

Extrapulmonary Tuberculosis

PICO Question 7: Does the use of adjuvant corticosteroids in tuberculous pericarditis provide mortality and morbidity benefits?

Recommendation 7: We suggest initial adjunctive corticosteroid therapy not be routinely used in patients with tuberculous pericarditis (*conditional recommendation; very low certainty in the evidence*).

PICO Question 8: Does the use of adjuvant corticosteroids in tuberculous meningitis provide mortality and morbidity benefits?

Recommendation 8: We recommend initial adjunctive corticosteroid therapy with dexamethasone or prednisolone tapered over 6–8 weeks for patients with tuberculous meningitis (*strong recommendation; moderate certainty in the evidence*).

Tuberculosis can involve virtually any organ or tissue in the body. The principles underlying the treatment of pulmonary tuberculosis also apply to extrapulmonary disease. Chemotherapy for extrapulmonary tuberculosis is initiated with INH, RIF, PZA, and EMB in an initial 2-month phase. After 2 months of 4-drug therapy, for extrapulmonary tuberculosis known or presumed to be caused by susceptible strains, PZA and EMB may be discontinued, and INH and RIF continued during a continuation phase. Increasing evidence, including randomized controlled trials, suggests that 6–9 month INH and RIF-containing regimens are effective for the majority of extrapulmonary sites of disease. The exception is tuberculous meningitis where the optimal duration of therapy has not been established through randomized controlled trials, but most experts and society guidelines prescribe 12 months of treatment [78,292]. The opinion of experts is that the preferred frequency of dosing for extrapulmonary tuberculosis is once daily for both the intensive and continuation phases. No randomized controlled trials have studied intermittent drug administration for extrapulmonary tuberculosis. If intermittent regimens are used, experts believe that highly intermittent, once-weekly regimens should be avoided because of insufficient experience with this regimen in extrapulmonary tuberculosis. In regard to treatment monitoring, bacteriologic evaluation is often limited by the difficulty in obtaining follow-up specimens. Sputum specimens are obtained when there is concurrent pulmonary involvement, otherwise, response to treatment in extrapulmonary diseases is often judged on the basis of clinical and radiographic findings.

Lymph Node Tuberculosis

We believe a 6-month regimen is adequate for initial treatment of all patients with drug-susceptible tuberculous lymphadenitis [293–298]. Affected lymph nodes may enlarge and new nodes can appear during or after therapy without any evidence of bacteriological relapse [293,295,296,299]. Therapeutic lymph node excision is not indicated except in unusual circumstances. For large lymph nodes that are fluctuant and appear to be about to drain spontaneously, aspiration has been reported by some experts to be beneficial, although this approach has not been examined systematically. Incision and drainage techniques applied to cervical lymphadenitis, however, have been reported to be

associated with prolonged wound discharge and scarring [300]. Of note, the majority of lymphatic cases of mycobacterial disease in US children are caused by nontuberculous mycobacteria [301].

Bone, Joint, and Spinal Tuberculosis

Six- to 9-month regimens containing RIF for treatment of bone, joint, and spinal tuberculosis are at least as effective as 18-month regimens that do not contain RIF [302–304]. Because of the difficulties in assessing response, however, some experts tend to favor the 9-month duration, and in the setting of extensive orthopedic hardware, some experts extend the duration of treatment further to 12 months. Several trials found no additional benefit of surgical debridement in combination with chemotherapy compared with chemotherapy alone for spinal tuberculosis [80,303–306]. As such, uncomplicated cases of spinal tuberculosis are managed with medical rather than surgical treatment. However, based on expert opinion, surgery can be considered in situations in which (1) there is poor response to chemotherapy with evidence of ongoing infection or ongoing deterioration; (2) relief of cord compression is needed in patients with persistence or recurrence of neurologic deficits; or (3) there is instability of the spine [307]. Spinal tuberculosis with evidence of meningitis is managed as tuberculous meningitis, including consideration of adjunctive corticosteroids (see Tuberculous Meningitis).

Pericardial Tuberculosis

A 6-month regimen is adequate for patients with pericardial tuberculosis. Based on small studies that have shown mortality and morbidity benefits [71–73], corticosteroids have previously been universally recommended as adjunctive therapy for tuberculous pericarditis, however, a recent placebo-controlled randomized clinical trial with 1400 participants did not find a difference in the combined primary endpoint of the trial, which included mortality, cardiac tamponade, or constrictive pericarditis, between patients treated with adjunctive corticosteroids vs placebo [74]. A subgroup analysis, however, did suggest a benefit in preventing constrictive pericarditis. Similarly, a systematic review conducted to obtain evidence in support of this guideline did not find a statistically significant benefit in terms of mortality or constrictive pericarditis from the use of corticosteroids (see [Supplementary Appendix B, Evidence Profile 14](#)) [71–75]. Therefore, we suggest that adjunctive corticosteroids should not be used routinely in the treatment of patients with pericardial tuberculosis (Recommendation 7: *conditional recommendation; very low certainty in the evidence*). However, selective use of glucocorticoids in patients who are at the highest risk for inflammatory complications might be appropriate. Such patients might include those with large pericardial effusions, those with high levels of inflammatory cells or markers in pericardial fluid, or those with early signs of constriction [76].

Pleural Tuberculosis

A standard 6-month regimen (Table 2) is also adequate for treating pleural tuberculosis. Some clinicians consider using