active tuberculosis has been excluded, usually by negative cultures.

In general, for complicated diagnostic or management situations, consultation with local and state health departments is advised. In the United States, the CDC's Division of Tuberculosis Elimination funds tuberculosis regional training and medical consultation centers (http://www.cdc.gov/tb/education/rtmc/), which provide medical consultation to programs and health providers on management of tuberculosis. In Europe, the WHO and ERS Tuberculosis Consilium (https://www.tbconsilium.org) provides similar consultation services regarding the diagnosis and treatment of tuberculosis.

Regimens

The preferred regimen and other choices are listed in Table 2. Patient factors should be considered when selecting administration schedule (intermittency), and in some instances regimen composition. Feasibility of DOT is sometimes an additional consideration when selecting frequency of administration. Regimens for adults and children are identical except in uncommon circumstances where it may be acceptable to omit EMB from the initial treatment regimen for young children (see "Children"). For all regimens, patients are treated until they have received the specified total number of doses for the treatment regimen (ie, not solely based on duration of treatment).

Preferred Regimen

The preferred regimen for treating adults with tuberculosis caused by organisms that are not known or suspected to be drug resistant is a regimen consisting of an intensive phase of 2 months of INH, RIF, PZA, and EMB followed by a continuation phase of 4 months of INH and RIF [3, 36, 37]. To reduce the risk of relapse, the continuation phase of treatment is extended for an additional 3 months for patients who had cavitation on the initial (or follow-up) chest radiograph and, in addition, are culture positive at the time of completion of the intensive phase of treatment.

The intensive phase of treatment consists of 4 drugs (INH, RIF, PZA, EMB) because of the current proportion of new tuberculosis cases worldwide caused by organisms that are resistant to INH [38–41]; however, if therapy is being initiated after drug susceptibility test results are known and the patient's isolate is susceptible to both INH and RIF, EMB is not necessary, and the intensive phase can consist of INH, RIF, and PZA only. EMB can be discontinued as soon as the results of drug