120 Kul Bhushan: ASSESSMENT OF BCG VACCINATION IN INDIA: THIRD REPORT Indian J Med Res 1960, 48, 406-17.

Under the auspices of the Indian Council of Medical Research, a third **assessment of the mass BCG campaign** in India was carried out from **1955-58**. It is a continuation of the work started by the WHO, of evaluating the level of allergy among groups vaccinated in the campaign. WHO team used 5 TU RT 14, 20, 21, while the present assessment team used 5 TU RT 22. A total of 18,367 school children distributed over 262 schools in 169 different localities were retested for **post vaccination tuberculin sensitivity**. The groups were vaccinated in mass BCG campaign with 91 different batches of vaccine produced in Madras. The interval between vaccination and retest varied from 1½ to 42 months.

The mean size of reactions varied from 8.3 to 16.6 with overall mean of 12.5 mm. Less than 10% of the mean values were under 10 mm and less than 10% over 15 mm. Analysis also showed that BCG vaccination was responsible for an increase of 6-7 mm in the mean size of reaction over the pre-vaccination level of the non-infected. One third of the groups had their sensitivity increased upto 6 mm and two third by 7-11 mm. Comparing with the highest attainable degree of tuberculin sensitivity in the infected 1/3rd of the vaccinated group fell short of it by 5-9 mm, whereas 2/3rd were within 4 mm of this level. There is no appreciable difference in the post vaccination allergy according to the state and prevalence of non specific tuberculin sensitivity. However, there is an increase in allergising capacity of the BCG vaccine after introduction of modifications in the production procedures in 1955 and again in 1956 in the BCG Laboratory at Madras. Waning of allergy upto 20 months after vaccination and **boosting** thereafter probably due to super infection was also observed. Findings show that a large proportion of the vaccinated groups retested have achieved attainable allergy with the vaccine used. In view of the above, there is an urgent need to produce freeze dried vaccine than the present liquid vaccine for achieving high levels of allergy.

Freeze dried vaccine holds out promise for use in the mass BCG campaign. A continued and expanded research is needed into the protective value of BCG vaccination with the level of allergy which the mass campaign can produce under the epidemiological circumstances existing in India and other technically developed countries. KEY WORDS: BCG VACCINATION, ASSESSMENT, TUBERCULIN SENSITIVITY, TUBERCULIN ALLERGY, LIQUID BCG, FREEZE DRIED BCG.

121 Raj Narain, Kul Bhushan & M Subramanian: ALLERGY PRODUCING CAPACITY OF MADRAS AND DANISH BCG VACCINES AS SEEN AMONG SCHOOL CHILDREN IN BANGALORE Indian J TB 1961, 7, 1-15.

In all, 1,259 students aged 11-19 years from three boys high school of Bangalore, formed the study group. They were tuberculin tested with 1 TU RT 23 containing Tween 80. Boys with a reaction of 13 mm or less to tuberculin test and willing for BCG vaccination were allocated in 3 groups: (i) to be vaccinated with **Madras vaccine** (211), (ii) to be vaccinated with **Danish Vaccine** (236), (iii) **control with saline injection** (231) (placebo). Strength of Madras and Danish vaccines used was same, 0.075 mg per dose. After 3 months of vaccination, second tuberculin test with 1 TU RT 23 with Tween 80 was given to 575 boys included in both the vaccinated groups and in the control group. A **follow-up at one year** after vaccination was done among 328 boys, who were again tuberculin tested.

analysis of data shows that the mean size The of post-vaccination tuberculin test induration among Madras BCG vaccinated group was 11.8 mm and among Danish BCG vaccinated group, it was 11.9 mm, the standard deviation were 3.8 and 4.5 mm respectively. The above differences between the 2 vaccinated groups were not statistically significant. Similarly, the post-vaccination allergy in the two BCG vaccinated groups at the end of one year was not significantly different. The mean size of the scar produced by two vaccines were also smaller. The post-vaccination allergy among persons whose pre-vaccination tuberculin induration was 9 mm or more to 1 TU RT 23 with Tween 80, did not increase by more than 4 mm after vaccination. While the group whose pre-vaccination tuberculin induration was below 9 mm, had an increase of post-vaccination allergy of a little over 8 mm. It is concluded that the allergy producing capacity of the Danish and Madras vaccines was not different.

KEY WORDS: BCG VACCINE, POST VACCINATION ALLERGY, MADRAS VACCINE, DANISH VACCINE.

122 GVJ Baily: DOOR TO DOOR BCG VACCINATION Bull Dev Prev TB 1962, 9, 12-15.

The objectives of the presentation were to understand the **operational efficiency of the centre type of BCG mass campaign** in India and how the efficiency especially the BCG vaccination

coverages could be improved through adopting a house-to-house or door to door approach. The material from three different sources are examined. Firstly, the reports from the mass campaign showing the **reported** coverages in different age groups; secondly, the presence of **BCG scars** (as an evidence of vaccination) as seen in an epidemiological survey done shortly afterwards and finally the coverages as obtained in an operational study of door to door BCG vaccination.

While the mass campaign reported that 35% of the total population was tuberculin tested (vaccination coverage reports were not available) the epidemiological survey showed that shortly after the mass campaign only about 19% of the children aged 0-9 years had BCG scars, while about 97% were tuberculin negative and eligible for vaccination. On the other hand in the house-to-house campaign 80% of the children aged 0-19 years could be vaccinated. The major **disadvantage of a house-to-house programme** is low output of work due to time taken up for registration of every household member. This can be improved by limiting registration to 0-19 years and by simplifying registration form.

KEY WORDS: HOUSE TO HOUSE BCG, MASS BCG CAMPAIGN, OPERTIONAL EFFICIENCY.

123 Kul Bhushan: TRIAL ON EXPERIMENTAL BATCHES OF FREEZE-DRIED BCG VACCINE PRODUCED AT GUINDY LABORATORY Bull Dev Prev TB 1962, 9, 16-19.

Government of India set up a plant for producing freeze-dried vaccine at BCG Vaccine Laboratory, Madras in 1959. Before releasing the freeze-dried vaccine to the mass campaign it was necessary that it is subjected to various tests. This paper deals with two such trials. The first study planned in this connection was for the **assessment of allergising properties of two lots each of four batches of freeze-dried vaccine.** The second study was to investigate the **stability** of two lots of a batch of freeze-dried vaccine in relation to storage at different temperatures for varying periods.

The results indicate that though the liquid vaccine has on the whole produced slightly higher allergy than the freeze-dried vaccine, the **level of allergy achieved with the freeze-dried vaccine is quite adequate**. Levels of post-vaccination allergy in the lots containing glutamate and tween 80, show that increase in storage temperature has resulted in higher loss of potency of vaccine. No definite trend is indicated regarding the lots containing glutamate alone.

KEY WORDS: FREEZE-DRIED BCG, CLINICAL TRIAL, POTENCY, STABILITY.

124 Kul Bhushan: ALLERGY AFTER BCG VACCINATION Proceed 18th Natl TB & Chest Dis Workers Conf, Bangalore, 1962, 286-89.

In view of the variable and low levels of post-vaccination allergy elicited in the Indian Mass BCG Campaign vaccinated groups as observed by WHO and Indian BCG Assessment Teams, some studies were carried out to investigate some of the factors considered having influenced the levels of post-vaccination allergy. The reasons were potency and storage of vaccine, techniques, interval between vaccination and retesting and Potency of the vaccine: Madras vaccine was tuberculins used. compared with Danish vaccine. The retest done at 3 months with 1 TU RT 23 showed 11.8 mm induration with Danish and 11.9 mm with the Madras vaccine. Test done after one year with 20 TU induration was 18.3 mm for both the vaccines. It is reasonable to assume that the vaccine produced at Madras is as potent as Danish vaccine. Storage of vaccine: A comparison of post vaccination allergy in respect of storage of vaccine by the ICMR Assessment Team and by Mass Campaign Teams was carried out in five groups of villages in the neighbourhood places where five BCG teams were working in Tamil Nadu. The non reactors were vaccinated randomly by vaccines stored by either team and with the placebo-III group as control. The retest done after 3 months showed that in all the five groups combined the mean size of indurations vaccinated with vaccine stored by Assessment Team were more in the vaccine stored by Mass Campaign Team. The loss of potency was 0.7 mm per week in vaccine stored by Assessment Team and 1.5 mm per week stored by Mass Campaign Team. Techniques: The above study was extended to five more groups vaccinated and tested by the Mass Campaign Team. Assessment Team also vaccinated separate groups with the same vaccine and tested on the same day. Mean size induration for groups combined was higher for assessment team but not significant. So, the techniques do not seem to make much difference. Interval between vaccination & retesting: Analysis of data collected on post vaccination allergy in the groups vaccinated by the Mass Campaign Teams retesting according to intervals showed that the mean size induration decreased with the increase in interval between vaccination and retesting from 1-20 months. Thereafter, it rose again. These results indicate a tendency for the allergy after vaccination to wane with passage of time. The rise is presumably due to super infection or difference in batches of vaccine. In the third year (not included in this paper) greater proportion of people had bigger reactions. Besides, tuberculin used for retesting is also found to give differences in mean size induration. Tuberculin 5 TU RT 22 gave larger reactions than 1 TU RT 23 with tween, the differences were above 3 mm.

It can be concluded that at present Madras vaccine is

satisfactorily potent, the post vaccination allergy is influenced by storage of vaccine, by interval between vaccination and retesting and type of tuberculin used for eliciting the allergy. Technique of testing, reading and vaccination may not influence the results. Under Indian climatic conditions the liquid vaccine should not be used for more than 2 weeks. There is a need for freeze dried vaccine.

KEY WORDS: POST VACCINATION ALLERGY, LIQUID BCG, FREEZE DIRED BCG, MASS BCG CAMPAIGN.

125 GD Gothi, Kul Bhushan, SS Nair & GVJ Baily: BCG WITHOUT TUBERCULIN TEST Proceed 19th Natl TB & Chest Dis Workers Conf, New Delhi, 1964, 138-62.

In the BCG Mass Campaign low outputs and coverages of BCG vaccination done after tuberculin test were due to slowness of the campaign because of two visits to an area, the fear of two pricks and tuberculin tested absenting themselves from reading of the test. It was thought that if BCG vaccination could be given without prior tuberculin test and without causing any complications then the speed of work and outputs could be more than doubled and coverages improved appreciably. For this, the following three studies were carried out: In the first study 1,891 persons belonging to a rural population were randomly divided into four groups (i) those tuberculin tested and vaccinated, (ii) tested but not vaccinated, (iii) not tested but vaccinated, and (iv) neither tested nor vaccinated. Induration site of tuberculin test and vaccination were read on the 3rd, 6th and 90th day. Later on, another tuberculin test was done on the 90th day and read 3 days later. Both axillae were examined on 0, 14th and 90th day and X-ray pictures were taken on 0 day, 90th day and after one year. Tuberculin indurations on 3rd day were compared with BCG induration on 3rd, 6th, 14th and 90th day. Majority of tuberculin reactors had large BCG indurations upto 14th day. By 90th day very few persons have large indurations left. Among non reactors also large BCG reactions were seen in 25% - 53% of the persons. There were no differences as regards to the size of lymph nodes (regional reactions) between reactors and non-reactors; neither was there any evidence of exacerbation of existing disease nor any flaring up of dormant foci (Primary complex) in the form of new disease as shown by X-ray.

In the **second study** out of 1,520 persons from 4 villages, 1,186 were both **tuberculin tested and simultaneously vaccinated**. Examination of local reactions daily from one to nine days, on 19th and the 29th day, confirmed the findings of first study with regard to the local reactions. In this study neither axillae were examined nor X-ray pictures taken. In the **third** **study**, influence on acceptability of direct BCG vaccination due to large local reactions was tested. Twelve villages in Gubbi taluk of Tumkur district were taken in pairs. Vaccination of 2nd village of each pair was done after 1-4 weeks of the vaccination in 1st village to observe the influence of BCG reaction on the people. Vaccinations were given to 5363 (64.2%) persons from the total registered population with Madras liquid vaccine. The large local reactions showed no adverse effect on the acceptability of BCG vaccination in the neighbouring villages, rather a slight improvement in BCG vaccination coverages with time was seen.

KEY WORDS: RURAL POPULATION, DIRECT BCG VACCINATION, APPLICABILITY.

126 Kul Bhushan: TECHNICAL ASPECTS OF BCG VACCINATION CAMPAIGN Bull Dev Prev TB 1965, 11, 31-35.

During the 7th All India BCG Conference held at Ahmedabad in February 1965 various points regarding the technical aspects of BCG Campaign were put forward by the author of this article. The issues discussed were related to specific age-group to be vaccinated; direct vaccination; vaccination of new-borns; techniques of testing, reading and vaccination; preservation of biologicals, freeze-dried vaccine; pilot and research studies; assessment and training.

Some of the suggestions given on the above aspects described briefly were: (1) Only 0-20 years might be taken up because that was the most vulnerable age group for infection from the natural sources. (2) **Direct BCG vaccination** in 0-20 years age group could be carried out in the first round followed by vaccination of population below 7 years of age (0-6 years) in the subsequent rounds. (3) Infant vaccination practiced at that time in some of the major cities only, would not contribute greatly to the control of tuberculosis unless it is extended to the rural areas also. (4) Results of vaccination should be exceedingly good provided vaccine was maintained properly, used within 2 weeks of manufacture, shaken well before opening, a drop ejected out before vaccination and proper dosage injected correctly. (5) The vaccine must be kept under refrigeration during storage, transport and use. (6) The personnel engaged in the use of freeze-dried vaccine had to be **trained** properly in its aseptic reconstitution. (7) Operational studies in respect of BCG work in cities; practicability and feasibility of setting up training centres in the states, assessment of programme by the states etc., were required to be undertaken. (8) Uniformity of techniques and procedures of BCG vaccination and proper assessment of Mass BCG Campaign by an independent agency would be required. The author in his article also stressed that no changes should be brought into operation without assessment.

KEY WORDS: BCG VACCINATION, MASS BCG CAMPAIGN, DIRECT BCG VACCINATION.

127 Kul Bhushan, GVJ Baily & VB Naidu: SIMULTANEOUS SMALLPOX AND BCG VACCINATION Indian J TB 1968, 15, 52-56.

A study was carried out in Bangalore city corporation area with the following objectives; when BCG vaccination is administered simultaneously with primary smallpox vaccination to infants; (i) whether any immunological interferences take place as indicated by the development of vaccination lesion and post-vaccination allergy due to BCG vaccination and the development of the local lesion (take rate) of smallpox vaccination; (ii) whether the incidence of complications are higher among those simultaneously vaccinated and, (iii) whether the population will accept a procedure involving two vaccinations. BCG technicians and the smallpox vaccinators registered all the eligible children after house to house visit and randomly allocated to three groups. A total of 789 children aged below one year were admitted to the study. While 315 were vaccinated simultaneously with BCG and smallpox vaccines (BCG on the right arm and smallpox on the left), 255 were vaccinated with smallpox vaccine only and 219 with BCG vaccine. All 789 children were followed-up on the 5th, 21st, 90th and 93rd day of vaccination. The 5th and 21st day followups were to study the development and healing of smallpox vaccination lesions, whereas the 21st, 90th and 93rd day followups were for BCG vaccination lesions. The 90th and 93rd followups were for tuberculin testing and reading.

It was found that there was **no evidence of immunological** interference between the two vaccines when administered simultaneously i.e., the development of lesion of smallpox vaccination among the simultaneously vaccinated group was similar to the development of the smallpox vaccination lesion the only smallpox vaccinated group among and, the post-vaccination allergy due to BCG among the simultaneously vaccinated group was similar to the **post-vaccination allergy** among the only BCG vaccinated group. The complications due to vaccinations were very few and similar among the simultaneously vaccinated as compared to the other respective groups. The acceptability of simultaneous vaccination was higher than BCG alone. The above study has demonstrated that BCG and smallpox vaccinations can be administered simultaneously.

KEY WORDS: SIMULTANEOUS BCG & SMALLPOX VACCINATION, ASSESSMENT, ACCEPTABILITY, COMMUNITY.

128 Kul Bhushan, SS Nair & KT Ganapathy: ASSESSMENT OF POST-VACCINATION ALLERGY AMONG THOSE BCG VACCINATED WITHOUT PRE-VACCINATION TUBERCULIN TEST Indian J TB 1970, 17, 18-31.

The conventional methods of assessment of post vaccination allergy by doing tuberculin testing among the vaccinated group are inapplicable in case of BCG vaccination without prior tuberculin test (Direct BCG). Because of obvious technical and operational advantages of direct BCG vaccination a search for a method of technical assessment of BCG vaccination is important. Hence, a study was carried out by the BCG Assessment Team of National Tuberculosis Institute in Tumkur district of Mysore state where Mass BCG Campaign was going on. Four groups of persons aged 0-20 years, each group belonging to two BCG Technicians area and vaccinated one day prior to visit of assessment team, were randomly selected. Besides, persons (0-20 years) from 2 unvaccinated villages of adjacent area were included as control groups. All persons were registered simultaneously tuberculin tested with 1 TU RT 23 and 5 TU RT 22 within 24 hours of BCG vaccination (for pre vaccination allergy) and retested with tuberculin 5 TU RT 22 at the end of 3 weeks and 3 months (for post vaccination allergy). The four vaccine groups were vaccinated with vaccine batch Nos. 977, 978, 981 and 984 respectively. Classification of the directly vaccinated persons into previously infected and non-infected by tuberculin test administered within 24 hours of vaccination and about 12 weeks later, elicitation of post-vaccination allergy only among the non-infected, has been considered as the **Reference Test** for judging the suitability of other methods of assessment studied. The main findings are: (1) The Reference Test showed that the four batches of BCG vaccine used had induced varying levels of allergy. (2) Assessment based on the mean size of post-vaccination reactions among 0-4 years age group, which consists predominantly of previously non-infected persons, showed a different pattern of differences between the four batches of vaccine as compared to the Reference Test. Moreover, to get adequate number of children aged 0-4 years, it will be necessary to cover a comparatively large population. (3) The method of using the mean size of post-vaccination reactions among those classified as non-infected on the basis of vaccination reactions of size 0-13 mm at the site of BCG $\,$ vaccination on the 4th day of vaccination showed results similar to the Reference Test. But this method has only a marginal operational advantage over the Reference Test. (4) Using size of induration at the site of vaccination on 21st day of vaccination did not give the same results as the Reference Test. Operationally this method would have been most suitable as it

involved only one visit to the group. (5) Differences between mean size of post vaccination tuberculin reactions among directly vaccinated persons and mean size of (natural) allergy in reactors among neighbouring unvaccinated areas showed the same results as the Reference Test. This method has the operational advantage but needs further investigations. (6) Tuberculin testing of all directly BCG vaccinated persons including the natural reactors about 12 weeks after vaccination compared favourably, with the reference method, as the tuberculin reactors contributed less than 1 mm over and above the allergy in the vaccinated non-reactors. This method would be useful when rate of tuberculin reactors is less than 20% in 0-20 years age group and their mean size is also less than 20 mm. Operationally, it is a simpler method next only to No.4 above. Further investigations are considered necessary for final selection of this or any of the other methods.

KEY WORDS: BCG, POST VACCINATION ALLERGY, ASSESSMENT, DIRECT BCG VACCINATION.

129 Kul Bhushan, MN Mukherjee, SP Chattopadhya & KT Ganapathy: A COMPARISON BETWEEN LONGITUDINAL AND TRANSVERSE DIAMETERS OF TUBERCULIN TEST INDURATIONS

Indian J Med Res 1972, 60, 1724-30.

The purpose of this investigation was to compare the corresponding longitudinal and transverse diameters of tuberculin test and study the influence of reader variations, size of reaction and the age specific infection rates, in order to understand the effect of switching over from the transverse to longitudinal readings. The study was carried out in villages in south India where no BCG or tuberculin testing had been undertaken. A total of 1240 persons were given tuberculin test with 1 TU RT 23 in both longitudinal and horizontal diameters. The indurations were read after 2-4 days by two readers independently. The study showed that though the longitudinal diameters were bigger than the corresponding transverse diameters, these differences did not influence infection rates calculated at 10 mm or more induration level. In National Tuberculosis Institute (NTI), Bangalore the practice of reading transverse diameter was altered to longitudinal diameter in the epidemiological surveys as it was comparatively easier to read the longitudinal diameter. Obtaining almost similar infection rates at the 10 mm or more level of induration in this study, irrespective of readers and diameters has minimized the effect of the changeover from transverse to longitudinal diameter reading in the epidemiological surveys at NTI. This would also not pose any problem in comparing the results of NTI studies with other research studies by any national or international organisation where transverse diameters have been measured.

KEY WORDS: TUBERCULIN TEST, LONGITUDINAL, TRANSVERSE, TUBERCULIN INDURATION SIZE.

130 Kul Bhushan, SS Nair, KT Ganapathy & Vijay Singh: A COMPARISON OF THE COPENHAGEN AND MADRAS LIQUID BCG VACCINES Indian J TB 1973, 20, 4-9.

Liquid BCG vaccine produced upto 1955 at the BCG Laboratory, Guindy, Madras induced low and variable levels of post vaccination allergy. However, subsequent to improvement in production, its potency was adjudged as equivalent to Danish BCG vaccine. Later on, lower levels of post vaccination allergy in Mass BCG vaccination campaign and in research studies were observed. A study was planned to compare the Madras BCG vaccine with Danish vaccine in terms of the potency of the strains, production efficiency of the laboratory and stability on storage. This was done by comparing the allergising capacity and size of vaccination lesions. On a predetermined date in each of four consecutive months, both laboratories supplied to the Research Team one week of fresh vaccines from their respective BCG strains and also fresh vaccine of strains borrowed from the other laboratory. With these six vaccines every month, in two consecutive weeks randomly, vaccinations were given to 2,978 tuberculin non-reactors. Post-vaccination allergy was elicited 10 weeks later when size of BCG lesion was also noted. Viable counts on all vaccines were done by Madras Laboratory.

Though the Indian and Danish BCG vaccines induced similar levels of allergy, on further analysis it was found that Madras BCG strain was inferior to the Danish strain and that Madras Laboratory produced better vaccine than Copenhagen Laboratory. The vaccine produced from Copenhagen strain in Madras Laboratory induced the highest level of allergy. The stability of vaccines produced from Madras strain was found to be unsatisfactory. Results according to vaccination lesion size and their correlation with tuberculin reaction more or less confirmed the above findings. They were however not corroborated in terms of viable counts. Considering that the inferior quality of Madras BCG strain was due to mutation over time, seed lots of suitable BCG strain would ensure uniformly potent vaccine from Madras Laboratory.

KEY WORDS: BCG VACCINE, POTENCY, DANISH STRAIN, MADRAS STRAIN.

131 Baily GVJ, Kul Bhushan, GE Rupert Samuel & BK Keshav Murthy: INTEGRATION OF BCG VACCINATION IN GENERAL HEALTH SERVICES IN RURAL AREAS Indian J TB 1973, 20, 155-60.

BCG vaccination is being conducted as a mass campaign. It is difficult to maintain a high coverage of the population at risk i.e., new borns. This can best be done by integrating the BCG vaccination services with the general health services. The present investigation was planned to study the feasibility of routine BCG vaccination of the new borns by the Primary Health Centre personnel using the normal records maintained by them. In a rural population of 33,128 persons (1971 census), served by PHC Bettahalasur of Bangalore district, BCG vaccination was administered to 0-15 months old children by 2 Block Health Workers (BHWs) and 3 Auxiliary Nurse Midwives (ANMs) after training them for about 3 weeks. They used a compact specially designed BCG kit and employed a conventional intradermal technique for BCG vaccination. Routine work was not to be disturbed in any way. Each worker prepared a list of children eligible for BCG vaccination from the register of unprotected children and updated the list for those not found registered. National Tuberculosis Institute (NTI) field staff registered a sample population, allotted to each worker for estimation of eligibles. Three months later they also examined BCG vaccination lesions in a sample of children. BHWS and ANMS were interviewed by a medical officer from NTI regarding their opinion on integrated work.

The findings showed that the ANMS and BHWS had already registered nearly 50% of the new borns in their records with variation in registration from 21 to 80% by the field workers; ANMS understandably having registered lesser numbers. All of them were, however, able to update the registrations to a level They could pick up the BCG vaccination technique of 82%. easily. Of the total eligibles, ANMS and BHWS could contact 86.4% and vaccinate 77%; remaining 23% either refused or were excluded from vaccination. In the total eligibles registered, however, the vaccination coverage was 66.6%. Of the children reported vaccinated, 96% had evidence of BCG vaccination indicating a high degree of **reliability of reporting**. The opinion of all the 5 field workers on integration was favourable. All the ANMS and BHWS workers, on interview, stated that they had done BCG work without detriment to their other duties and would be easily able to do so in future. The field workers can accumulate the new borns for a year and vaccinate them during a month. This has mainly operational advantages including less vaccine wastage. For urban areas a different operational design with the same principles may become necessary.

KEY WORDS: INTEGRATION, BCG VACCINATION, HEALTH SERVICES, RURAL POPULATION.

132 GD Gothi, SS Nair, Kul Bhushan, GVJ Baily & GE Rupert Samuel: BCG VACCINATION INDURATION SIZE AS AN INDICATOR OF INFECTION WITH MYCOBACTERIUM TUBERCULOSIS Indian J TB 1974, 21, 145-51.

After the introduction of direct BCG vaccination,

assessment of post vaccination allergy and information about prevalence of infection could not be obtained. Few methods were tested i.e., i) retesting of persons with 0-13 mm reaction at site of vaccination on 4th day of vaccination, ii) retesting of all vaccinated persons of age 0-10 years. It is not only necessary to find out the size of BCG lesion that could separate them but also the day after vaccination on which the tuberculin reaction size best correlates with the BCG vaccination size. With this in view, two studies with regard to direct BCG vaccination done in India have been examined further. In Study I, 816 eligible persons were tested with 1 TU RT 23 read on 3rd day and vaccinated with either Indian or Danish vaccine. The vaccination lesions were examined on the 3rd, 6th and 90th day of vaccination. On the 90th day post vaccination tuberculin test was done and read on 3rd day. In **Study II**, a total of 691 who had no previous BCG scar were simultaneously tuberculin tested with 1 TU RT 23 and vaccinated with either Indian or Danish vaccine. The BCG lesions were examined every day and on 39th and 90th day.

The correlation of pre-vaccination tuberculin test and BCG lesion size showed that sixth day in first study and fifth day in second study was the highest. Tuberculin reaction size of 10 mm or more correlated well with 14 mm or more induration size of BCG in classifying the persons as infected and noninfected. Correlation between the size of BCG scar at 3 months and size of pre-vaccination tuberculin reaction was poor. Considering the two studies together vaccination induration of 14 mm or more on 5th or 6th day appears to be the best criterion for demarcating the infected from non-infected. Some other choices are 12 or 14 mm levels on 2nd day, 10 and 12 mm levels on 5th day and 10 mm levels on 8th day seems to be nearly as good and operationally useful.

A BCG Vaccination induration size of 14 mm and above between 5th and 6th day of vaccination, for all practical purposes may be considered satisfactory for **demarcating persons infected with M.tuberculosis from those non-infected**. It can be concluded that **estimation of prevalence of infection**, when BCG vaccination is given to all without prior tuberculin testing, can be made on the basis of BCG vaccination induration size of 14 mm or more.

KEY WORDS: BCG VACCINATION, M.TUBERCULOSIS, INFECTION, TUBERCULIN INDURATION, RURAL POPULATION.

133 Kul Bhushan, GVJ Baily, SS Nair, KT Ganapathy & Vijay Singh: FREEZE DRIED BCG VACCINE SEALED IN PRESENCE OF NITROGEN Indian J Med Res 1975, 63, 1335-43.

The freeze dried BCG vaccine manufactured in India is sealed under vacuum. This though adds to its stability involves expensive production procedures. Sealing in presence of nitrogen is both simpler and economical. Before producing this vaccine for use on a large scale, it was considered necessary, to study the influence of storage at higher temperatures on the allergy inducing capacity on the basis of the size of local lesion and viable counts of freeze dried BCG vaccine sealed either in vacuum or in the presence of nitrogen. For this, half of the ampoules of a batch of vaccine prepared in Madras BCG Vaccine Laboratory were sealed in **vacuum** and the other in presence of **nitrogen**. Randomly selected ampoules of both types of vaccine were exposed to 37° and 44° for 2, 6, and 18 weeks and another set at $4^{\circ}C$ for 18 weeks. Two batches of liquid BCG vaccine were made as controls: 16 types of ampoules thus obtained were randomly repeated 5 times according to Standard Lattice Design. About 3000 school children without BCG scar, aged 5-14 years In Bundi and Kota districts of Rajasthan were vaccinated as per the study design. Post vaccination allergy with 5 TU RT 22 by measuring the size of vaccination lesions was recorded 3 months later. Viable counts on samples of ampoules from freeze dried BCG vaccines exposed differently were done in the production laboratory after 18 weeks of storage.

The vaccine in 16 types of ampoules was significantly different. Liquid BCG vaccine resulted in higher level of allergy and larger vaccination lesions than freeze dried BCG vaccine sealed under either method. The study has shown that freeze dried BCG vaccine sealed under either method vacuum or nitrogen, gave satisfactory level of post vaccination allergy and induration size of vaccination lesions, provided the vaccine was preserved at 4°C. Storage at 37° for more than 2 weeks and even 2 weeks storage at 44°C affected both types of vaccine badly as shown by post vaccination allergy and viable counts. However, decrease in viable count with time and temperature was more pronounced in vaccine sealed in presence of nitrogen. Hence, there is a need to provide cold chain facility for freeze dried vaccine all throughout the period.

KEY WORDS: LIQUID BCG, FREEZE DRIED BCG.

134 Kul Bhushan: NORMAL AND ABNORMAL BCG REACTIONS NTI Newsletter 1978, 15, 65-69.

All artificial immunizations lead to more or less specific reactions. These reactions may occur at the site of administration of immunising agent: regionally in the area around it: at sites far removed, in the viscera specifically concerned with immune response and those to which the dissemination of the immunising agent may occur.

Normal BCG Reaction: In the uninfected individuals the

reaction starts about 2-4 weeks after vaccination and all the stages from erythema, nodule, pustule, ulcer, crust and scar formation are over in 4-6 weeks period in that sequence at the site of BCG vaccination. Regional lymph glands enlargement depends upon the exact location of injection. Entire sequence of occurrences are painless and uneventful. In previously infected persons or repeat BCG vaccination results in exaggerated and accelerated reaction of similar nature as The reaction starts within hours of described above. vaccination and healing of ulcer to scar formation is over within 2 weeks time without any lymph gland involvement. BCG organisms are also absorbed into the blood stream and produce multiple reactions at different sites.

Abnormal Reactions: Reactions other than those described above or those which do not conform to the stated time schedule are recognised as abnormal reactions or complications. The causes of these complications are attributed to the degree of attenuation, dose, concentration of vaccine, subcutaneous or instead of intradermal, infection of muscular ulcer, constitution of the subject and tuberculo hypersensitivity manifestiations anywhere in the body. The complications are of three types. i) local, ii) regional and iii) general. Local Complications: Undulating ulcer, abscess formation due to deep vaccination, Eczematous lesion, lupoid reaction and keloid formation. Regional Complications: enlargement of lymphnode, sinus formation. General Complications: Erythema nodosum, phlyctenular conjunctivitis, BCG Osteoitis, generalised tuberculosis disease among children with compromised or deficient immune system etc. The abnormal reactions are very uncommon and many of them rare.

KEY WORDS: BCG REACTIONS, COMPLICATIONS.

135 Kul Bhushan: PRIMARY COMPLEX AND BCG VACCINATION Souvenir of Shri A.V.Jasani TB Hospital, Kotharia: 1978, 1-7.

The article deals with primary complex and BCG vaccination. Lodgement or implantation of tubercle bacilli, at any site, in the body of an animal or human being is called primary infection. The tissue response by accumulation of polymorphonuclear leucocytes at the site of primary infection is termed as **primary focus.** The tubercle bacilli are transported from the primary focus to the lymph node through lymphatics. The primary focus, the lymphangitis and regional lymphadenitis together constitute primary complex. In 95% of cases it occurs in the lung: the initial polymorphic leucocytic reaction in the primary focus and the lymph nodes are soon augmented by large monocytes then epitheloid cells and the Langhans' giant cells. In about 2-4 weeks the reticuloendothehal system develops cell mediated immunity and tuberculo hypersensitivity. Most of the

primary complexes (lesions) become innocuous after a short time harbouring the tubercle bacilli with arrested activity, but live and potentially virulent. There is always a lurking danger of these bacilli flaring up in the future to progressive tuberculous disease. BCG vaccination is aimed at establishing a controlled primary complex by intradermal injection of attenuated (harmless) live, bovine strain of tubercle bacilli in an attempt to forestall the infection with virulent tubercle bacilli among the uninfected persons. At the site of vaccination, the lower half of the left deltoid region, a primary focus is created from where some bacilli are transported to axillary lymph node through the lymphatics and complete the formation of primary complex. In 2-4 weeks time cell mediated immunity and delayed hypersensitivity are initiated and is completed in about 6-8 weeks time and the vaccinated persons show positive reaction to tuberculin test. The BCG lesion heals in 4-6 weeks time.

The advantages of primary complex established with BCG vaccination prior to a chance of natural infection are: i) primary tuberculosis disease caused by it can be ruled out; ii) there is no chance of spread of disease to adjoining parts i.e., haematogenous dissemination of disease leading to milliary, meningeal, bone tuberculosis etc., is prevented; iii) also the danger of future local flare up and thereby chances of disease after infection are reduced. To obtain maximum advantage from the BCG vaccination, it should be given at the earliest possible time in life of an individual.

KEY WORDS: PRIMARY COMPLEX, BCG VACCINATION.