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LOCAL COMPLICATIONS OF BCG VACCINATION IN PRE-SCHOOL CHILDREN AND NEW-BORN BABIES

C. T. HSING, M. D.

Chief, Preventive Department,
Taipei Tuberculosis Control Center,
Taipei, Taiwan

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SYNOPSIS

The local complications resulting from BCG vaccination in new-born babies and pre-school children in Taiwan are discussed. The author points out that severe local reactions at the site of vaccination are rare, but that the frequency of regional glandular enlargement and abscess formation is alarmingly high—particularly among new-born babies—and there is a danger of the prestige of BCG vaccination being lowered in consequence.

During the past four years, more than 1,800,000 people, including adults, schoolchildren, pre-school children, and new-born babies, have been vaccinated with BCG in Taiwan. Among the vaccinated school students, aged 6-19 years, only a few cases have developed a comparatively severe reaction at the site of vaccination and in the corresponding lymph-gland. In the 1,160 primary-school children examined 17-18 weeks after vaccination, 0.17% developed local abscesses of 10-14 mm at the site of vaccination and 2.6% developed regional glandular enlargement on the side that the vaccination was done.[1] These glands, after remaining enlarged for a month or so, subsided gradually. The writer has not seen one case of perforated enlarged gland among the vaccinated students of school age during the past four years.

Among the children of pre-school age, especially those under 2 years, and in new-born babies, the picture is entirely different. The glandular abcess produced by BCG vaccination is so alarming that it endangers the prestige of the vaccination. The writer has made a detailed study of this matter and is presenting it here, in order to attract more attention to this particular problem.

Procedure and Technique

The Mantoux technique for tuberculin tests was adopted for this study. The tuberculin used was a purified protein derivative supplied by the

Statens Seruminstitut, Copenhagen. The stock solution, 50,000 tuberculin units (TU) per ml, was diluted locally with buffer solution to a concentration of 50 TU per ml. The diluted solution was kept in a brown glass bottle and stored in a refrigerator. It was used within two weeks after dilution. 5 TU was used as a single screening-dose, 0.1 ml being injected intradermally, as superficially as possible, at the middle third of the dorsal aspect of the left forearm. A definite white wheal of 8-mm diameter was produced at the site of injection. No disinfectant was used on the skin. The needle was sterilized before each injection by passing it through the flame of a spirit-lamp.

The reaction of the tuberculin test was read after 72 hours. The size of the Mantoux induration was measured and recorded in millimetres at the widest transverse diameter. Induration of 5-mm diameter or more was considered positive. Induration less than 5 mm in diameter was considered negative. Only negative reactors to tuberculin tests received BCG vaccination.

0.1 ml of fresh vaccine (1 mg/ml) was injected intradermally, as superficially as possible, at the middle of the left deltoid region, immediately after the reading of the tuberculin test. A definite white wheal of 8-mm diameter was produced at the site of injection. No disinfectant was used on the skin. The needle was sterilized in the same way as before the injection of tuberculin.

New-born babies were not tuberculin-tested before being vaccinated with 0.1 ml in the left deltoid region.

The vaccine, containing 1 mg of BCG per ml, was prepared by Dr. J. S. Sumpaico of the BCG Laboratory, Alabany, Rizal, Philippines, every Friday, and was flown to Taipei in an air-conditioned container on the following Tuesday. It was immediately stored in the refrigerator, and was used within ten days after production.

Analysis of Results

Table I gives the results of post-vaccination tuberculin testing for three age-groups—namely, new-born, 1 month to 2 years, and 3 to 6 years. The percentage of positive reactors after vaccination decreases slightly with age from 96.7% in the new-born to 89.7% in children 3-6 years of age.

Among the 263 vaccinated children aged from 3 to 6 years, 206 were examined 11-24 weeks after vaccination; 7 (3.4%) of these children developed axillary glandular enlargement of the size of a walnut or smaller (see table II). These glands all subsided gradually by themselves. Among the 422 vaccinated children aged from 1 month to 2 years, 355 were examined 11-24 weeks after vaccination; 43 (12.1%) of these children developed glandular enlargement, in 35 cases in the left axillary region, in 2 in the

TABLE I. RESULTS OF TUBERCULIN TESTS 11-24 WEEKS AFTER BCG VACCINATION

Age-group	Number vaccinated	Number tuberculin-tested after vaccination	Number positive	Percentage positive
New-born	482	301	291	96.7
1 month to 2 years .	422	326	302	92.6
3 to 6 years	263	195	175	89.7

right, and in 6 on both sides. Of these 43 cases of glandular enlargements, 8 suppurated and perforated; all the rest subsided gradually. This shows that 2.3% of the children examined under two years of age had a significant local glandular reaction after BCG vaccination.

TABLE II. GLANDULAR ENLARGEMENT 11-24 WEEKS AFTER BCG VACCINATION

Age-group	Number vaccinated	Number examined after vaccination	Number with enlarged glands	Percentage with enlarged glands	Number with perforated glands	Percentage of total number of children examined with perforated glands
New-born	482	344	80	23.3	80	23.3
1 month to 2 years .	422	355	43	12.1	8	2.3
3 to 6 years	263	206	7	3.4	0	0

Of the 482 new-born babies who were vaccinated intradermally with BCG within 3 days after birth, 344 (71.3%) came back for follow-up examination 11-24 weeks afterwards. Among these 344 cases, 80 (23.3%) developed regional glandular enlargements.

A baby sometimes developed one or more enlarged glands either at the same time or in succession. In this series of cases, 27 babies had one enlarged gland, 37 had two, 10 had three, 5 had four, and 1 had five. All the glands suppurated and ruptured during the period of the follow-up examination. Only one case had an adhesion, and no case had secondary pyogenic infection.

The earliest appearance of an enlarged gland was two weeks after vaccination. Usually the enlargement showed up between 4 and 8 weeks

after vaccination, but one case developed as late as 16 weeks afterwards (see table III).

TABLE III. TIME OF APPEARANCE OF GLANDULAR ENLARGEMENT AFTER BCG VACCINATION IN THE 80 NEW-BORN BABIES

Time of appearance of enlarged glands (weeks after vaccination)	?	2	4	6	8	10	12	14	16
Number of cases	29	2	10	11	11	4	7	5	1

As to the location of the glandular enlargement, there were 72 cases in the axillary region, 1 in the cervical region, 6 in both the cervical and the axillary region, and 1 in the left scapular region.

The size of the local reaction at the site of vaccination in new-born babies was also measured in millimetres, and was recorded as discoloration, induration, ulcer, and scar.

Table IV shows the size of the tuberculin reaction and of the local vaccination lesion in babies with and without glandular abscesses. The average diameter of the tuberculin reaction in babies without glandular abscesses was 10.9 mm and in those with glandular abscesses was 13.1 mm. The average diameters of the local vaccination lesion in babies without glandular abscesses and with glandular abscesses were 7.1 mm and 8.1 mm, respectively, for discoloration; 1.4 mm and 1.5 mm, respectively, for induration; 0.5 mm and 0.1 mm, respectively, for ulcer; and 3.1 mm and 3.4 mm, respectively, for scar.

Discussion

When BCG are injected into human beings who have not previously been infected with tubercle bacilli, the bacilli multiply rapidly and develop pathological processes at the site of injection, and then pass rapidly through the lymph-glands. The primary complex—the reaction at the site of vaccination and in the corresponding lymph-gland—produced by BCG has no practical ill-effects unless it becomes too severe and unpleasant. Too frequent occurrences of severe and unpleasant reactions would certainly harm the prestige of BCG vaccination. Reports from different parts of the world show that the frequency of local abscess formation at the site of vaccination is different in different places. Tørnell [4] reported that it varied from 0.5% to 25%. The frequency of occurrence of abscesses after BCG vaccination depends a great deal on the technique of the vaccinator. Too deep injections will produce more abscesses.[2,3] The local abscess formation at the site of vaccination in Taiwan is low. As mentioned earlier, only

TABLE IV. SIZE OF POST-VACCINATION TUBERCULIN REACTIONS AND VACCINATION LESIONS IN NEW-BORN BABIES 11-24 WEEKS AFTER BCG VACCINATION, ACCORDING TO PRESENCE AND ABSENCE OF GLANDULAR ABSCESSES

Diameter of reaction or lesion (mm)	5 TU post-vaccination Mantoux reaction		Vaccination lesion							
			discoloration		induration		ulcer		scar	
	without abscess	with abscess	without abscess	with abscess	without abscess	with abscess	without abscess	with abscess	without abscess	with abscess
0	1				201	64	251	78	111	33
1							1			
2	1							1	5	
3	2		1	1	9				5	4
4	6		14	5	12	1			33	5
5	18	1	46	6	12	4	1		51	10
6	14	2	71	11	11	5			36	13
7	20	4	45	10	5	1			9	10
8	16	5	43	18	5	1		1	9	4
9	10	4	14	4	5	2			3	
10	33	6	14	11	1	1			1	1
11	10	4	5	6	1		11			
12	21	15	4	5						
13	9	4	1	1	1					
14	8	4	4	1	1					
15	17	14	1							
16	3	2								
17	5	4								
18	7	4								
19	5			1		1				
20	9	3								
21		1								
22	3									
23	2									
24		1								
25	1	1								
26		1								
33									1	
34			1							
Total	221	80	264	80	264	80	264	80	264	80
Average diameter	10.9	13.1	7.1	8.1	1.4	1.5	0.5	0.1	3.1	3.4

0.17% of the 1,160 elementary-school children examined 17-18 weeks after vaccination developed local abscesses at the site of vaccination.[1]

In regard to the regional glandular enlargements, Winge [6] found that 9 cases (0.27%) developed glandular abscesses among the 3,369 individuals vaccinated from 1935 to 1942. In the mass BCG-vaccination campaign conducted by the Joint Enterprise in Europe, Ustvedt [5] reported that 0.1%-0.5% of the vaccinated individuals developed glandular abscesses. Among the 1,160 children mentioned above, 30 (2.6%) had enlarged glands on the side that the vaccination was done, and 10 (0.86%) had them on the opposite side. Fortunately, however, these glands subsided gradually after a month or so and caused no trouble. Whether all these glandular enlargements were due to BCG or whether some were due to skin or other infections is difficult to say. Skin infections are very common in Taiwan, especially in the summer, and about 1% of our healthy schoolchildren have been found to have enlarged axillary glands due to these or other infections; in my opinion, enlarged glands due to BCG are nearly always on the side of vaccination.

Among the pre-school children from 3 to 6 years old, some cases developed enlarged glands, but the latter were considered insignificant since they subsided gradually. Glandular enlargement without suppuration is considered " normal " in BCG vaccination. Of the children under 2 years of age, 12.1% developed enlarged glands, but only 18.6% of these glands perforated; all the rest subsided gradually. The rate of significant glandular abscess formation was 2.3%. The follow-up work in this group has not been very complete or satisfactory, but the writer has the impression that the actual percentage of glandular abscesses after BCG vaccination in this group is not likely to be much higher than the figure given here.

On the other hand, the result of BCG vaccination in new-born babies was, as we have seen, alarming, and is a matter causing great concern. In all the 80 cases (23.3%) of glandular enlargement, the glands ruptured, and then took a few months to heal. Sometimes a gland would heal in one month, but would rupture again a few weeks later and discharge from time to time. The babies themselves never complained, but it was extremely difficult to convince the mothers about the harmlessness of BCG vaccination. No matter where the abscess was located, it produced the same anxiety and disturbed all the people concerned.

From table IV it would seem that there is little relation between the presence of glandular abscesses and the severity of vaccination lesions. The local reaction at the site of vaccination depends, at least to some extent, on the technique of vaccination, too deep injection producing more severe local lesions. In this series of cases, the local vaccination lesions at the site of injection are about the same in babies with glandular abscesses as in those without, but the follow-up work for new-born babies was extremely difficult, as it was not easy to arrange for them to come back

in a short period. This follow-up examination took three months, so that the local reaction at the site of vaccination was in different stages of development. The average level of tuberculin allergy produced by BCG was slightly higher in babies with glandular abscesses (13.1 mm) than in those without (10.9 mm).

All the vaccine used was produced by the same laboratory. The average number of viable units per ml was reported to be 3.5 million (Sumpaico, personal communication). What role the dosage of BCG played is difficult to say from this study. Age seemed to be the determining factor—the younger the child, the more frequently glandular abscesses occurred; the exact reason is not clearly known.

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RÉSUMÉ

Au cours des quatre dernières années, plus de 1.800.000 personnes — adultes, écoliers, petits enfants et nouveau-nés — ont été vaccinées au BCG à Taïwan. Les réactions locales et ganglionnaires à la vaccination ont varié suivant l'âge. Dans le groupe d'âge de 6 à 19 ans, ces réactions n'ont été observées que rarement. Entre 3 et 6 ans, 7 sur 206 enfants (3,4%) présentaient, à l'examen postvaccinal, des hypertrophies ganglionnaires qui se résorbèrent par la suite. Chez les enfants d'un mois à deux ans, on observa 43 cas de réactions ganglionnaires parmi 355 enfants examinés (12,1%); huit de ces cas donnèrent des abcès suppurants. C'est dire que 2,3% des enfants de ce groupe d'âge examinés après vaccination, avaient des réactions postvaccinales sérieuses.

Chez les nouveau-nés, vaccinés par voie intradermique 3 jours après la naissance, ces complications ont revêtu un caractère particulièrement grave. A l'examen de contrôle auquel furent soumis 344 enfants, on releva 80 cas d'hypertrophie ganglionnaire. Tous ces cas évoluèrent en donnant des abcès suppurants, dont la guérison fut lente et demanda parfois plusieurs mois. Ces complications ont alarmé la population et jeté un certain discrédit sur la vaccination par le BCG. L'auteur désire attirer l'attention sur ce problème.

Il n'a pas été possible de préciser la cause de cette fréquence excessive de réactions graves chez les nouveau-nés. Il semble que l'âge soit un facteur essentiel puisque les complications ganglionnaires ont été d'autant plus fréquentes et plus graves que les enfants étaient plus jeunes.

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