immunosuppression who develop new symptoms shortly after ART is initiated (within 3–6 months), despite evidence of good HIV control (increased weight and CD4 count, reduced viral load). TB IRIS represents a temporary exacerbation of symptoms and occurs in two clinical scenarios. In patients who have occult TB before ART initiation, TB may be unmasked by subsequent immune recovery.[131] This unmasking or incident TB IRIS usually occurs within 3 months of ART initiation, and the pathogen typically is detectable.[132] TB IRIS also can result in paradoxical clinical worsening of TB disease after ART initiation in patients with TB/HIV coinfection; treatment failure because of microbial resistance or poor adherence also must be excluded in these cases. In prospective observational studies, IRIS occurred in nearly 5% to 10% of children, usually within 4 weeks of ART initiation, resulting mostly from atypical mycobacteria, BCG (in young vaccinated infants) and TB (more prevalent in older children).[133,134] Mild-to-moderate symptoms of IRIS can be treated symptomatically with nonsteroidal anti-inflammatory agents, while short-term use of systemic corticosteroids can be considered in more severe cases **(expert opinion)**[125-128,135,136]; treatment for TB and ART should not be discontinued.

Managing Treatment Failure

Most children with TB, including those with HIV, respond well to standard treatment. If clinical response is poor, then adherence to therapy, drug absorption, and the possibility of drug resistance should be carefully considered. Mycobacterial culture, DST, and assessment of serum concentrations of TB drugs should be done whenever possible. Drug resistance should be suspected in any child whose smear or culture fails to convert from positive to negative after 2 months of DOT, and alternative diagnoses or dual pathology should also be considered.

Preventing Recurrence

TB recurrence can represent relapse or re-infection disease. The relapse rate is low in children with drug-susceptible TB who receive DOT and ART. Recurrence within 6 to 12 months of treatment completion should be regarded as relapse and managed the same as treatment failure **(expert opinion).** Recurrence more than 6 to 12 months after treatment completion might be due to re-infection with *M. tuberculosis*, especially after a new exposure to a person with TB disease or a visit to a TB-endemic setting. Re-infection should be managed the same as the first episode of TB disease. Regular TB exposure screening should continue after completion of treatment, and preventive therapy should be considered whenever repeat exposure occurs.

International Guidelines

These guidelines were developed for the United States. Guidelines for resource-limited countries may be different and are available from WHO.[26]

Additional Resources

- CDC Division of TB Elimination
  https://www.cdc.gov/tb
  800-CDC-INFO (800-232-4636)
  TTY: 888-232-6348
  24 Hours/Every Day
  cdcinfo@cdc.gov