

Need for a BCG trial in Canada's native populations

RAJ NARAIN,* MB, BS, TDD, FAMS (INDIA)

For over 30 years most of the 7000 registered Indians and 550 Inuit born in Canada each year have been vaccinated with BCG (bacille Calmette-Guérin).¹ During the past three decades the prevalence of tuberculosis has dropped and its treatment has become more effective. In view of these changes it appears necessary to review briefly the history of mass BCG vaccination in the native populations of Canada to determine whether vaccination is still cost-effective and whether some modifications in the existing program are warranted.

BCG vaccine was first used in France in 1922, and by 1925 France had adopted a large-scale vaccination program.² With a grant from the Canadian National Research Council (NRC) Baudouin gave BCG vaccine orally to 20 000 infants in Montreal between 1926 and 1938. The data collected were reviewed by a committee appointed by the NRC. Regular follow-up was available for 793 children who had been in contact with active tuberculosis. The incidence of tuberculosis in these children and in 1200 children, mostly from the same families, who had not been vaccinated was compared after adjustments had been made for the differences between the two groups; it was found that BCG vaccine afforded substantial protection against tuberculosis.²

Towards the end of the last century tuberculosis was rampant among the native populations of Canada. In 1890 the rate of death from tuberculosis was 90/1000 in these groups, whereas their rate of death from all causes was 1.37/1000.^{2,3} By 1927, however, their rate of death from tuberculosis was only 8/1000,² and the prevalence was probably twice as high. It was virtually impossible to segregate the large number of patients to institute the long and rather ineffective treatment. Therefore, the NRC suggested that the efficacy of BCG vaccine be tested in the native Indian population without segregating the patients. A BCG trial, supported by a grant from the NRC, was conducted among Indian infants in Saskatchewan between 1933 and 1947. The vaccine was given at random to 306 infants from homes where a member of the family had tuberculosis. All but 21 infants were given the vaccine intracutaneously. Another 303 infants were left unvaccinated. Vaccination was found to offer 80% protection.⁴

Mass BCG vaccination of the native Indian and Inuit populations was started in the late 1940s. Since 1965 the vaccine has been administered only intradermally.⁵

Does BCG vaccination still offer protection against tuberculosis? One might assume that if it offered protection in the 1930s and 1940s it would also do so today. However, this assumption may not be valid for the following reasons:

- The two trials I have cited were conducted mostly

among contacts living in areas where tuberculosis was widespread and patients were usually not segregated. In the Saskatchewan trial 68.7% of the controls became infected at an average age of 9 years. Around 1950 the risk of infection among the Inuit in Canada was about 15% per year, in 1971 it was about 3% to 4% and in 1974 it was 1.5% to 2%.⁶ Springett⁷ has suggested that BCG vaccination may offer protection only when the risk of infection is high. With the marked reduction in the risk of infection in Canada the amount of protection offered by the vaccination may have changed.

- With the great reduction in the risk of infection, infancy may no longer be the best time for vaccination. Theoretically, the vaccine should be given a few weeks before the expected time of infection so that postvaccination allergy is at its maximum at the time of infection with *Mycobacterium tuberculosis*.⁸ However, postvaccination allergy wanes rapidly in infants.⁹ It is likely that at present few Indian or Inuit infants become infected soon after birth and that less than 10% are infected by the time they are 10 years of age. In fact, one BCG trial, performed in Great Britain, included only persons of school-leaving age, since it was considered that the risk of infection in younger persons was too small to merit BCG vaccination.¹⁰ However, this hypothesis has yet to be tested.

- More recent BCG trials have shown conflicting results, the degree of protection varying from 80% to none at all,¹⁰⁻¹⁶ and opinion seems to have shifted away from BCG vaccination. Recently the executive director of the International Union Against Tuberculosis wrote that BCG vaccination had not proved very effective in reducing the transmission of infection; it only prevented the noninfective form in children.¹⁷ Styblo and Meijer¹⁸ estimated that annually BCG vaccination prevented only 0.3% to 2.0% of infective cases. The largest BCG trial, conducted in India under international auspices with strict research discipline, showed that the vaccine offered no protection.¹⁶

- When a strain of BCG has been repeatedly subcultured to produce vaccine, it may change its characteristics and lose its potency,¹⁹ thereby offering less protection.²⁰⁻²² The strain used in Canada appears to have undergone such a change. In 1975 postvaccination allergy and the protection offered by vaccination were very poor in Inuit children; among those 0 to 7 years of age more than half showed little or no reaction to tuberculin, and 13% had tuberculosis.⁵

- The protection afforded by BCG vaccination has always been a mixed blessing. It renders the tuberculin test, a valuable diagnostic tool, practically useless; even as little as a 10th of the usual dose of the vaccine obliterated the distinction between infected and uninfected individuals.²³ With the marked reduction in the prevalence of tuberculosis, the tuberculin test has become very important in the diagnosis and control of the

*Former director, Tuberculosis Prevention Trial, India

Reprint requests to: Dr. Raj Narain, 3014-1 Meadowbrook Lane, Windsor, Ont. N8T 3G8

disease and in epidemiologic studies. Other methods, such as roentgenography and sputum examination, have become extremely costly in terms of the numbers of cases found. During the 1930s and 1940s the loss of the value of the tuberculin test was compensated for by the substantial protection offered by BCG vaccination. However, the position may be different now.

• Because BCG vaccination may offer little or no protection, its complications, which occasionally include death, cannot be disregarded.

The incidence of tuberculosis among Canada's native populations is still very high. From 1970 to 1974 the incidence rose among registered Indians, from 140.8/100 000 to 166.2/100 000, an annual average increase of 2.3%, while it decreased among all other Canadians, from 19.3/100 000 to 14.9/100 000. Thus, measures for preventing tuberculosis are still needed in the registered Indian population. However, if the protection afforded by BCG vaccination is low, we may be unwise to expend scarce resources on its use.

The value of BCG vaccination can be defined only by another trial in Canada, conducted among Indians and Inuit; such a trial would produce data that would help in the planning of more effective and economical control measures in keeping with the advances in technical knowledge during the last 30 years. The costs of such a trial could be contained if existing services and programs were used. To select a group other than infants would be impractical because, since most would have already been vaccinated at birth, an adequate number of unvaccinated controls would not be available. In the new study, infants would continue to be vaccinated at birth at the various health centres and hospitals involved. Placebo injections would be given to a proportion of the infants under rigidly controlled double-blind techniques. Both groups would be followed up with surveillance and periodic tuberculin testing. According to Statistics Canada, from 1975 to 1979 about 40 cases of tuberculosis occurred per year in children less than 5 years of age among the Indians and Inuit. If we assume that the average age at the time of diagnosis was about 2.5 years, 40 cases should develop in both cohorts within

3 years, and 150 cases within 5 to 6 years. These numbers should be adequate to show statistically significant results.

Tuberculosis experts, manufacturers of BCG vaccine and agencies responsible for health care in the North should be interested in determining the effectiveness of BCG vaccination in Canada's native populations.

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