Results of Controlled Investigations on BCG Vaccination

By
D.N. SHIVPURI,
Medical Officer,
Tuberculosis Clinic, Queens Road, Delhi.

In Malta, 36,320 BCG vaccinations were done in 1950, and records of follow-up were kept. (Zammit 1952) Out of these 54 (0.15%) got glandular enlargements in the armpit two to four months after vaccination, which became soft and were aspirated. All eventually healed, without leaving any permanent damage or defects. Twenty-three cases (0.075%) developed a tiny ulcer at the site of vaccination between the 30th and the 53rd day, but all healed eventually. Two developed some fever and constitutional symptoms for a few days only. None developed blindness or tuberculosis or any permanent defect. There was no death on account of BCG.

It is important to note that there were no major complications. The enlargement of armpit glands or formation of a tiny ulcer at the site of vaccination in about 0.2 per cent of cases is the expected normal rate of slight inconveniences met with in this vaccination, and is less than the fever and the swelling met with in many other vaccinations.

2. Animal Experiment

Since 1930 several bacteriologists have made repeated attempts in their laboratories to see if the organism in the BCG vaccine can again become virulent and dangerous either in cultures or in animal bodies. None of these attempts have so far succeeded and the BCG organisms could not be made virulent or dangerous.

Some persons have quoted Pierce and Dubo’s (1955) recent work in which they mention that substrains of BCG obtained from 4 different laboratories differed in the degree of tissue invasiveness in guinea pigs but these critics have conveniently ignored quoting that part of the work of these authors (Tubercle, April 1955) which mentions that although these substrains of BCG differed in degree of tissue invasiveness, they were all found to give rise to self-limited lesions in healthy guinea pigs even when they were injected by intravenous route. That is, they did not produce progressive disease even in guinea pigs, who are many times more susceptible than human beings.

Other experiments done to test the effects of BCG vaccination on guinea pigs are as follows:

One group of the guinea pigs was given vaccination and another group was left unvaccinated. After 8 to 12 weeks a challenge infection of virulent tubercle bacilli was injected in equal doses into both groups. Both the groups were kept under similar conditions and were observed for several weeks. It was found:

1. The average period of survival of vaccinated group was much greater than that of the non-vaccinated group.
2. Same guinea pigs were killed from each group at equal intervals after challenge infection, and on post-mortem it was seen that the number and the extent of pathological lesions were much less in the vaccinated group than in the non-vaccinated group.

3. Lastly, the bacterial population in these lesions was much less in the vaccinated group than in the non-vaccinated group.

These comprehensive experiments show that the vaccinated group due to the increase of its specific resistance by BCG vaccination enjoyed a greater degree of protection than the non-vaccinated group.

Experimental work published in “The American Review of Tuberculosis” (Abstracts, Sept., 1953) showed that tubercle bacilli multiplied freely within the cells (monocytes) taken from normal guinea-pigs or rabbits by contrast, intra-cellular multiplication of tubercle bacilli was retarded or completely inhibited within the cells taken from animals previously vaccinated with BCG.

**Controlled Experiments on Human Beings**

Clinical evidence has been collected from observation among the following categories: (1) Red Indian children; (2) Red Indian infants; (3) Danish girls; (4) Canadian nurses; (5) English children; (6) American children; (7) Swedish Army recruits; (8) Japanese young adults and children.

Joseph D. Aronson, of the Henry Phipps Institute, University of Pennsylvania U.S.A., and C.E. Palmer report in “The American Review of Tuberculosis” (1946, 1948) that Red Indian American children are said to have very little resistance against tuberculosis. Morbidity from tuberculosis among them is high. Therefore, it was decided to increase their specific resistance by BCG vaccination and find out whether they get any increased protection from this deadly disease.

Two groups of non-infected Red Indian children in the U.S.A. and Alaska of school and pre-school age, were selected. One group of 1,550 children received BCG protection, the other group of 1,457 children received only normal saline injection.

They were allowed to continue their natural way of life before and after vaccination. Both groups were followed up and examined annually from 1937 to 1951 (13 to 15 years). Almost an equal number of children were followed in both groups for this long period. Here are the results of this scientifically controlled observation lasting for more than a dozen years.

In the BCG vaccinated group, six died of tuberculosis, whereas in the group which did not receive BCG vaccination, 52 died of tuberculosis during the same period. In other words, the vaccinated children enjoyed a protection which was about 8.7 times greater than that enjoyed by the non-vaccinated.

2. Further, the same author gives the results of BCG vaccination on new born infants observed between 1939 and 1941 in the same community and area. During the period, out of the 123 BCG vaccinated infants none died of tuberculosis but seven died of non-tubercular diseases. Of the 139 unvaccinated infants, four died of tuberculosis and 11 from non-tubercular diseases.

This observation is doubly important. First, it shows that BCG vaccinated new-born infants compared with unvaccinated enjoyed four times the protection
against tuberculosis. Secondly it proves that BCG does not give rise to any serious complications, for the number of deaths due to all causes, besides tuberculosis, was also less among the vaccinated infants than in the non-vaccinated.

This observation must satisfy those who are trying to prove that all ailments which children get after BCG vaccination, are due to that vaccination.

3. Hyge, from Denmark, reported in 1947 that in a school in that country an unsuspected female case of open tuberculosis was working as a teacher or two months before she was diagnosed. She had come in intimate contact with about 200 girl students during that time. At that time all these student contacts were also examined. It was found that 106 girls had already been BCG vaccinated and 94 were non-vaccinated. Full records of these girls were kept and they were examined at intervals. It was found that of the vaccinated group two developed tuberculosis. But in the unvaccinated group, 41 developed tuberculosis.

There cannot be more convincing proof of the safety and efficacy of BCG vaccination than this unfortunate accidental experiment by nature without the previous human knowledge or plan.

4. Ferguson, of Saskatchewan, Canada, after 24 years follow-up ‘reported in 1949, in ‘Tubercle’ that among 1,005 BCG-vaccinated nurses, 0.9 per cent acquired tuberculosis, whereas of 1,368 unvaccinated tuberculin negative nurses, 4 per cent acquired tuberculosis, that is, about four times as many.

5. R. Stevenson Doig (School Medical Officer, Stornoway, England) reports in the “Lancet” of April 2, 1955, that in 1950 a group of 3,000 children were vaccinated and another group of 2,814 children who were also tuberculin-negative were not vaccinated.

Both the groups were followed up for four years and careful records were kept. It was found that by 1954 none of the vaccinated group had developed tuberculosis whereas nine children from the unvaccinated group had developed tuberculosis.

6. Stein and Aronson carried out scientifically controlled observations at the Henry Phipps Institute, University of Pennsylvania. They reported in “The American Review of Tuberculosis” (Nov, 1953) that 1,540 persons were BCG vaccinated and 1,450 tuberculin-negative were not vaccinated. The two groups at the beginning of the study were comparable in age, sex and economic condition. They were followed up for about a period of nine to 11 years and x-ray and other examinations were done at yearly intervals. It was found that 4.1 per cent of the BCG vaccinated developed tuberculosis during this period.

7. Next we come to a study on Swedish Army recruits by Dahlstrom and Difs (1951,) which for its thoroughness and details has been compared to a controlled laboratory experiment. During 1941—44 they followed up and investigated 36,235 vaccinated and 25,239 unvaccinated tuberculin negative young recruits who lived under practically similar environments. They have made several interesting and instructive discoveries as the result of their exhaustive studies. Briefly, however, their finding was that during these 4 year period of observation there occurred 0.3% cases of tuberculosis in the BCG group and 0.7% in the unvaccinated group, that is the vaccinated group enjoyed a protection which was 2.3 times over the unvaccinated.

Regarding deaths from tuberculosis during the same period the vaccinated group enjoyed the protection which was 3 times than the non-vaccinated group.
8. Finally, it is interesting to note that the largest controlled study on effects of BCG vaccination in human beings has been done in an Asian country, namely Japan. Crawford has published the details of this study in the “American Journal of Public Health” (July 1954). He mentions that tuberculosis was a leading cause of death in Japan up to 1951. The mortality rate was 282 per lakh of population in 1945. It was found that about 30 million of people between the ages of 0-29 years were tuberculin negative. 27 million of them were vaccinated between 1945-1951. The death rate from tuberculosis dropped from 282 per lakh in 1945 to 82 per lakh in 1952. That is within seven years there was a startling drop of 70%. Practically all this drop occurred between the ages 0-29 years. This is all the more startling when it is remembered that all environmental factors including overcrowding, malnutrition and collapse of normal living caused by destruction in war should have caused an increase in death rate, as it did cause an increase in war-ravaged European countries. All this emphasizes the importance of BCG in mitigating the menace of tuberculosis even under adverse environmental conditions. No one denies that raising the standard of living and isolation of sputum positive cases in hospital beds is of prime importance. But while these important measures are also being attended to they will take a quarter to half a century to develop. Therefore BCG vaccination is a necessary supplementary measure to meet the present day emergency in our country where tuberculosis has become a leading cause of disability and death.

BIBLIOGRAPHY