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Tuberculin (Mantoux) Test Reaction in BCG-vaccinated Children

VA NOTTIDGE*, A AL HIBSHI** AND H AL SWAT**

Summary

Nottidge VA, Hibshi AL A and Swat AL H. Tuberculin (Mantoux) Test Reaction in BCG-vaccinated Children. *Nigerian Journal of Paediatrics* 1994; **21**:12. The present study was undertaken in order to assess the rate of tuberculin conversion in a society where BCG vaccination had been compulsory for 10 years. Out of 148 children who were Mantoux-tested, 59 satisfied the criteria for analysis and of these, 96.6 percent were negative, while 1.7 percent was positive. Since most of the children were younger than five years, this finding suggests that there might have been some faults in the BCG programme. It is therefore, recommended that further sample Mantoux-testing, shortly after BCG vaccination, should be undertaken so as to determine the exact BCG conversion rate. If this rate is confirmed to be equally low, then there would be justification in reviewing the storage and transportation arrangements for the vaccine.

Introduction

IN 1979, Saudi Arabia promulgated the first Royal decree on immunization, making immunization compulsory for BCG, DPT, and oral polio vaccines before a birth certificate could be issued (personal communication from the Director General of Health Centres, Riyadh, Saudi Arabia). In 1982, another royal decree included measles in the immunization programme, while hepatitis B was included in 1988, when the Primary Health Care programme also became the official policy in the country. National cluster sample surveys have shown that by 1989, after 10 years of compulsory BCG vaccination at birth, BCG coverage was 96 percent, while overall vaccine coverage was 84 percent (Dr Yacob Mazrou, Ministry of Health, personal communication).

Successful BCG vaccination at birth in a community, should result in a high percentage of tuberculin conversion, especially in early life. However, contrary to expectation, our preliminary observation in Taif Children's Hospital in 1989, indicated that tuberculin test negativity, even in infants, was almost 100 percent. As we were then midway between Alma-Ata [1] and the year 2000, it seemed relevant to take the opportunity to assess the success of BCG immunization in Taif. The

Children's Hospital, Taif, Saudi Arabia

Department of Paediatrics
* Consultant Paediatrician
** Resident in Paediatrics

Correspondence: VA Nottidge
Department of Paediatrics
University College Hospital
Ibadan, Nigeria.

present study was, therefore, designed to determine the rate of BCG conversion in vaccinated children and examine the policy implications of the results.

Subjects and Methods

The study was conducted in the Children's Hospital, Taif, a city that is located in the western region of Saudi Arabia. The hospital is a second level referral institution. During the two- month period of the study, beginning from February 15, 1990, all children admitted into the hospital who were not disqualified by the exclusion criteria, were included in the study, if they satisfied the following criteria:
(a) informed parental consent, (b) patient was delivered within Saudi Arabia, (c) verifiable age, (d) at least, two months old and at least, two months after BCG vaccination, (e) immunization undertaken within Saudi Arabia and (f) a BCG scar, or an immunization card, to verify BCG vaccination. Exclusion criteria comprised malnutrition and past or current steroid therapy. In the absence of a BCG scar, the test was administered only if the parents promised to bring the immunization card for verification; the result was excluded from analysis, if the card was not presented. Particulars of BCG vaccination and the vaccine used were obtained from the parents and confirmed from the immunization card, where available.

Mantoux test was administered as an injection of 0.1ml (2 tuberculin units - TU) of PPD red label with 0.01 percent Chitosol and 0.005 percent TWEEN 80 as additives, obtained from Statens Serum Institute, Denmark (Batch No RT 23), using a plastic insulin syringe and gauge 26 steel needle. The injection site was the middle third of the anteromedial aspect of the left forearm. A fresh syringe and needle were used for each patient and all tests were read on the third day. Testing was postponed till three to four days after recovery in severely ill children. Some parents of qualified children could not wait for that long before discharge, but such children were included in the study, if they were brought back for testing about one week later. Each parent was requested to bring the child back for reading three days after that. Similarly, all parents of tested children were requested to bring the children back for reading, if the child was discharged earlier than the third day after Mantoux testing.

An induration, measuring between zero and 4mm, was interpreted as a negative, between five and 9mm as an intermediate and 10mm or more as a positive result.[2] Children who had a positive, or intermediate reaction were further studied with chest radiographs as well as gastric washing and tracheal aspirate for TB culture and Z-N staining.

Results

There were 148 children who satisfied the criteria for inclusion into the study; these subjects were therefore, Mantoux-tested, but only 81 were available for the reading of the result. There were 22 of these children whose vaccination status could not be verified because the parents did not produce their immunization cards; these were all Mantoux-negative, but were excluded from the final analysis. Thus, data on 59 children (36 males and 23 females, ratio 1:6:1) were available for analysis. The ages ranged from two months to 11 years, but 40 (67.8 percent) of the children were between two months and two years old. Eight of these subjects were two months to six months old, while 14 were aged between seven and 12 months. Six children were older than five years (Table). Forty-five (76.3 percent) of the 59 children were vaccinated in hospital, while the rest were vaccinated at health centres. Fifty (84.7 percent) of the 59 children were Saudis.

A $4^{1/2}$ -month old Saudi boy with non-tuber-

culous right upper lobe pneumonia, had the only positive response, measuring 12mm. The intermediate response (8mm) was obtained in a one-year old Saudi girl with a diagnosis of non-tuberculous bronchopneumonia. Thus, 57 (96.6 percent) of all the BCG-vaccinated children, had a negative reaction to tuberculin. It is to be noted, in particular, that 51 (96 percent) of the 53 children, aged less than five years and 20 (91 percent) of the 22 infants in the study had a negative reaction.

TABLE

Age Distribution of 59 Mantoux-tested Children

Age Group (months)	*No of Children*	*Percent of Total*
2 - 24	40	67.8
25 - 60	13	22.0
61 - 120	5	8.5
≥120	1	1.7
Total	59	100.0

Nine of the 37 children with respiratory disease had bronchial asthma without atopy, while one had lung abscess and the rest had bronchopneumonia or upper respiratory tract infection. Neurological diseases among the children comprised five cases of febrile seizure and one each, of epilepsy and cerebral palsy, while cardiac diseases included two cases of congenital heart disease and one case of cardiomyopathy. The miscellaneous group comprised gastro-enteritis (three), brucellosis (two) and one each, of orbital cellulitis, chronic renal failure, Henoch-Schonlein purpura, idiopathic thrombocytopenic purpura, shigellosis, sickle-cell anaemia and rickets.

Discussion

A number of studies has been carried out on the epidemiology of tuberculosis, including tuberculin reactivity, in Saudi Arabia.[2] The age selection in these earlier studies excluded children less than five years of age. However, the interpretation of tuberculin-test results in the older children, aged between five and 14 years that were studied, had assumed a successful primary vaccination, namely: vaccination followed by a satisfactory level of allergy on sample testing carried out a few months later. Our present findings in the hospital were at variance with this assumption in children, especially during the first five years of life. The possibility of anergy in some of the children was noted, but they were not excluded because (a) they satisfied the inclusion oriteria, (b) there was no history of atopy, malnutrition or steroid therapy and (c) it has been shown that, even though the presence of chest disease could affect an individual patient's test result, it does not vitiate the overall evaluation of Mantoux reaction significantly, for the whole of a given population.[3,4] In the present series, a (96.6) percent negative test was obtained, while there was only 1.7 percent positive and intermediate result, respectively. Since these two subjects were non-tuberculous, it is reasonable to conclude that the positive reaction was probably due to an atypical mycobacterium,[4,5] while the intermediate reaction may have been due to the BCG vaccination.

The high negative tuberculin-testing in the present study has confirmed our preliminary observation and concern as expressed above. In earlier studies,[2,6] 90 percent and 71 percent negativity were reported among vaccinated older children, aged between five and 14 years in the northern and eastern provinces of Saudi Arabia, respectively; the authors explained this finding on the basis of waning reactivity after five years from vaccination. In another study, however, that compared tuberculin sensitivity two months after vaccination and that at five years, it was shown that the allergic response was unchanged by five years.[7] This allergic response may be boosted minimally, by repeat tuberculin testings.[8] Alarm

has been signalled that 32 percent of the children tested in the northern province of Saudi Arabia, had not received BCG even though BCG vaccination at birth, is mandatory. [2] This may be a common problem in many areas of the country as well as a warning against complacency.

The incidence of positive tuberculin reaction among non-BCG vaccinated children (tuberculosis index: TI) was highest in the western province at nine percent, [9] compared to the northern province at four percent [2] and the eastern province at five percent. [6] This higher prevalence has been attributed to the periodic influx of large numbers of pilgrims from all over the world into the western province for the Hajj pilgrimage. It has therefore, been suggested that these pilgrims might introduce foci of infection into the country and some of them evade regulatory authorities to merge into the local population in violation of their short-tem visas. [9] Even though the country would be classified in the middle prevalence category of two to 14 percent TI, according to the International Union against Tuberculosis, [10] there is cause for concern that 97 percent of vaccinated young children in the present study had negative reactions in this area of relatively higher prevalence. Such children therefore, constitute a window of vulnerability in contact with foci of infection. Since there is no policy requirement for sample-testing after BCG vaccination, to confirm tuberculin conversion, it is suggested that a national policy review may be indicated. This would include such sample-testing, after confirmation of our results by other studies involving large numbers of young children.

It has been shown that tuberculin sensitivity depends on the tuberculin-testing technique, [11] the BCG vaccine and its dose, as well as, on shipment and storage. [7] The technique in our study was careful and precise and besides, the tuberculin used (RT 23 from Statens Serum Institute, Denmark and the dose of 2 TU) has been shown by others [12 13] to be effective. However, we would like to suggest that, if further post-vaccination tuberculin-testing by others in the country does not show a satisfactory level of conversion, the storage and transportation of the BCG vaccine used should be evaluated.

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References

1 WHO Declaration of Alma-Ata. In: From Alma-Ata to the year 2000: reflections at the midpoint. Geneva: WHO (publishers) 1988: 7-10.

2 Al-Kassimi FA, Abdullah A, Al-Orainey I, Al-Hajjaj M, Baghee EAA and Bener AB. Mantoux reaction survey conducted in the northern region of Saudi Arabia. *Ann Saudi Med* 1991; **11** 315-21.

3 Bener A. Prevalence of tuberculosis in Abha and Baha. *Eur J Epidemiol* 1990; **6**: 376-81.

4 Lind A, Larsson LO, Bentzon MW, Magusson M, Olofson J, Sjogren I, Strannegard TI and Skoogh BE. Sensitivity of sensitins and tuberculin in Swedish children. I.A study of school children in an urban area. *Tubercle* 1991; **72**: 29-36.

5 Larsson LO, Skoogh BE, Bentzon MW, Magnusson M, Olofson J, Teranger J and Lind A. Sensitivity to sensitins and tuberculin in Swedish children II. A study of pre-school children. *Tubercle* 1991; **72**: 37-42.

6 Al-Kassimi FA, Abdullah AK, Al-Orainey IO, Lambourne A, Bener AB and Al-Hajjaj MS. Tuberculin survey in the eastern province of Saudi Arabia. *Resp Med* 1991; **85**: 111-6.

7 Horwitz O and Unch-Chistensen K. Correlation between Tuberculin sensitivity after two months and five years among BCG-vaccinated subjects. *Bull Wld Hlth Org* 1972; **47** 49-58.

8 Guld J, Waaler H, Sundaressan Tk, Kaufmann C

and Ten Dam HG. The duration of BCG-induced tuberculin sensitivity in children and its irrelevance for revaccination. *Bull Wld Hlth Org* 1968; **39**: 829-36.

9 Al-Kassime FA, Abdullah AK, Al-Hannah MS and Al-Orainey IO. Tuberculosis epidemiology in the western region of Saudi Arabia. *Thorax* 1989; **44**: 869.

10 Tuberculosis Association of India, eds. Textbook of Tuberculosis. New Delhi: Vikas Publishing House (Publishers) 1981; 63-4.

11 American Thoracic Society, The tuberculin skin test: Official ATS statement. *Am Rev Resp Dis* 1991; **124**: 356-63.

12 Mitinskaia LA and Iavorski K. Disseminated tuberculosis of the lungs in children. *Probl Tuberk* 1991; **4**: 32-4.

13 Toppet M, Malfroot A, Hofman B, Casimir G, Cantraine F and Dab I. Tuberculosis in children: a 13-year follow-up of 1714 patients in a Belgian home-care centre. *Eur J Pediatr* 1991; **150**: 331-5.