the sigmoidoscopic appearances before treatment. Normal or improved sigmoidoscopic appearances were more frequent in the cortisone group. Similarly, for 51 patients examined by barium enema at the end of treatment, improvement in the radiological appearances was more common in the cortisone-treated patients.

Deaths were less frequent among the cortisone group than among the controls; brief details are given of the fatal cases.

Follow-up information is available for an average period of eighteen months in respect of 205 patients out of the original 210.

Nine months after the trial period patients treated with cortisone in the first attack preserved a clear advantage over the corresponding control group. By contrast, relapse cases treated with cortisone had lost the initial advantage they showed at the end of the trial period.

At the end of the follow-up period, essentially the same pattern existed as at nine months, but with a slight worsening of the general picture.

About one-fifth of the original group had been treated by ileostomy by the end of the study. Of these 44 patients, 14 (31.8%) were dead at the end of the study.

Cortisone is a valuable addition to the medical treatment of ulcerative colitis. We think it likely that better short-term results than we have obtained in the present trial could be achieved by the use of higher doses when necessary. However, its effect is far from permanent, particularly in the established disease, though it is possible that more prolonged treatment than we have so far used will give better long-term results.

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SUPPURATIVE LYMPHADENITIS FOLLOWING INTRADERMAL B.C.G. VACCINATION OF THE NEWBORN

A PRELIMINARY REPORT

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Suppurative lymphadenitis is generally regarded as the most critical local complication of B.C.G. vaccination and has been shown by numerous workers (de Bruijne *et al.*, 1952; Mande and Huët, 1952; Biering-Sørensen, 1953; Gaisford and Griffiths, 1954; W.H.O. Tuberculosis Research Office, 1955) to vary in frequency and severity with the age of the child and the dose of vaccine. In general, the younger the child and the stronger the dose of B.C.G., the higher the frequency of enlarged or perforated glands—and this seems to be true whether vaccination is made by intradermal injection, multiple puncture, or scarification (Mande, 1954). Few studies have, however, been made on the relation between the dose of vaccine and the degree of B.C.G.-induced tuberculin sensitivity in newborn infants.

The present paper is a preliminary report of an investigation being carried out in the newborn. It was designed to study the frequency and severity of glandular involvement (and of the local vaccinal lesion) and the degree of tuberculin sensitivity after intradermal B.C.G. vaccination in relation to the dose of vaccine and the vaccination procedure. For this purpose more than 1,500 newborn babies have been vaccinated with various doses of B.C.G., either by a single injection or by dividing the dose into two, giving 0.1 ml. into each shoulder. The first babies to enter the study were born (and vaccinated) in November, 1953, and each week thereafter for the following 14 months (up to and including January, 1955) newborn babies have been added to the study. A one-year follow-up of all vaccinated babies will be completed in January, 1956.

The study is a joint effort of the Public Health Nurses Agency of Copenhagen (Københavns Sundhedsplejerske Institution), the B.C.G. Department of the State Serum Institute of Denmark (Statens Seruminstitut), and the W.H.O. Tuberculosis Research Office (T.R.O.). The work is being carried out in co-operation with the two municipal maternity hospitals of Copenhagen. A preliminary report of the findings, together with a broad outline of how the work is being done, seemed warranted at the present time because of the immediate practical implications of the results obtained so far.

Material and Methods

Babies born in the two maternity hospitals during the period November, 1953, to January, 1955, inclusive, and for whom permission for B.C.G. vaccination had been

given by both the mother and hospital staff, have been included in the study. Decision regarding the eligibility of each baby rested with the hospital staff, who were responsible for obtaining the mother's permission and for excluding those with medical contraindications such as prematurity, illness, tuberculous milieu, etc. Babies to be included in the study were listed by the hospital staff, and the list was followed by the vaccinating team.

B.C.G. Vaccine

The B.C.G. vaccine used in the study consisted of batches prepared every second week at the State Serum Institute and used five and twelve days after harvest. Seven different dilutions were prepared for the study: 2/1, 1/1, 1/2, 1/4, 1/8, 1/16, and 1/32 of the standard strength vaccine. (The standard strength contains 0.75 mg. per ml.) To ensure as uniform a vaccine product as possible for the 31 batches used throughout the vaccination period of 15 months, all of the batches were prepared by the same person according to the standard technique used in the Institute since January, 1952, and the diluting procedure was the same for all batches.

All vaccines used in the study were subjected to the same control measures applied by the Institute for all current batches. Among these measures was the determination of the content of viable bacillary units based on colony counts after inoculation into Löwenstein-Jensen medium. The counts have not revealed any notable variation from batch to batch in the number of viable organisms.

Vaccination Procedures

The vaccination was carried out without a previous tuberculin test. Six different doses of vaccine were given: 0.15 mg. of B.C.G., which when divided in two injections has been recommended for the vaccination of newborn infants in Denmark until now; 0.075 mg., the Danish "standard" dose for schoolchildren and adults; and 1/2, 1/4, 1/8, and 1/16 of this standard dose. Each of the six doses was given as a single injection of 0.1 ml. or as two injections of 0.1 ml. each with vaccine half as strong, thus making a total of twelve different groups vaccinated intradermally (as listed in Table I). All vaccinations were given in the most superficial layer of the skin overlying the lower insertion of the deltoid muscle of one or both shoulders.

The twelve different combinations of vaccine strength and vaccination procedure were allocated to the babies according to a strict randomization scheme, each combination being given to about the same number of children.

All vaccinations were given by one experienced nurse from the T.R.O. All vaccine ampoules were labelled in code, the significance of which was unknown to the vaccinator. The vaccinator was accompanied by a statistical clerk, who verified that the vaccinator gave the vaccination as specified in accordance with the randomization scheme.

Follow-up Procedures

The follow-up was carefully planned and organized in advance to assure that a sufficiently high proportion of the babies could be followed and the demands for objectivity in making observations could be met. The follow-up includes periodic examination of regional lymph nodes, quantitative measurement of B.C.G.-induced tuberculin sensitivity, and examination of the local vaccinal lesion.

Examination of axillary and cervical lymph nodes is being made by the 65 nurses of the Public Health Nurses Agency of Copenhagen. The nurses visit all babies born in Copenhagen at regular intervals during the first year after birth. At seven of the visits—those made at one, two, three, four, six, nine, and twelve months—a special examination has been included for babies in the study: both right and left axillae and right and left cervical regions are carefully palpated, and enlarged nodes are graded, by size, by reference to a set of three wooden balls carried by each nurse. The balls are 9 mm., 16 mm., and 25 mm. in diameter, and palpable lymph nodes are classified as smaller than ball number 1, between balls 1 and 2 in size, between balls 2 and 3, or larger than ball 3. Skin changes overlying enlarged nodes (infiltration of the skin, etc.) are also described, and the presence of perforation or scar after perforation or incision of glandular abscesses is noted on the record cards.

While the health nurses would in most cases be able to see whether a baby had been vaccinated in one or both shoulders, they have no way of knowing what strength of vaccine was used. Nor do they retain a record of their findings from one examination period to the next: immediately after each examination the results are sent by mail to the T.R.O.

Tuberculin-testing and examination of the local vaccinal lesion is being done by a T.R.O. team, arrangements for the team's home visit being made in advance by the public health nurses. Each baby is scheduled to have a tuberculin test once during the follow-up period. In order to study the development of post-vaccination allergy, the time interval

TABLE I.—Number in Each of the 12 Vaccination Groups and Extent of Follow-up Examinations by February 1, 1955, for 1,513 Newborn Babies Vaccinated during the Period November, 1953, to January, 1955

Vaccination Group			No. Vaccinated	Examination of Post-vaccination Allergy and Vaccinal Lesions				Examination of Glands							
Strength of Vaccine in Fractions of Standard (0.75 mg./ml.)	No. of Injections	Total Dose of B.C.G. (mg.)		Examination Scheduled				No. of Infants Examined at (Months)							
				Dec. 15, 1953–Feb. 1, 1955			Feb. 1, 1955–Feb. 1, 1956 No.	1	2	3	4	6	9	12	
				No. Visited*		No. Not Visited									
				Tuberculin-tested	Not Tuberculin-tested										
2	1	0.15	124	59	13	14	38	106	98	88	77	64	42	13	
1	2	0.15	129	63	5	28	33	113	96	89	77	65	41	13	
1	1	0.075	126	71	5	23	27	107	102	85	82	72	47	14	
1/2	2	0.075	127	70	5	17	35	116	102	89	78	69	44	15	
1/2	1	0.0375	130	65	13	18	34	121	110	99	85	76	49	8	
1/4	2	0.0375	133	80	6	19	28	124	112	100	88	77	44	14	
1/4	1	0.0188	122	45	8	20	49	103	93	82	69	57	34	7	
1/8	2	0.0188	122	71	7	21	23	105	96	87	84	65	44	11	
1/8	1	0.0094	132	67	7	28	30	109	104	98	89	74	46	16	
1/16	2	0.0094	128	65	9	22	32	115	102	95	79	64	33	11	
1/16	1	0.0047	119	63	10	14	32	109	96	87	79	69	39	18	
1/32	2	0.0047	121	73	7	7	34	114	107	96	86	66	43	16	
Total			1,513	792	95	231	395	1,342	1,218	1,095	973	818	506	156	

* All infants visited, except two, were examined for vaccinal lesions.

between vaccination and the tuberculin test is varied: about half of the total group are tested between one and four months after vaccination, the remaining half between four and twelve months; and, within these two broad intervals, about an equal number are tested during each three-weeks period. The time set for each baby was picked at random so there would be no systematic relation between a particular vaccination procedure and the interval between vaccination and testing.

The tuberculin test is made by intradermal injection of 0.1 ml. of a 5 T.U. (0.0001 mg.) dilution of P.P.D., RT XIX-XX-XXI, from the State Serum Institute. The nurse who gives the tests also examines the vaccinal lesion by measuring and recording the widest transverse diameter of induration and of an ulcer, scab, scar, or any other finding. Four days later another nurse reads the tuberculin reactions by palpating and measuring the transverse diameter of induration without knowing the strength of vaccine used.

Study Population

A total of 1,513 babies have been vaccinated from 1 to 11 days after birth during the period November, 1953, to January, 1955, and, as shown in Table I, they are rather evenly distributed throughout the 12 vaccination groups. The home visits scheduled for 1,118 babies during the first half (December 15, 1953, to February 1, 1955) of the follow-up period were carried out in 887. The 95 who were not tuberculin-tested either had recently been tested elsewhere or had some intercurrent disease at the time scheduled for examination; and most of the 231 not visited were no longer accessible for follow-up. As few refused the follow-up examination there is no reason to believe that the losses can prejudice the results of the study.

Results

Regional Lymph Nodes

Both left and right axillary and cervical regions are examined for enlarged or perforated lymph nodes or skin changes overlying the nodes at seven intervals during the follow-up period: at one, two, three, four, six, nine, and twelve months after vaccination. The results are shown in Fig. 1 for the three strongest doses at all except the twelve-months examination period—the number examined at twelve months is still small. Some enlarged lymph nodes* have been noted within the first few months after vaccination, but the frequency increases sharply up to the ninth month. Extrapolation of the trend makes it probable that some glandular abscesses will perforate as late as one year after vaccination.

The frequency of enlarged and perforated glands shows a pronounced dependence on the dose of vaccine. Among all the babies given one of the three weakest doses (not shown in the figure) only one had a perforated gland, three had skin changes overlying glands, and two had enlarged glands.

For a better estimate of the relation between the dose of vaccine and the frequency of glandular complications a preliminary analysis has been made of the findings in the current total of 834 babies examined at one or more of the six-, nine-, and twelve-months periods. The results are shown in Table II. The infants have been grouped according to the total dose of B.C.G. injected and, for each dose, whether it was given in one or two injections. The frequency of glandular complications cannot be shown to differ statistically whether the total dose of B.C.G. was given in one or two injections.

The relation between total dose of B.C.G. and the frequency of complications is clear from Fig. 2: the 0.15-mg. dose has given rise to complications in 25% of the babies examined, the 0.075-mg. dose in 10%, and the 0.0375-mg. dose in less than 5%; the weaker doses have caused only an occasional enlargement or perforation. If attention

is directed only to perforated glands and to skin changes (which in practically every case have signalled impending perforation) the frequencies are about 20%, 6%, and 2% for the three strongest doses of B.C.G. used in the study.

Almost all of the perforated glands have been found in the axillary region; only 2 out of a total of 37 perforations observed after six months have occurred in cervical regions.

The frequency of glandular complications is higher for five-day-old vaccine than for 12-day-old vaccine, as shown in Table III, giving the frequency of complications for the three strongest doses of B.C.G. for the two different intervals between harvest of the organisms and use of the vaccine.

Tuberculin Sensitivity

The tuberculin sensitivity produced by the various vaccine doses and procedures is shown in Fig. 3, where the horizontal scale gives the time in weeks after vaccination (birth),

FIG. 1.—Frequency of enlarged and perforated glands among infants at different times after B.C.G. vaccination. The number above each block indicates the number examined.

FIG. 2.—Frequency of enlarged and perforated glands among infants examined six months or later after vaccination, according to total dose of B.C.G. vaccine. The number above each block indicates the number examined.

*Only glands classified as larger than ball number 2 (16 mm. in diameter) are regarded as enlarged in this connexion.

TABLE II.—*Most Severe Finding among Infants Examined at Least Once, Six Months or Later after Vaccination**

Most Severe Finding	Total Dose and No. of Injections																	
	0.15 mg.			0.075 mg.			0.0375 mg.			0.0188 mg.			0.0094 mg.			0.0047 mg.		
	1	2	Total	1	2	Total	1	2	Total	1	2	Total	1	2	Total	1	2	Total
Size of gland:																		
0	41	12	53	53	53	106	70	51	121	52	65	117	72	56	128	69	66	135
<1 or 1-2	8	38	46	12	10	22	7	21	28	6	2	8	2	7	9	—	3	3
2-3 or >3	4	4†	8†	1	3	4	—	1	1	—	—	—	—	1	1	—	—	—
Skin change	2	2	4	1	1	2	—	1†	1†	—	—	—	—	—	—	—	—	—
Perforation or scar after perforation	11	11	22	6†	3	9†	—	5	5	—	—	—	—	1†	1†	—	—	—
Total	66	67	133	73	70	143	77	79	156	58	67	125	74	65	139	69	69	138

* For infants given two injections, observations on both sides are included. The 20 perforations after vaccination with two injections occurred in 14 children. Only the most severe observation is included for each side.

† Including one observation in the cervical region.

TABLE III.—*Most Severe Finding among Infants Vaccinated with the Three Strongest Doses According to Storage Period* of the Vaccine*

Most Severe Finding	Total Dose: 0.15 mg.			Total Dose: 0.075 mg.			Total Dose: 0.0375 mg.		
	Vaccine Stored for 5 Days	Vaccine Stored for 12 Days	Total	Vaccine Stored for 5 Days	Vaccine Stored for 12 Days	Total	Vaccine Stored for 5 Days	Vaccine Stored for 12 Days	Total
Size of gland:									
0	19	34	53	53	53	106	57	64	121
<1 or 1-2	29	17	46	14	8	22	16	12	28
2-3 or >3	7†	1	8†	2	2	4	1	—	1
Skin change	4	—	4	1	1	2	1†	—	1†
Perforation or scar after perforation	16	6	22	7	2†	9†	1	4	5
Total	75	58	133	77	66	143	76	80	156

* The storage period is defined as the period between harvest and use.

† Including one observation in the cervical region.

FIG. 3.—Mean size of induration of reactions to 5 T.U. among infants according to time after B.C.G. vaccination.

FIG. 4.—Mean size of induration of reactions to 5 T.U. among infants, 18-50 weeks after vaccination, according to total dose of B.C.G. vaccine.

and the vertical scale the mean size of induration of reactions to the intradermal 5 T.U. test. The three curves give the results grouped according to total dose of vaccine, regardless of whether that dose was given in one or two injections. Each point† on a curve represents the mean response of a different group of babies, as each baby in the study was tested only once during the follow-up period.

The mean size of the tuberculin reactions increases during the first four months—more sharply with the stronger than with the weaker doses—and then remains unchanged up to the end of the year. Comparisons of the degree of allergy produced by the different vaccine doses and procedures are therefore based on observations made between the 18th and the 50th week after vaccination; and such comparisons are made in Fig. 4 according to the total dose of B.C.G. injected. Frequency distributions by size of induration for the 12 groups are given in Table IV.

The level of allergy produced by intradermal vaccination is clearly related to the dose of vaccine injected. Halving the dose results in a reduction of about 1 mm. in the mean tuberculin reaction size; and this seems to be true whether vaccination is made with one or two injections. It would also appear that the degree of post-vaccination allergy is slightly higher when a prescribed total dose of vaccine is given in two 0.1-ml. injections rather than in a single 0.1-ml. injection.

In contrast with the frequency of glandular complications, the degree of allergy does not appear to be affected by whether the vaccine was stored for five or twelve days before use (Table V).

Vaccinal Lesions

The character of the vaccinal lesion changes considerably with time: an infiltrated area soon appears at the vaccination site, and develops in its centre a superficial ulceration which may be open and moist but more often is covered with a crust beneath which the ulcer persists for some time. The lesion finally heals, leaving a permanent scar. For

† Each point (except the last) is based on 24 to 63 observations; the last point on each curve is based on 10 to 18 observations.

TABLE IV.—Distribution by Size of Reaction to the 5 T.U. Test, 18–50 Weeks after Vaccination, for the 12 Vaccination Groups

Size of Induration (mm.)	Total Dose of B.C.G. Injected (mg.) and No. of Injections											
	0.15		0.075		0.0375		0.0188		0.0094		0.0047	
	1	2	1	2	1	2	1	2	1	2	1	2
0	—	—	—	—	—	—	—	—	—	—	—	—
1	—	—	—	—	—	—	—	—	—	—	—	—
2	—	—	—	—	—	—	—	—	—	—	—	—
3	—	—	—	—	—	—	1	1	—	—	—	—
4	—	—	—	—	—	—	—	—	—	—	2	—
5	—	—	—	—	—	—	1	—	—	1	—	1
6	—	—	—	1	—	—	1	2	—	2	3	1
7	1	—	1	—	—	—	—	—	2	2	—	1
8	—	—	—	—	—	1	—	2	—	1	2	1
9	1	—	1	—	4	3	—	—	1	2	2	3
10	1	—	—	1	3	1	—	1	3	1	2	1
11	1	3	4	5	1	—	1	1	—	—	2	2
12	2	—	4	3	2	2	2	4	2	3	1	1
13	1	—	7	1	1	1	1	3	1	3	—	1
14	—	1	1	1	1	1	1	4	3	1	2	—
15	1	—	1	1	1	1	1	1	1	—	—	—
16	—	1	2	2	2	2	1	1	2	1	—	—
17	2	3	3	2	1	1	2	—	—	—	—	—
18	—	—	—	—	—	—	—	—	—	—	—	—
19	2	—	—	1	2	1	—	—	—	1	—	—
20	—	—	—	—	—	1	—	1	—	—	—	—
21	—	1	1	2	—	—	—	1	—	—	—	—
22	—	—	—	—	—	—	—	—	1	—	—	—
23	1	—	—	—	—	—	—	—	—	—	—	—
24	—	1	—	—	—	1	—	—	—	—	—	—
25	—	1	—	—	—	—	—	—	—	—	—	—
26	—	—	—	—	—	—	—	—	—	—	—	—
27	1	—	—	—	—	—	—	1	—	—	—	—
>27	—	—	—	—	—	—	—	—	—	—	—	—
Total	14	17	24	22	19	19	12	24	18	16	18	17
Mean (mm.)	15.1	17.0	14.1	14.5	13.1	13.9	12.0	13.0	13.4	11.3	9.9	11.3
Standard deviation (mm.)	5.6	4.4	3.1	4.3	3.6	4.2	5.0	5.2	3.5	3.7	4.1	4.0

TABLE V.—Mean Size of Induration of Reactions to 5 T.U. 18–50 Weeks after Vaccination According to Storage Period of Vaccine*

Vaccine Stored or (Days)	Reactions to 5 T.U.	Dose of B.C.G. Injected (mg.)					
		0.15	0.075	0.0375	0.0188	0.0094	0.0047
5	No.	17	25	20	17	19	22
	Mean (mm.)	16.2	14.2	13.4	12.6	12.1	12.2
12	No.	14	21	18	19	15	13
	Mean (mm.)	16.1	14.3	13.6	12.7	12.9	7.8

* The storage period is defined as the period between harvest and use.

present purposes the extent of the ulceration has been taken as a quantitative measure of the vaccinal lesion: the diameter in millimetres of the ulcer or crust or scar.

Results are presented according to strength (rather than total dose) of vaccine, as babies who were given two injections have two lesions, and each lesion is taken as a separate finding. As shown in Fig. 5, the size of the lesion increases rapidly during the first six weeks after vaccination and then tends to remain relatively stable.

Fig. 6 compares the mean size of the vaccinal lesion during the period 6–50 weeks after intradermal vaccination for the different strengths of vaccine used in the study. As the lesions in babies given two injections did not differ in size from the lesions in babies given only one injection with the same strength of vaccine (as shown in Table VI), a single curve can be shown to describe the findings. The lesion size is clearly related to the strength of the vaccine: the strongest vaccine (2/1 standard) gives lesions averaging 6.5 mm. in diameter, the weakest (1/32 standard) averaging 3 mm. smaller.

Discussion

Although the follow-up of the study had not been completed when this report was written, the findings so far available bring out a number of critical points relating to intradermal vaccination of newborns.

The present study was designed to permit careful examination of the development of allergy and glandular complications during the first year after vaccination. The

Fig. 5.—Mean size of vaccinal lesions among infants according to time after B.C.G. vaccination.

Fig. 6.—Mean size of vaccinal lesions among infants, 6–50 weeks after vaccination, according to strength of B.C.G. vaccine.

maximum size of the tuberculin reactions was observed at about four months after vaccination; hence, assessment of post-vaccination allergy in infants should probably be delayed until at least four months after vaccination if a quantitative measure is desired. The findings differ from those in schoolchildren, in whom the tuberculin reactions reach a maximum size at two months or even earlier (Edwards *et al.*, 1953). Whether the delay in infants is due

to a prolonged period of allergy production or simply that the reactions increase in size as the infants grow older, it is not possible to determine from this material; but there is no doubt that infants can respond to B.C.G. vaccination with the development of a strong degree of tuberculin sensitivity. With the product and procedures used in the present study, we have not met with the difficulties described by Jensen (1942) in making infants tuberculin-positive through B.C.G. vaccination.

The glandular complications also develop many months after vaccination, a large proportion at six months or later and very few before three months. In an earlier study of pre-schoolchildren (W.H.O. Tuberculosis Research Office, 1955) it was found that some glands perforated as early as 10 weeks after vaccination and that all glands that perforated at a later period had been enlarged at 10 weeks. This may mean that glandular complications, like tuberculin sensitivity, develop later in infants than in older children.

Vaccinating the infants by dividing the total dose into two injections, a procedure recommended by some workers, does not seem advantageous. The frequency of glandular complications is at least as high, and the allergy is only slightly stronger.

Results of the present study suggest that a glandular complication may not be a strictly local phenomenon. If it were, one would expect twice as many enlarged glands in babies given two injections as in those given only one injection of the same strength vaccine, but the babies given two injections had *more* than twice as many complications as the others. Whether or not this finding proves significant must await completion of the follow-up for the entire study group.

The period of time that the vaccine was stored before it was used affected the frequency of glandular complications but not the post-vaccination allergy: 5-day-old vaccine gave a significantly higher frequency of perforated and enlarged glands than 12-day-old vaccine, yet no difference could be demonstrated in the degree of allergy produced by the two. A similar trend has also been found by further analysis of material previously published on B.C.G. vaccination in schoolchildren (Edwards and Gelting, 1950). This seems to indicate that the factors responsible for glandular involvement are not entirely the same as those responsible for the production of tuberculin sensitivity.

The total intradermal dose of B.C.G. vaccine affects the frequency of lymph-node complications as well as the degree of tuberculin sensitivity: both increase with an increase in the dose. But the *relative* increase in frequency and severity of lymphadenitis is much greater than the *relative* increase

in degree of sensitivity. Within the range of doses from 0.0375 to 0.15 mg., the frequency of lymph-node complications increases from less than 5% to around 25%, while the average size of tuberculin reactions increases by about 2-3 mm. The size of the vaccinal lesion also shows a relatively slight increase with increasing dose of vaccine.

Similar results have been reported by Gaisford and Griffiths (1954), who also used Danish vaccine but varied the total dose from 0.15 mg. to 0.0375 mg. by varying the amount of standard strength vaccine (0.075 mg. per 0.1 ml.) injected. They report a reduction in glandular abscesses from about 12% to less than 1% by reducing the amount injected (as a single dose) from 0.2 ml. to 0.05 ml., and the tuberculin sensitivity, as judged by the Mantoux 100 T.U. test, was "perfectly satisfactory" from ten weeks onwards: all of the babies reacted with at least 5 mm. of induration, about half of them with 15 mm. or more.

The preliminary results reported here would leave little doubt that the total dose of B.C.G. injected is of paramount importance in affecting the frequency of suppurative lymphadenitis in the newborn. Moreover, the frequency can be dramatically reduced with relatively little effect on the degree of post-vaccination tuberculin sensitivity by judicious adjustment of vaccine dosage.

Summary

A preliminary report is given of a study of B.C.G. vaccination in newborn infants. The study was designed to investigate the frequency and severity of lymph-node involvement and the degree of post-vaccination tuberculin sensitivity in relation to the dose of B.C.G. given by intradermal vaccination. A total of 1,513 newborn babies have been vaccinated within 11 days of birth by one of twelve procedures: injection in one or both deltoid regions with six different total doses of B.C.G. vaccine ranging from 0.15 to 0.0047 mg. The one-year follow-up, which includes periodic examination of regional lymph nodes, quantitative measurement of tuberculin sensitivity, and examination of the local vaccinal lesions, will not be completed for all babies until January, 1956. A report of the results obtained so far seemed warranted because of their immediate practical implications for vaccination of the newborn.

The relation between total dose of B.C.G. and the frequency of lymph-node involvement is clear: the strongest dose (0.15 mg.) has given rise to enlarged or

TABLE VI.—Distribution by Size of Vaccinal Lesion 6-50 Weeks after Vaccination According to Strength of Vaccine

Size of Vaccinal Lesion (mm.)	Strength of Vaccine in Fractions of Standard (0.75 mg./ml.) and No. of Injections											
	2/1	1/1		1/2		1/4		1/8		1/16		1/32
	1	1	2	1	2	1	2	1	2	1	2	1
0	—	—	—	2	2	1	7	3	7	10	17	19
1	—	—	—	—	—	—	—	—	1	—	—	7
2	—	2	1	3	4	—	5	2	7	5	11	10
3	2	2	10	4	5	1	14	8	18	11	20	24
4	4	6	16	12	23	10	27	14	33	10	31	31
5	8	17	22	13	26	11	35	14	30	6	22	15
6	8	22	17	14	26	12	23	8	23	3	11	6
7	18	8	24	12	8	5	12	7	8	8	3	—
8	8	4	13	3	7	1	3	—	6	3	2	—
9	2	2	1	2	1	—	2	2	1	—	—	—
10	4	1	2	—	2	—	—	—	—	—	—	—
11	—	—	3	—	—	—	—	—	—	—	—	—
12	1	—	1	—	—	—	—	—	—	—	1	—
13	—	—	—	—	—	—	—	—	—	—	—	—
14	—	1	—	—	—	—	—	—	—	—	—	—
15	—	—	—	—	—	—	—	—	—	—	—	—
16	—	—	—	—	—	—	—	—	—	—	—	—
17	—	1	—	—	—	—	—	—	—	—	—	—
>17	—	—	—	—	—	—	—	—	—	—	—	—
Total ..	55	66	110	65	104	41	128	58	134	56	118	112
Mean (mm.) ..	6.7	6.0	5.9	5.2	5.2	5.2	4.7	4.6	4.5	3.8	3.7	3.0
Standard deviation (mm.)	1.8	2.3	2.0	1.9	1.7	1.4	1.8	1.9	1.8	2.4	2.0	1.8

perforated nodes in 25% of the babies examined at six months or later after vaccination, the 0.075-mg. dose in 10%, and the 0.0375-mg. dose in less than 5%; the weaker doses have caused only an occasional enlargement or perforation. For perforated nodes and overlying skin changes only, the frequencies are 20%, 6%, and 2% for the three strongest doses.

The degree of tuberculin sensitivity is also directly related to the dose of vaccine, although halving the total dose results in a reduction of only about 1 mm. in the average size of the reaction to the 5 T.U. intradermal test. The reactions increased in size up to about four months after vaccination, then remained stable throughout the remainder of the year.

Vaccinal lesions were largest, averaging 6.5 mm. in diameter, with the 0.15-mg. intradermal dose and about 3 mm. smaller with the weakest dose.

Little advantage was found in giving the total dose of B.C.G. in two injections, one in each shoulder, rather than in a single injection.

An indication was also found that the B.C.G. vaccine used five days after harvest produced a slightly higher frequency of glandular complications than vaccine used twelve days after harvest, while the degree of allergy was apparently no different.

The present results confirm reports of other workers that the frequency of glandular complications is markedly reduced by reducing the dose of B.C.G. by one-half or one-quarter. Moreover, the present study has shown that such a reduction has only a slight effect on the degree of post-vaccination tuberculin sensitivity.

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A total of 1,972 beds with an additional 170 beds in mental hospitals were set aside for tuberculosis patients in 1954, records the annual report of Liverpool Regional Hospital Board Regional Tuberculosis Service. The number of deaths from respiratory tuberculosis has dropped from 1,286 in 1948 to 465 in 1954. Admissions totalled 3,192 for respiratory tuberculosis, a substantial decrease over the previous year, and 214 for non-respiratory. The waiting-list for admission to regional hospitals was down to 109 patients; it was 453 in 1949. Total attendances at chest clinics and hospitals where tuberculosis cases are seen for examination, follow-up, and treatment numbered 189,299. There were 19,899 registered patients on December 31, 1954. New cases diagnosed during the year were 2,389 respiratory and 245 non-respiratory. 879 major surgical operations for tuberculosis were performed. The work of the four mass radiography units has proceeded on similar lines to previous years.

A PLEA FOR SIMPLICITY*

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I believe that in many circumstances anaesthetic apparatus is unnecessarily bulky and complex, and I think that a plea for simplicity is likely to commend itself.

I have introduced the phrase "in many circumstances" to placate those of you who do not believe there is virtue in simplicity for its own sake. As a Dutch colleague remarked to me, "Why make it simple when you can keep it complicated?" And to these I would make it clear that I am not concerned here with what anaesthetists do in London, New York, or Toronto. I am prepared to concede that in favoured centres, where maintenance technicians are always to hand and supplies present no problem, elaborate apparatus, on occasions, gives some modest benefit to the patient; but I do hold the view that in more backward communities substantially comparable results can be obtained with something much more simple.

Basic Equipment

I freely admit that a few items of equipment are highly desirable. I was invited to Spain in 1937, during their Civil War, and it soon became evident that certain surgical procedures—I have in mind, for example, repair of wounds of the head and neck—had to be carried out at considerable disadvantage to patient, surgeon, and anaesthetist because of lack of apparatus. During the six weeks I was there I did not see a cylinder of oxygen or of any other gas, and literally no other apparatus but an Ombrédanne, which is nothing more nor less than an outrageous French copy of the inhaler which Clover (1877) described 31 years before Ombrédanne (1908). Luckily I had brought with me a laryngoscope and endotracheal tubes—for these, too, were locally unavailable; and I don't suppose anyone will dispute the statement that endotracheal intubation is practically essential for safe and tranquil anaesthesia for a large number of operations above the level of the clavicle.

For operations on the head and neck any anaesthetic apparatus must be set at a slight distance from the patient so as to allow the surgeon reasonable access to the field of operation. I improvised a vaporizer from a tin can (a tip I learned from Flagg) and connected it by tubing to the proximal end of the endotracheal mount (Macintosh and Pratt, 1939). The only means by which the vapour in the primitive inhaler can be conveyed to the lungs is the inspiratory effort of the patient. A good deal of rebreathing is inevitable, and this is necessarily accompanied by accumulation of carbon dioxide and a decrease of oxygen in the inspired mixture. One sensed at once the great handicap of not having some *vis a tergo* in the form of a flow of gases to carry the vapour to the patient, and to clear the breathing-tube of carbon dioxide.

Disadvantages of Elaborate Apparatus

That is one side of the apparatus question. The range of surgical activity can be restricted, and indeed the safety of the patient may be jeopardized because of the absence of a few small and inexpensive pieces of anaesthetic equipment; but, on the other hand, I deplore the development of apparatus along what I call battleship lines. During the war I was responsible for advising the D.G.M.S. of the

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