

Tuberculin reaction and BCG scar in children vaccinated at birth

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تفاعل التوبركولين وندبة لقاح ب ث ج لدى الأطفال الذين لُقِّحوا وقت ولادتهم
علي صديقي حسن أبادي ونيجين هادي ومهرزاد ياقوت

خلاصة : في هذه الدراسة أجري اختبار التوبركولين لدى 1576 طفلاً أصحاء تقل أعمارهم عن ست سنوات، وكانوا قد لُقِّحوا عند مولدهم بلقاح BCG . وكانت ندبة لقاح BCG لاتزال موجودة لدى حوالي 71.5% من بينهم. وكان متوسط حجم تفاعل التوبركولين في المجموعة التي احتفظت بندبات اللقاح، أكبر منها في الآخرين، وكانت الفروق ذات معنوية إحصائية ($P < 0.05$). أما التواتر النسبي للأطفال الذين كان تفاعلهم سلبياً فقد ارتفع مع زيادة العمر، فعند سن أربع سنوات كان حوالي 68% من الأطفال الملقَّحين سلبيين. وكانت هناك علاقة خطية موجبة بين حجم ندبة لقاح BCG وبين قُطر تفاعل التوبركولين. وهكذا ينبغي الاشتباه في عدوى السل بعد السنة الرابعة من العمر، إذا كان اختبار التوبركولين إيجابياً، وخاصة إذا زاد حجم التفاعل عن عشرة ميليمترات.

ABSTRACT In this study, 1576 healthy children under 6 years who had received BCG at birth were tuberculin tested. About 71.5% had retained their BCG scar. The average size of tuberculin reactivity was larger in the group with BCG scar than without, the difference being statistically significant ($P < 0.05$). The relative frequency of children showing a negative reaction increased with age; at 4 years about 68% of vaccinated children were negative. There was a positive linear relation between the size of BCG scar and diameter of tuberculin reactivity. After 4 years, tuberculosis infection should be suspected with a positive tuberculin test, especially if the reaction size is >10 mm.

La réaction tuberculique et la cicatrice BCG chez les enfants vaccinés à la naissance

RESUME Dans cette étude, on a procédé à un test tuberculique chez 1576 enfants sains âgés de moins de 6 ans qui ont reçu le BCG à la naissance. Environ 71,5% d'entre eux avaient conservé leur cicatrice vaccinale. La taille moyenne de la réaction tuberculique était plus grande dans le groupe des enfants qui avaient une cicatrice que dans le groupe des enfants qui n'en avaient pas, la différence étant statistiquement significative ($P < 0,05$). La fréquence relative des enfants montrant une réaction négative augmentait avec l'âge; à l'âge de 4 ans, environ 68% des enfants vaccinés avaient une réaction négative. Il y avait une relation linéaire positive entre la dimension de la cicatrice et le diamètre de l'induration. Après l'âge de 4 ans, une infection tuberculeuse devrait être suspectée en cas de résultat positif, en particulier si la réaction tuberculique est plus large que 10 mm.

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Introduction

One million new cases of tuberculosis are reported worldwide each year but it is estimated that the true figure is around 8 million with a mortality of about 4 million people; 95% of the cases are among people living in the poorest areas of the world [1]. When we consider the prevalence of infection with the tubercle bacillus to be about 1800 million with 50 million resistant cases, the problem is clearly a major public health concern.

In the Islamic Republic of Iran, it is estimated that the annual risk of tuberculosis infection is about 0.5%, giving an annual incidence of 40 000 with 22 000 sputum positive cases [2]. The easiest and most practical way to conduct an epidemiological investigation for the estimation of tuberculosis risk in the community is to use the pattern of tuberculin reaction in children. On the other hand, one of the preventive measures used in countries such as the Islamic Republic of Iran is to employ bacille Calmette-Guérin (BCG) vaccination at birth and to repeat it at entry to primary school. In view of the many controversies regarding the tuberculin reaction after BCG vaccination [3,4] and because of the differences found in different parts of the world, we decided to study the pattern of the reaction at different time intervals after BCG vaccination. This should provide answers to questions about the kind of reaction that should be considered positive (due to infection) and about the shortcomings of BCG vaccination and purified protein derivative (PPD) testing.

Subjects and methods

The study included 1576 children under 6 years of age (783 boys and 793 girls) who

were brought to nine urban health centres in Shiraz during a 10-month period. The inclusion criteria were as follows:

- under 6 years of age
- BCG vaccination at birth
- healthy at the time of the study.

The information gathered included name, birth date, sex and diameter of BCG scar measured in millimetres. Tuberculin testing was done using 5IU PPD provided by the Pasteur Institute, Teheran. Every child was tested with 0.1 ml of the PPD (1 ml syringe with a 25 or 26 gauge needle), which was injected intradermally on the anterior aspect of the left forearm, midway between the elbow and the wrist. All the injections were done by one expert vaccinator.

The diameter of induration was measured in millimetres 72 hours after PPD injection. The reaction was reported as "positive" if the diameter of induration was ≥ 10 mm, "suspicious" if it was 5–9 mm and "negative" if it was < 5 mm. Those who were not present at the time of reading the test (68 children) were omitted. Thus, we had 1576 cases for scar determination and 1508 for the tuberculin reaction study.

Results

The average PPD reaction size decreased with age in both sexes and the trend of this reduction was statistically significant until the age of 36 months ($P < 0.05$). The trend continued for girls, while the boys showed an increase starting at the age of 4 years (Table 1).

The average reaction size in those with a BCG scar was greater than those without a scar (5.98 mm versus 1.13 mm) in all the children under study and in the different age groups (Table 2); the difference was

Table 1 Average size of tuberculin reaction in vaccinated children by age and sex

Age (months)	Male ^a			Female ^b		
	Number tested	Mean reaction size (mm)	s (mm)	Number tested	Mean reaction size (mm)	s (mm)
<12	32	7.78	4.92	26	7.85	4.62
12-23	278	6.11	5.49	280	6.16	5.67
24-35	170	4.26	4.97	175	3.78	5.11
36-47	135	2.80	4.51	131	3.36	4.90
48-59	122	3.07	4.83	129	3.14	4.96
60-71	15	3.53	5.09	15	2.27	4.38
Total	752	4.62	5.2	756	4.58	5.43

^aF = 13.32, P < 0.05

^bF = 11.88, P < 0.05

s = standard deviation

Table 2 Average size of tuberculin reaction in children with and without BCG scar by age in those vaccinated at birth

Age (months)	With scar ^a			Without scar ^b		
	Number tested	Average reaction size (mm)	s (mm)	Number tested	Average reaction size (mm)	s (mm)
<12	48	9.12	3.86	10	1.50	3.37
12-23	464	6.93	5.50	94	2.10	3.96
24-35	235	5.41	5.24	110	1.10	2.95
36-47	180	4.3	5.12	86	0.55	2.11
48-59	135	5.10	5.40	116	0.78	2.83
60-71	18	3.84	5.57	12	1.42	2.57
Total	1080	5.98	5.44	428	1.13	3.05

^aF = 11.73, P < 0.05

^bF = 2.77, P < 0.05

s = standard deviation

again statistically significant ($P < 0.05$). The majority of the children with negative reaction showed absolutely no reaction (zero), and the majority of children with positive reaction had a reaction size between 10 mm and 14 mm.

In the study, 1127 children (71.5%) had retained their BCG scar and 449 children (28.5%) showed no scar. There was a statistically significant reduction in the average size of BCG scar with age ($P < 0.001$)

Table 3 Distribution of BCG scar size in vaccinated children by age

Age (months)	BCG scar size (mm)								Total	
	0		≤ 2		3-5		≥ 6		No.	%
	No.	%	No.	%	No.	%	No.	%		
< 12	13	19.4	5	7.5	21	31.3	28	41.8	67	100
12-23	93	15.9	114	19.5	178	30.4	200	34.2	585	100
24-35	115	32.3	65	18.2	72	20.2	105	29.4	357	100
36-47	94	33.8	54	19.4	54	19.4	76	27.3	278	100
48-59	121	46.5	33	12.7	35	13.5	71	27.3	260	100
60-71	13	44.8	5	17.2	6	20.7	5	17.2	29	100
Total	449	28.5	276	17.5	366	23.2	485	30.8	1576	100

$P = 0.00001$

Table 4 Average BCG scar size in vaccinated children with scar by age

Age (months)	Number	Average scar size (mm)	s (mm)
<12	54	5.54	2.2
12-23	492	4.74	2.5
24-35	242	4.71	2.6
36-47	184	4.57	2.7
48-59	139	4.80	2.7
60-71	16	4.16	2.6
Total ^a	1127	4.80	2.5

$P = 0.00001$

^a Excluding 449 cases with no scar

(Tables 3 and 4). This relation was found to follow the equation: scar size (mm) = $2.07 - [5.48 \times \text{age (months)}]$. The difference in the size of scar between the two sexes was not significant ($P = 0.06$) (Table 5). The relation between the size of the BCG scar and PPD reaction size was studied and the relation was found to be as follows (Table 6): PPD reaction size (mm) = $1.37 + [2.07 \times \text{scar size (mm)}]$

Discussion and conclusion

In our study, 71.5% of the vaccinated children who had been given the BCG vaccination at birth had retained a scar. This proportion is higher than reported in 1991 in the Islamic Republic of Iran (27.2%) but lower than reports from other countries (91.5%–97.0%) [5–8]. Most of the authorities in this field believe that BCG vaccination should result in a long-standing scar in more than 90% of the cases [9]. The differences could be attributed to the type of vaccine, immune response of the children and the method of vaccination.

Evaluation of the size of reaction in different age groups showed that 27.2% of the children under the age of 12 months were negative, of which 87.5% had absolutely no reaction. This indicates that the conversion rate after BCG vaccination in Iranian children was less than others [10–12]. Positive reactions, even in children under one year, were concentrated between 10 mm and 14 mm; reactions > 15 mm were rarely observed. Thus any reaction > 15 mm should strongly indicate tuberculosis infection and further evaluation should be carried out to see if chemoprophylaxis is needed.

Table 5 Distribution of BCG scar size in vaccinated children by sex

Sex	BCG scar size (mm)								Total No.	Mean	s (mm)	
	0		≤ 2		3-5		≥ 6					
	No.	%	No.	%	No.	%	No.	%				
Male	201	25.7	143	18.3	183	23.4	256	32.7	783	100	1.34	1.05
Female	248	31.3	133	16.8	183	23.1	229	28.9	793	100	1.26	1.07
Total	449	28.6	276	17.5	366	23.2	485	30.8	1576	100	1.30	1.06

P = 0.064

Table 6 Relationship between the size of tuberculin test reaction and the size of BCG scar in children vaccinated at birth^a

Average BCG scar size (mm)	Number	Average reaction size (mm)	s (mm)
0	428	1.13	3.05
≤ 2	260	3.69	1.82
3-5	352	5.99	5.29
≥ 6	459	7.29	5.49

^aExcluding children who were absent at the time of reading the test

According to our observation, the PPD reaction reaches its lowest level around the age of 3½ to 4 years and at this age about

68% of the vaccinated children showed a negative tuberculin test. Therefore, at this age any positive reaction should suggest the possibility of tuberculosis infection.

Finally, in spite of widespread BCG vaccination, the tuberculin skin test can still be used as a useful measure in the epidemiology of tuberculosis.

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References

1. WHO report on the tuberculosis epidemic 1995: stop TB at the source. Geneva, World Health Organization, 1995.
2. Salek S. Tuberculosis in Iran. *World health magazine*, 9th year N(1), 27:1373 (in Farsi).
3. Koch A. BCG mass vaccination in Tanzania: tuberculin allergy conversion and waning rate. *East African medical journal*, 1973, 50(9):537-42.
4. Lifschitz M. The value of the tuberculin skin test as a screening test for tuberculosis among BCG-vaccinated children. *Pediatrics*, 1965, 36(4):624-7.
5. Karalliedde S, Katugahalo LP, Uragodo CG. Tuberculin response of Sri Lankan children after BCG vaccination at birth. *Tubercle*, 1987, 68:33-8.

- 2 months and 5 years among BCG-vaccinated subjects. *Bulletin of the World Health Organization*, 1972, 47:49-58.
7. Sedaghatian MR, Shanda IAK. Evaluation of BCG at birth in the United Arab Emirates. *Tubercle*, 1990, 71:177-80.
 8. Kroger L, Katila ML, Baander E. Rapid decrease in tuberculin skin test reactivity at preschool age after newborn vaccination. *Acta paediatrica*, 1992, 81:678-81.
 9. Grindulis H et al. Tuberculin response 2 years after BCG vaccination at birth. *Archives of disease in childhood*, 1984, 59:614-9.
 10. Ormerod LP, Garnett JM. Tuberculin response after neonatal BCG vaccination. *Archives of disease in childhood*, 1988, 63:1491-2.
 11. Plotkin AS. *Textbook of vaccines*. Philadelphia, WB Saunders Company, 1988:376-85.
 12. Menzies R, Vissandjee B. Effect of BCG vaccination on tuberculin reactivity. *American review of respiratory diseases*, 1992, 145:621-5.

BCG Vaccination

Over 80 per cent of the world's children have been given the BCG vaccination against TB as part of the United Nation's Expanded Programme on Immunization. While the vaccination is relatively effective in preventing serious but noninfectious forms of childhood TB and must be maintained as an element in child health programmes, its value is limited mainly to early childhood.

Source: WHO Report on the Tuberculosis Epidemic, 1995 (WHO/TB/95.183)