It is suggested that the excretion of large amounts of dopamine metabolites, homovanillic acid, and 3-methoxytyramine may indicate that the phaeochromocytoma is malignant.

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Conversion After Freeze-dried B.C.G.

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If it can be shown that the appearance of a local reaction at the site of vaccination can be regarded as a criterion of successful B.C.G. vaccination, as is the accepted practice in vaccination against smallpox, the time and money spent on post-vaccination testing and reading would be saved. In an earlier paper (Irvine and Barr, 1960) we showed that 99.6% of 13-year-old schoolchildren who developed a papule at the site of vaccination after intracutaneous Danish fresh (liquid) B.C.G. converted from Heaf-negative to Heaf-positive. From this we concluded: "The presence of any local reaction to intracutaneous vaccination with Danish fresh vaccine may be regarded as an indication of successful vaccination. Only persons with no local reaction to vaccination require a conversion test."

The short life of fresh vaccine and its heat-sensitivity raised transport problems which severely limited its use, especially in the tropics. The introduction of a reliable freeze-dried B.C.G. which is more heat-stable and has a life of 12 months has been a great advance. This is a report of a trial similar to the earlier one with Danish fresh vaccine but using British freeze-dried vaccine.

Material and Method

The analysis is based on 11,199 vaccinations carried out during the school year 1960–1. A Heaf test was given before and after vaccination; the standard Heaf P.P.D. issued by the Ministry of Health was used and the test was normally read at seven days as recommended by the British Tuberculosis Association (1959), though readings up to 10 days were accepted. The apparatus used was East's automatic gun with a de Hamel nose-piece.[1] Induration at the site of four of the six punctures was the minimum criterion of a positive reaction. Negative reactors to the pre-vaccination Heaf test were given 0.1 ml. of reconstituted Glaxo freeze-dried vaccine intracutaneously by some 50 school medical officers. Forty-two batches were used whose viable counts ranged from 4.0×10^6 to 12.8×10^6. The post-vaccination Heaf test was carried out 35 to 63 days after vaccination and was read at 42 to 70 days. In one school 29 children had to be tested at 34 days and read at 41 days; they all proved positive. The local reaction to vaccination was inspected when the post-vaccination Heaf test was read, and the mean width of the indurated papule in millimetres was measured with callipers. None of the children was in contact with known open tuberculosis at the time of vaccination.

The work was carried out by the B.C.G. Control Centre. This was set up in 1958 at the request of the Ministry of Health when Glaxo freeze-dried vaccine was first released for use in this country, so that the laboratory control of each batch could also be checked clinically. The results were collated and analysed by the Regional Records Department of the Oxford Regional Hospital Board. The clinical work of the Control Centre was carried out by the medical officers of health and school medical officers listed below.

Results

Of the 11,199 children vaccinated 10,893 converted, giving a conversion rate of 97.3%. As will be seen from Table I, the differences between the conversion rates recorded at different intervals after vaccination showed no obvious trend —so confirming that this is a satisfactory range of time for post-vaccination testing. However, reports from vaccinators suggested that there was a small proportion of schoolchildren who converted late after dried vaccine. It was therefore decided to retest as many of the 306 non-converters as possible when the next B.C.G. session was carried out at each school.

TABLE I.—*Width of Vaccination Reaction and Conversion Rate Read at Different Intervals after Vaccination*

Days after Vaccination	No. of Vaccinations	Mean Width of Indurated Papule (mm.)	Standard Error of Mean (mm.)	Standard Deviation	Conversion Rates (%)
<43	1,812	9·18	0·07	2·86	95·6
43–	3,331	9·58	0·06	3·56	98·0
50–	2,789	9·11	0·06	3·39	97·6
57–	1,885	8·44	0·08	3·57	96·4
64–70	1,382	9·11	0·09	3·23	98·2
All	11,199	9·15	0·03	3·40	97·3

As was to be expected, some of the 306 non-converters had left school by the next visit; nevertheless the school medical officers succeeded in testing 239 (78.1%). Of these, 183 (76.6%) were found to be positive and 56 negative. These retests were carried out 5 to 17 months after vaccination with

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[1] Made by Messrs. H. G. East and Co. Ltd., 37a Oxford Road, Cowley, Oxford.

the exception of one which was carried out at 16 weeks and proved positive. A further 183 conversions can thus be added to the original 10,893, making a total of 11,076. The corrected conversion rate is therefore 98.9%.

The relation of this corrected conversion rate to the size of the papule at the site of vaccination was then studied. The results, which are given in Table II, show that conversion occurred in all except 0.7% of those with any local reaction, but in only about half of those with no local reaction.

TABLE II.—*Relationship of the Vaccination Reaction to Conversion*

Group	Vaccination Reaction (Width of Indurated Papule in mm.)	No. of Vaccinations	Positive Reactors	
			No.	%
Post-vaccination heaf test	0	95	37	39·0
	1–10	8,640	8,434	76·2
	11–20	2,406	2,364	82·6
	21+	58	58	100
Post-vaccination negative reactors retested later	0	50	17	34·0
	1–10	151	128	84·8
	11–20	38	38	100
Corrected totals after retest	0	95	54	56·8
	1–10	8,640	8,562	99·1
	11–20	2,406	2,402	99·8
	21+	58	58	100
Corrected totals condensed	No reaction (0)	95	54	56·8
	Any reaction (1+)	11,104	11,022	99·3

Discussion

In discussing the validity of the conversion rate of 99.3% for those who showed any reaction to vaccination, it might be questioned whether this applied to as small an induration as 1 mm. A detailed analysis of the vaccination reactions shows that this is justified. Whereas only 54 of the 95 children who showed no vaccination reaction ultimately converted, there were 24 conversions in the 25 children recorded as having vaccination reactions of only 1 mm.

It is also worth noting that the conversion rate increased with the size of the papule, eventually reaching 100% for vaccination reactions of 21 mm. or over.

Between vaccination and retesting 5 to 17 months later some natural conversions may have occurred even in non-contact children. Even a 3% yearly natural conversion rate would only have reduced the total number of B.C.G. conconversions from 11,022 to 11,015. On the other hand, there were 67 negative reactors who escaped retesting; in the absence of evidence to the contrary, these have been left in the negative-reactor group. If in fact 76.6% of these had become positive reactors, the total number of conversions would be increased from 11,022 to 11,075. As the latter would only make an increase of 0.3% in the conversion rate and the former a decrease of 0.06%, these sources of error have little influence on the findings.

The relationship demonstrated between the local reaction to vaccination and the conversion rate is striking; only 0.7% of children with vaccination reactions failed to convert. Provided the Glaxo freeze-dried vaccine maintains these standards, it seems reasonable to suggest that where evidence of successful vaccination is required inspection of the vaccination site 6 to 10 weeks after vaccination could replace conversion testing. A test would then be required only for those vaccinations that have no local reaction.

Summary and Conclusions

In the school year 1960–1 the B.C.G. Control Centre vaccinated 11,199 13-year-old schoolchildren with Glaxo freeze-dried vaccine. A post-vaccination Heaf test 6 to 10 weeks after vaccination gave a conversion rate of 97.3%. Retesting of 239 of the 306 non-converters 5 to 17 months after vaccination added a further 183 late reactors, giving a corrected conversion rate of 98.9%.

Children with no local reaction to vaccination had a conversion rate of 57% : children with a local reaction, however small, had a conversion rate of 99.3%.

The presence of any local reaction to intracutaneous vaccination with Glaxo freeze-dried vaccine may be regarded as an indication of successful vaccination. Only children with no local reaction to vaccination require a conversion test.

The figures for the school year 1960–1 and the subsequent retests are the work of the Medical Officers of Health of the County Boroughs of Oxford and Reading and of the Counties of Berkshire, Gloucestershire, Northamptonshire, Oxfordshire, and Wiltshire, together with their school medical officers. These formed the B.C.G. Control Centre at this period. This paper is the collation of their findings; without their willing co-operation, conscientious work, and careful records these results could not have been obtained. We thank them all sincerely. We also thank the staff of the records and statistics department of the Oxford Regional Hospital Board for their co-operation, and the Ministry of Health, who set up the B.C.G. Control Centre and gave grants to one of us (K. N. I.).

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Medical Memoranda

Herpes Gestationis

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An annotation in the *British Medical Journal* (1963) suggests that the following notes on three recently observed consecutive cases of this rare skin disease of pregnancy may be of general interest.

CASE I

A para-5 aged 42 was admitted to the Rotunda Hospital, Dublin, at 21 weeks' gestation on 12 May 1960. For six weeks she had had an intensely itchy rash with large blisters, mainly on her limbs and lower trunk. Examination revealed a typical polymorph bullous rash of herpes gestationis. A biopsy was reported as showing "subepithelial eosinophil accumulations; epithelium shows intra-epithelial vesicles containing eosinophil leucocytes." Corticosteroids, either triamcinolone 24 mg. daily or prednisolone 20 mg. daily, gave good control of itching and fair control of the rash.

On 22 August, at 35 weeks, she was delivered of a macerated foetus. An exacerbation of the rash followed at once, and was again controlled with triamcinolone. This was gradually withdrawn and finally stopped one month later, by which time the rash had almost cleared. A severe recurrence soon followed and triamcinolone was again resumed with good response.

Six weeks after delivery she was discharged home with no irritation and no active rash but a good deal of residual pigmentation. She