

in infants in South Africa. Results published in 2013 showed that MVA-85A was well tolerated and modestly immunogenic but did not confer significant protection against clinical TB or *M. tuberculosis* infection. A second, more promising candidate vaccine, M72/AS01_E, a subunit vaccine pairing two *M. tuberculosis* antigens (32A and 39A) with the adjuvant M72/AS01_E, was recently tested in a randomized trial among 3575 patients with *M. tuberculosis* infection to prevent development of active disease. TB developed in 13 participants among those receiving the vaccine and in 26 among those receiving placebo with an estimated efficacy of 49.7% at 36 months. Adverse events were not different in the two groups. This vaccine is now being considered for further development.

As of the end of 2020, 14 candidate vaccines were in various stages of clinical trials. They included whole-cell or mycobacterial whole-cell or lysates, viral vector vaccines, and adjuvant recombinant protein vaccines. Several challenges must be faced in the development of a TB vaccine. For instance, the lack of predictive animal models and protection correlates renders trials long and expensive. Furthermore, the decision about whether a candidate vaccine should be developed for prevention of infection (preexposure) or prevention of reactivation (postexposure) without an exact understanding of its precise mechanism of action is complex. Therefore, introduction of a new vaccine on a large scale is not likely in the near future. This step will require an intensified and much larger investment in research and development.

■ TB PREVENTIVE TREATMENT (TPT)

It is estimated that 1.7 billion people—more than one-quarter of the human population—have been infected with *M. tuberculosis*. Although only a small fraction of these infections will progress toward active disease in a lifetime, new active cases will continue to emerge from this pool of infected individuals. Therefore, TPT (also called *chemoprophylaxis* or *preventive chemotherapy*, and previously referred to as *treatment of latent TB infection*) is a fundamental intervention in TB control and elimination strategies.