

Pharmacological advances also include the scheduling and trials of efficacy of known regimens and drugs in specific situations.

1. *Extrapulmonary TB (EPT)*: Two large multicenter studies from India have conclusively shown the efficacy of 6 month-RNTCP regimen (thrice weekly therapy – 2 R₃H₃Z₃E, 4 R₃, H₃) for tuberculous lymphadenopathy and pleural effusion.^{7,8} It was also shown that the resolution of tuberculous lymph nodes at the end of 12 months was similar in the group of patients given extended therapy for 9 months vs the group which was not extended beyond the 6 months treatment. There are ongoing studies to assess the efficacy of anti-TB regimes for management of other extra-pulmonary sites. A study on genital TB (GTB) from India concluded that the early institution of anti-tubercular treatment (ATT) for infertility (on the basis of positive endometrial TB-PCR) with no other demonstrable cause restored early fertility in a significant proportion of cases.⁹
2. *TB in patients in HIV positivity*: The WHO guidelines as well as some of the other recent studies have allayed the earlier fears of use of ATT in HIV-positive patients.^{10,11} Efavirenz based anti-retroviral treatment (ART) regimens are compatible with R based ATT; standard nevirapine (twice daily) also provides acceptable efficacy and safety. Rifabutin has lower effect on protease-inhibitor drugs used for HIV management. It is now recommended by the WHO that ART should be started after diagnosis of TB, irrespective of CD4 lymphocyte counts.¹⁰
3. *Other pharmacological interventions*: Investigations are on to develop alternate drug-delivery methods for longer duration of action (e.g. slow release polymer implants, liposomal encapsulation of drug particles and inhalable microparticles, etc.) as well as the use of supplementary drugs (such as vitamin A, Zinc and other nutritional supplements) for early recovery. None of these interventions have found the routine clinical application as yet.

A recent meta-analysis on adjuvant therapy with corticosteroids for all forms of tuberculosis has concluded that steroids could be effective in reducing mortality for all forms of TB.¹² It is rather a premature conclusion from insufficient data mostly from studies belonging to 1950s to 1970s when effective chemotherapy had not become available. Such results must be interpreted with great caution.¹³

Nonpharmacological Intervention

These advances have primarily rested on immunomodulation and immunotherapy. Use of anti-cytokine agents (thalidomide, pentoxifylline), protective cytokines and immunoenhancement with heat-killed Myco vaccae and other recombinant BCGs have been employed. None of these methods have been recommended in standard clinical practice.

TB Prevention

1. *Vaccination*: The use of BCG vaccination is limited to prevention of severer forms of childhood TB. With the use of innovative strategies to discover new protective antigens, adjuvants and delivery systems, there is a hope of developing an effective vaccine for TB.^{14,15} Some of these new recombinant and sub unit vaccines are already in the advanced trial stages.
2. *Chemoprophylaxis for latent TB*: In India, chemoprophylaxis is recommended for new born babies born to sputum smear positive mothers. Chemoprophylaxis for latent TB is not routinely recommended in India. Mantoux test or interferon gamma release assay test (IGRAs) are useful tests for diagnosis of latent TB.^{16,17} They do not however necessarily indicate the presence of active TB disease and requirement for treatment. Both Mantoux test and IGRAs are useful for diagnosis of latent TB in immunocompromised patients.¹⁸ These patients are routinely offered chemoprophylaxis in several Western countries.
3. *Strategies for air-borne infection control*: New developments in this area include the adoption of National Guidelines on Airborne Infection Control in Healthcare Settings in India.¹⁹ These guidelines are especially important in the MDR-TB wards and for prevention of spread of infection among healthcare workers in the hospitals.

SUMMARY

There have been several advances in the diagnosis and management of TB related to the understanding of pathogenesis, methods and interpretation of diagnostic tests, drugs and regimens for treatment. One can hope to control the menace using the newer strategies for treatment, control and prevention. There are grave challenges from development of multi- and severer forms of drug-resistance as well as of global economic crises to sustain the control/elimination programs.²⁰ The target of TB elimination is however distant, i.e. reduction of annual incidence to less than one case per million population by 2050.²¹ A more realistic target is to reduce the TB deaths to 1 per 100,000 population. This can possibly be achieved with effective measures and political commitment.

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