Annotations

BCG vaccination

Bacillus of Calmette-Guérin was developed after 13 years of research and more than 200 subcultures from an original strain of *Mycobacterium bovis*. It was first used in France in 1921 and since 1950 has played an important part in tuberculosis control programmes throughout the world. However the results of BCG trials have varied enormously and discouraging reports from a recent large field trial in south India¹ have provoked a reconsideration of BCG vaccination policies.

Controversy surrounding efficacy

Early observations in students and during epidemics in schools suggested that BCG immunisation reduced the incidence of primary tuberculosis² but during the last 50 years prospective controlled trials of mass vaccination with BCG have found a protective effect (reduction in incidence of tuberculosis in the vaccinated group) ranging from 80%³ to less than 5%.⁴ The Medical Research Council began a study in 1950 in which 54 239 British schoolchildren aged between 14 and 15 years participated; all were initially tuberculin negative. The protective effect was 78%, but the infection rate fell so much during the trial that it was impossible to assess efficacy beyond 15 years.⁵ In 1978 the British Thoracic Association reviewed the schools' programme and concluded that vaccination between ages 10 and 13 years still gave 70% protection for at least 10 years. However it estimated that as the infection rate had declined, 100 000 BCG vaccinations would prevent only 44 cases of tuberculosis in the next 15 years.⁶ Neither of these studies investigated the influence of race or place of birth on the protective effect.

The results of other trials, particularly those carried out in developing countries, have been less encouraging.⁷ The most recent and largest studied a rural population of over 250 000 near Madras in south India. The purpose of the trial was to test the efficacy of two widely used BCG vaccines. After 7½ years no protective effect could be seen with either vaccine. Only sputum-positive pulmonary tuberculosis was included in the analysis and no information was obtained about meningitis or miliary tuberculosis, so the study was not designed to assess the value of BCG in children.¹

The reasons for the disparate results of BCG trials are not known, but there are a number of variables which could have influenced the outcome. They include the age range, nutritional state, and prevalence of intercurrent infection in the study population, the potency of the vaccines used, the tuberculosis infection rate, and the prevalence of low grade tuberculin sensitivity (this was high in south India) presumably due to mycobacteria other than *Mycobacterium tuberculosis*.

Vaccination in the newborn

The rare complications of BCG vaccination—chronic ulceration, suppurative lymphadenitis, and osteomyelitis—occur more often in the newborn, and their immunological response judged by post-vaccination tuberculin testing is smaller than in adults. If the BCG dose is reduced the tuberculin response is further decreased. On the other hand some necropsy studies⁸ suggest that BCG protects by limiting the spread of tubercle bacilli, not by preventing the establishment of infection, and in studies where clinical disease has developed soon after infection the protective effect of BCG has been good. It follows that vaccination is potentially valuable in infants and young children who are at risk of rapidly developing disseminated disease.

There is little information about the efficacy of BCG vaccination in the newborn.

Two prospective controlled trials were done in the 1930s. The first was in North American Indians living in Saskatchewan. Paired families were allocated to BCG or control and their infants were vaccinated within 10 days of birth. During a 9- to 11-year follow-up period, 6 of 306 vaccinated children and 29 of 303 controls developed tuberculosis.⁹ The results of the second trial begun 4 years later in Chicago showed a similar protective effect. There were 17 cases of tuberculosis among 1716 vaccinated children and 65 cases among the 1665 controls.¹⁰ More recent evidence is available only from retrospective assessments, but studies in Germany, Britain, Taiwan, and Hong Kong suggest that vaccination in the newborn period gives considerable protection against childhood tuberculosis.¹¹

Current vaccination policies

BCG is compulsory in 64 countries and is officially recommended in a further 118 countries and territories. The most widely used programme is vaccination of the newborn. The United States Public Health Service does not recommend the routine use of BCG, and chemoprophylaxis with isoniazid is preferred.¹² The recent poor results from south India stimulated a review of existing policies by two WHO study groups.^{13 14} They recognised that there were situations in which the protective effect of BCG was uncertain, but felt that the Madras trial should not be interpreted as showing that BCG is ineffective under any circumstances. It was proposed that the kind of programme used should depend on the prevalence of infection (low dose tuberculin sensitivity) in 10- to 14-year-old children. If this was greater than 5% BCG should be given at birth, if it was between 2 and 5% vaccination should be given at school entry, and if the prevalence was less than 2% it should be given at between ages 12 and 14 years.

In the UK the overall prevalence of tuberculin sensitivity in 12-year-old children is about 1%. Vaccination is offered to all tuberculin-negative children at this age and is accepted by 80 to 90%. Because of the decline in incidence over the last 30 years it would now almost certainly be less expensive to stop the schools' vaccination programme and treat the resulting cases of tuberculosis. Infection rates vary in different parts of the country and in different ethnic groups, so the time may be approaching when vaccination policies could be determined by local rather than national circumstances. It seems reasonable to continue vaccinating groups at risk of exposure to infection—such as hospital and laboratory workers. Tuberculin-negative contacts of patients with tuberculosis should always be sought and vaccinated. Infants with a history of tuberculosis in the family should be vaccinated at birth. Babies born to mothers having treatment for tuberculosis should be given isoniazid for 6 to 8 weeks, and then given BCG if they remain tuberculin negative. It is the practice in some parts of the country to vaccinate newborn babies of Asian immigrant families. There is little information about the benefit of this, but a study by the British Thoracic Association found that among Asians who had been in close contact with tuberculosis, the infection rate was lower in those who had previously been vaccinated (1.6%) than in those who had not (3.8%).¹⁵

In some recent immunisation programmes BCG

has been given a few months after birth. Studies are being done to discover whether or not at this age vaccination induces a better immune response with less risk of complications, than in the newborn period.

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