WHO News and activities

WHO statement on BCG revaccination for the prevention of tuberculosis

The bacille Calmette–Guerin (BCG) vaccine is derived from a live, attenuated strain of Mycobacterium bovis and has been used for the prevention of tuberculosis in humans since 1921; approximately 3000 million doses have been given. BCG is the most widely used vaccine in the world; in the 172 countries where BCG immunization is practised, 85% of infants received the vaccine in 1993, with the average coverage ranging from 62% in Africa to 92% in South-East Asia and the Western Pacific Regions.

The use of BCG vaccine has been controversial for decades, largely owing to disparate results from clinical trials of its efficacy and the debate surrounding these differences. BCG vaccine is administered routinely in developing countries, whereas its use has been discontinued or has diminished in many industrialized countries in Western Europe and North America. The policies covering the use of BCG vary according to country and region, and different vaccine preparations are employed. It is most commonly administered at birth or in the first year of life; however, in some countries children are revaccinated with BCG at school entry, and in some regions, especially Eastern Europe, multiple revaccinations have been administered throughout childhood and adolescence. The present statement is intended to clarify WHO recommendations on BCG revaccination, based on currently available scientific evidence.

Efficacy of BCG vaccines

From 1927 to 1968, 21 controlled clinical trials of the efficacy of BCG vaccines were initiated in 10 countries, of which 19 were completed and evaluated. The protective benefit of BCG vaccination was extremely variable, ranging from 0 to 80% with different vaccines in different settings. In the most recent and largest trial, performed in Chingleput, India, with over 200 000 participants, the results were disappointing, since BCG showed no protective effect. Of seven trials that reported on survival, the protective effect against death ranged from 7% to 88%, although in most studies there were few deaths.

In trials that reported specific morbidity, protection against meningitis or miliary tuberculosis in children ranged from 46% to 100%. In the past decade, there have been 14 case–control studies in 12 countries that have compared cases of tuberculosis with selected controls by BCG vaccination status. BCG efficacy against tuberculosis ranged from 2% to 83%, and against meningitis or miliary tuberculosis in children, from 58% to 100%. Evaluation of household contacts of known cases of tuberculosis has also shown 53–74% protective efficacy among contacts who received BCG vaccine.

BCG vaccine does not appear to prevent primary infection with M. tuberculosis, nor does it prevent an appreciable number of infectious pulmonary cases, and therefore does not significantly decrease transmission of tuberculosis within a community. Taken together with the variable efficacy noted above, BCG vaccination has a relatively low impact on the global control of tuberculosis.

Tuberculin skin testing and BCG revaccination

Tuberculin skin tests are positive in most recipients; the duration of this hypersensitivity is variable, and the size of induration wanes with time. In some programmes, negative tuberculin skin tests have been used as indicators for the need to revaccinate with BCG. However, there is poor correlation between skin test conversion rates or the induration and protective immunity, and there is no evidence that a reduction in post-BCG vaccination tuberculin sensitivity is associated with any reduction in protective immunity. Once an individual has been revaccinated, there is no reliable way of distinguishing tuberculin reactions associated with BCG from those caused by natural infection. The risk of administering BCG vaccine to persons with positive tuberculin reactions due to either prior BCG vaccination or to natural infection is minimal. Numerous studies have shown that direct vaccination, i.e., BCG vaccination without prior tuberculin testing, is safe and acceptable to populations being vaccinated.

Efficacy of repeated BCG vaccination

There is no definitive evidence that repeated BCG vaccination confers additional protection against tuberculosis. In Hungary, where systematic BCG revaccination was used from 1959 to 1970, the incidence of tuberculosis declined significantly. However, there was no comparative control group and other factors may have been responsible. In a retrospective analysis in Poland from 1965 to 1977, persons with tuberculin skin tests <5 mm in diameter who were

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Reprint No. 5663
WHO News and activities

...not revaccinated had a higher incidence of tuberculosis in the ensuing 12 years than a group who had been revaccinated. The number of incident cases were few, and the groups were not randomized and may not have been comparable. In Chile, where BCG revaccination is given at 6 years and 14 years of age, there was no difference in the proportion of young adults with 1, 2, or 3 BCG scars between patients with tuberculosis and controls, suggesting that there is no benefit from repeated vaccination. There are as yet no reports of prospective, comparative clinical trials that have assessed the efficacy of BCG revaccination.

Although BCG vaccine is relatively inexpensive, its administration after the first year of life or use of repeated vaccinations may incur significant additional costs and is probably not cost-effective. However, the cost-effectiveness of BCG vaccine is difficult to study owing to the variability in vaccine efficacy, BCG preparations, vaccination schedules, and the incidence of tuberculosis in different countries.

**Recommendations**

Based on the above information, the recommendations shown below reiterate and update previous WHO statements on the use of initial BCG vaccination and revaccination. Since BCG vaccination has variable efficacy, it should be considered an adjunct to national tuberculosis programmes. Rapid case detection and effective treatment remain the highest priorities for the control of tuberculosis in all countries.

- In countries where the prevalence and incidence of tuberculosis are high, BCG vaccination should be given to infants as soon after birth as possible, and in any case, within the first year of life.
- Where tuberculin skin testing is used to make decisions on BCG revaccination, the practice should be discontinued.
- For persons who have received BCG vaccination, repeat vaccination is not recommended, since available evidence does not support this practice. Multiple revaccinations are not indicated for anyone.

A list of relevant references is available on request from the Global Tuberculosis Programme, World Health Organization, 1211 Geneva 27, Switzerland.