BCG vaccination by bifurcated needle in a pilot vaccination programme*

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The bifurcated needle technique for BCG vaccination was compared with intradermal injection in a mass BCG and smallpox vaccination programme in Afghanistan. In all population groups the bifurcated needle technique produced substantial tuberculin sensitivity, which however was significantly inferior to that following intradermal injection. The advantages of the bifurcated needle technique did not result in a significant increase in vaccination coverage and output. Under the present circumstances vaccination by bifurcated needle would probably be more expensive than intradermal vaccination.

The bifurcated needle has been used successfully in smallpox vaccination programmes all over the world, and innumerable vaccinators have been trained in percutaneous vaccination with this instrument. Because of the operational convenience of this simple technique, and also because in many countries mass smallpox vaccination is coming to an end, the possibilities of using the bifurcated needle technique for BCG vaccination has been considered.

A number of controlled studies have been carried out (*1*, 2)[a] in which, as evidenced by the tuberculin sensitivity induced, the bifurcated needle technique appeared less satisfactory than the classical intradermal injection technique. However, in these studies the intradermal vaccinations were invariably administered by highly experienced staff, and the intradermal vaccine used for comparison was often the International Reference Preparation, which is known to be more allergenic than many routine batches of BCG vaccine. Moreover vaccination results observed in routine (intradermal) vaccination programmes are often inferior to those observed in trials. In view of this it was decided to compare the bifurcated needle technique and intradermal vaccination in a routine vaccination programme.

The investigation, which included an assessment of the operational aspects (output, coverage, cost), was carried out at the beginning of the mass BCG–smallpox (maintenance) vaccination programme in Afghanistan.

MATERIALS AND METHODS

The vaccination programme

The vaccinations were given by staff previously engaged in the Afghanistan Smallpox Eradication Programme. The established method was followed, i.e., mobile teams consisting of six vaccinators and a team leader (with one light four-wheel drive motor vehicle and driver) vaccinated village after village, where possible at collecting points, otherwise from house to house. All children up to the age of 15 years were eligible for BCG vaccination; those up to the age of 5 years, as well as those up to 15 years old without a smallpox vaccination scar, were eligible for smallpox vaccination. The vaccinators worked in pairs, one giving the BCG vaccinations, the other the smallpox vaccinations. This arrangement not only appeared to be the most practical in the opinion of the team leaders, but also, with regard to the present investigation, ensured that the pace of the

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[a] See also the unpublished document WHO/TB/73.5.

campaign was set by the BCG vaccinations, so that the operational aspects of the two BCG vaccination techniques could be compared.

The vaccination teams reported weekly on the numbers of vaccinations performed each day per vaccinator, and the area covered. The number of vaccinations performed by bifurcated needle was counted each day from the number of needles used. Vaccinations by injection were recorded on a tally sheet.

Four teams were included in the pilot programme, which was conducted in areas where mass BCG vaccination had not been carried out. They had previously received two weeks' training in intradermal injection of BCG vaccine. Furthermore, the investigation was preceded by a four-week trial period in which the teams practised BCG vaccination by bifurcated needle and by syringe alternately (simultaneously with smallpox vaccination). During this period the techniques and procedures were verified by inspection, and where necessary corrected.

The percutaneous BCG vaccinations were given in the same way as the smallpox vaccinations, i.e., a drop of reconstituted vaccine was taken from the ampoule by dipping the bifurcated needle into it; the drop was applied to the skin and fifteen perpendicular strokes were made through it. The intradermal BCG vaccinations were given according to the usual technique, i.e., 0.1 ml of the reconstituted vaccine was injected into the superficial layer of the skin by means of a graduated Omega syringe fitted with a 1-cm steel, 26-gauge needle. After the training period the supervision of the vaccination teams was not different from that scheduled for the routine programme; the vaccinators were aware of the fact that the programme was being evaluated on a sample basis.

The BCG vaccines used in the investigation had been prepared by the Statens Seruminstitut, Copenhagen, from seed lot 1173 P_2S. The vaccine for use with the bifurcated needle was prepared in four batches. It was freeze-dried in ampoules containing 80 mg, to be reconstituted with 0.25 ml of fluid. The intradermal vaccine was prepared from the same bacterial mass as one of the batches of concentrated vaccine, and freeze-dried in ampoules containing 3.75 mg to be reconstituted with 5 ml of fluid. The reconstitution fluid (diluted Sauton) was supplied in ampoules containing the correct amount. An extract of the results of the quality control examinations performed on the BCG vaccines is given in Appendix Table 1. The smallpox vaccine used was that routinely supplied to the Smallpox Eradication Programme (donated by the Government of the USSR).

The vaccines were kept in a central store (+2°C) in Kabul, where the ampoule boxes (5 ampoules each) of the four batches of intradermal vaccine were placed in random order. Every two weeks vaccine was taken from the store to the field in a cooled container, where it was stored in a refrigerator. From there the teams were supplied weekly. Vaccine remaining at the end of the week was collected and destroyed. Vaccine remaining in the field store at the end of each fortnight was replaced.

The pilot stage of the programme was scheduled for 16 weeks. Each of the teams used the bifurcated needle and the syringe for BCG vaccination alternately for four-week periods (see Table 1). For the first 8 weeks of the investigation (autumn) the vaccinators were assigned to Baghlan Province, which is to the north of the country; for the remaining 8 weeks (winter) they were transfered to Nangarhar Province, which is in the east and has a milder climate.

Evaluation

The programme was evaluated according to a method recommended by WHO,[a] which consists of determining, in a randomly selected cluster sample, the vaccination coverages, the size of the lesions, the complication rates, and the level of vaccination-induced tuberculin sensitivity, the latter as an indicator of the dose of BCG effectively introduced into the skin.

In a BCG vaccination programme, the vaccinated population can be recognized by the presence of BCG scars (or recent lesions) and thus the proportion of those found to have a scar provides a fairly accurate index of the vaccination coverage. In the present programme, where two different vaccination techniques were used, this could not be assumed since it has been observed that BCG vaccination by bifurcated needle does not always leave a distinct scar. Comparability was therefore ensured by classifying the children according to the fresh *smallpox* vaccination lesion; its presence or absence being considered independent of the BCG vaccination technique used in the vaccinated children.

Since smallpox vaccination was given systematically only to children under the age of 5 years, the

[a] Unpublished document WHO/TB/techn. guide/2. rev. 5.

Table 1. Schedule for the BCG vaccination techniques and allocation of clusters for evaluation [a]

Team	Week (cluster no.)															
	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16
A	i*	i	i	i	p	p	p*	p	i	i*	i	i	p	p°	p	p*
B	i	i	i*	i	p*	p	p	p	i	i°	i	i*	p	p*	p	p
C	p	p	p°	p*	i	i*	i	i	p*	p	p	p	i	i	i*	i
D	p	p*	p	p	i°	i	i	i*	p	p	p*	p	i*	i	i	i

[a] i = intradermal (syringe) vaccination; p = percutaneous (bifurcated needle) vaccination; * = selected as a cluster for evaluation; ° = selected for evaluation of coverage only.

evaluation was restricted to this age group. As regards determination of the level of post-vaccination tuberculin sensitivity, this was actually desirable, because only the lower age groups can be assumed to have had little pre-vaccination, naturally acquired sensitivity.

The coverages with BCG (as evidenced by the presence of a BCG vaccination scar) were also determined in a separate sample in the 0–15 year age group. The inclusion of this sample provided a check on the validity of evaluating coverage by determining the proportion of children with a BCG scar (for either technique).

Since the examination for a fresh smallpox vaccination lesion cannot be carried out simultaneously with post-vaccination tuberculin testing (which must be carried out some 10 weeks after vaccination), a special registration team, consisting of four experienced vaccinators, visited the selected samples 14 days after the vaccination teams. The clerks, working in pairs, went from house to house and completed individual cards for all children up to the age of 5; then the children were examined for the presence of a fresh smallpox vaccination lesion, an old smallpox vaccination scar, and a fresh BCG vaccination lesion. The absence or presence of the first two were recorded, the BCG lesion was measured (induration and tissue destruction), and the measurement was recorded. For each cluster a map, showing the houses visited, was prepared.

Ten weeks after registration, the individual cards, the maps, and further information on the cluster prepared by the registration team were handed over to the evaluation team. This team consisted of two registration clerks and two tuberculin testers. The two testers had received two months' special training in a WHO-assisted project in India. This team gave a tuberculin test to all the registered children (whether vaccinated or not) and also measured the BCG and the smallpox vaccination scars. In each cluster both testers worked separately. The measurements were made by the tuberculin testers and dictated to the clerks, who recorded them on the individual cards. The completed records were sent to Geneva for analysis. The tuberculin used was of batch RT23 (with Tween 80) in a dose denoted as 2 TU.[a]

The sample for the evaluation in the 0–5 year age group consisted of 16 clusters randomly selected according to a balanced design (unknown to the field staff), each cluster being defined as the area supposed to have been vaccinated by one team in one week in a four-week period. The details of the design are the following: for each team the work of one week was evaluated in every four-week period, once the work of the first week, once that of the second week, etc. Thus for each team each technique was evaluated twice, alternately, and for each team both techniques were evaluated once in the first and once in the second trial area. The total time intervals between the beginning of the study and the evaluations were the same for each technique. The allocation of clusters to teams is illustrated in Table 1.

The instructions for each week's selection of a cluster for evaluation were enclosed in sealed envelopes; the appropriate envelope was opened by the supervisor in the week following the vaccinations (and preceding the registration).

[a] In clusters 1 and 2 the dose was 1 TU; this has been disregarded in the analysis.

The evaluation of the coverage in the 0–15 year age group was undertaken by the registration team in four clusters not previously registered. One cluster was selected for each team and each four-week period in such a way that both BCG vaccination techniques were included twice (see Table 1).

RESULTS

Vaccination output

The reported numbers of vaccinations are shown in Table 2. Team D did not vaccinate in the first week of the study period, when it should have been using the bifurcated needle technique. Nevertheless, the total number of BCG vaccinations reported for the bifurcated needle technique was 11.6% higher than for the intradermal technique. Analysis of variance shows, however, that for the whole trial period the difference in output is statistically not significant. A possible real difference attributable to the technique may have been masked by the large differences between teams and between clusters. On the other hand, it will be observed that team C reported a higher output with the syringe-and-needle technique, and that for the other teams the higher output with the bifurcated needle technique

Table 2. Reported numbers of vaccinations by team and week of investigation—BCG and smallpox (SPX)

Cluster No. (week)	Team A		Team B		Team C		Team D	
	BCG	SPX	BCG	SPX	BCG	SPX	BCG	SPX
1	3 265 i	1 898	2 246 i	1 125	866 p	599	p	
2	2 714 i	1 546	2 151 i	1 032	655 p	386	1 128 p	442
3	2 909 i	1 989	1 623 i	690	1 533 p	834	2 221 p	1 420
4	2 492 i	1 649	3 004 i	1 418	1 965 p	1 101	2 034 p	1 573
5	2 425 p	1 680	1 908 p	952	1 174 i	770	2 102 i	1 276
6	1 814 p	870	1 716 p	749	1 385 i	787	1 146 i	677
7	2 011 p	1 064	2 084 p	968	1 510 i	726	456 i	250
8	1 988 p	997	1 980 p	721	858 i	508	804 i	316
Subtotal i	11 380	7 082	9 024	4 265	4 927	2 791	4 508	2 519
Subtotal p	8 238	4 611	7 688	3 390	5 019	2 920	5 383	3 435
9	4 243 i	1 681	2 434 i	732	3 516 p	1 463	2 431 p	1 129
10	3 713 i	1 638	2 767 i	1 125	2 325 p	874	2 588 p	1 221
11	1 982 i	1 010	2 332 i	984	1 565 p	702	2 295 p	1 202
12	1 745 i	870	2 169 i	857	1 771 p	943	2 433 p	1 214
13	5 819 p	2 534	3 016 p	932	2 544 i	1 095	2 297 i	1 168
14	3 274 p	1 303	3 560 p	1 432	2 290 i	848	2 234 i	1 143
15	4 410 p	1 825	4 859 p	1 509	2 690 i	1 094	1 709 i	1 027
16	4 450 p	1 663	3 932 p	1 091	3 463 i	877	1 939 i	558
Subtotal i	11 683	5 199	9 702	3 698	10 987	3 914	8 179	3 896
Subtotal p	17 953	7 325	15 367	4 964	9 177	3 982	9 747	4 766
Total i	23 063	12 281	18 726	7 963	15 914	6 705	12 687	6 415
Total p	26 191	11 936	23 055	8 354	14 196	6 902	15 130	8 201
Grand total	49 254	24 217	41 781	16 317	30 110	13 607	27 817	14 616

Total BCG = 148 962. Intradermal = 70 390. Percutaneous = 78 572. Total SPX = 68 757. Total Vaccinations = 217 719.

was not achieved over the whole study period, but mainly at the end (by teams A and B), when the population was easily reached.

In the sample population examined, the total numbers of children vaccinated with each technique were very similar: among the examined children with a fresh smallpox vaccination scar, 1846 had been vaccinated by syringe and 1852 by bifurcated needle (see Table 5).

Vaccination coverage

The coverage with BCG vaccination observed in the 0–5 year age group is shown in Table 3. It may be seen from the columns " A " that not all the children with a smallpox vaccination lesion had a BCG scar (or lesion) at the time of evaluation, although presumably they had all been vaccinated. Thus, counting BCG scars and lesions may give an underestimate of the vaccination coverage as expected. The absence of a scar was more frequent after vaccination with the bifurcated needle (4.9%) than after intradermal injection (2.8%). The independent evaluation of coverage in the 0–15 year age group is shown in Table 4. It appears that the coverage and the reported numbers of vaccinations are often inversely related. Moreover the coverage depended on the team and the area rather than on the vaccination technique.

BCG-induced tuberculin sensitivity

Post-vaccination tuberculin sensitivity. The results of the post-vaccination tuberculin tests, separately for each cluster by age group and sex are given in Appendix Table 2, and the summary results for the

Table 3. Coverage with BCG vaccination in the age group 0-5 years

	Intradermal				Bifurcated needle			
	Cluster	A [a]	B [b]	Coverage [c] (%)	Cluster	A [a]	B [b]	Coverage [c] (%)
Baghlan Province	1	99.4	91.4	92.0	2	96.0	77.5	80.7
	3	97.6	81.2	83.2	4	97.3	70.9	72.9
	6	98.8	60.4	61.1	5	95.4	64.5	67.6
	8	100	68.0	68.0	7	97.8	77.4	79.1
Nangarhar Province	10	95.6	64.3	67.3	9	95.2	52.1	54.7
	12	94.2	68.0	72.2	11	95.1	63.6	66.9
	13	95.8	67.4	70.4	14	94.1	73.3	77.9
	15	96.5	70.2	72.7	16	89.3	55.4	62.0
Total (mean)		97.2	71.4	73.5		95.1	66.8	70.2

[a] A = % with BCG scar ($\geq$ 2 mm) among those with fresh and late smallpox vaccination lesion.
[b] B = % with BCG scar ($\geq$ 2 mm) among all examined at the 10-week follow-up.
[c] Vaccination coverage = $\frac{100}{A} \times B\,\%$.

Table 4. Evaluation of BCG vaccination coverage according to presence or absence of a BCG scar, in the 0–15 year age group

Team	Week	Technique	No. examined	No. with scar	Coverage (%)	No. of reported vaccinations
A	14	Bif. needle	1647	1238	75.2	3274
B	10	Intradermal	1908	1471	77.1	2767
C	3	Bif. needle	983	883	89.8	1533
D	5	Intradermal	1205	1054	87.5	2102

Table 5. Tuberculin reactions (means in mm) to 2 TU of RT 23 (+ Tween) 10 weeks after vaccination, by vaccination technique, trial area, age, and sex in children with a fresh smallpox vaccination lesion at the time of registration

Province (technique)	Age < 1 year						Age 1-5 years						All ages up to 5 years					
	M		F		All		M		F		All		M		F		All	
	No.	Size	No.	Size	No.	Size	No.	Size	No.	Size	No.	Size	No.	Size	No.	Size	No.	Size
Baghlan (intradermal)	103	12.57	81	13.65	184	13.05	318	14.22	262	13.97	580	14.11	421	13.81	343	13.90	764	13.85
Baghlan (bifurcated needle)	78	10.35	101	10.60	179	10.49	305	11.11	320	11.38	628[a]	11.27	383	10.95	421	11.20	807[a]	11.10
Nangarhar (intradermal)	103	10.42	92	11.47	195	10.91	439	13.08	446	13.93	887[a]	13.52	542	12.58	538	13.51	1082[a]	13.05
Nangarhar (bifurcated needle)	139	9.46	104	8.87	244[a]	9.17	413	10.23	388	11.64	801	10.91	552	10.03	492	11.05	1045[a]	10.51
Total (intradermal)	206	11.50	173	12.49	379	11.95	757	13.56	708	13.94	1467[a]	13.75	963	13.12	881	13.66	1846[a]	13.38
Total (bifurcated needle)	217	9.78	205	9.72	423[a]	9.73	718	10.60	708	11.53	1429[a]	11.07	935	10.41	913	11.12	1852[a]	10.76

[a] Including those for whom the sex was not recorded.

different techniques by trial area, age, and sex in Table 5. The distributions (both sexes combined) are shown in Fig. 1. It was found that for both techniques the reactions in girls tended to be somewhat larger than in boys, and that in children under 1 year of age the reactions were slightly smaller than in older children. In both trial areas, both sexes, and both age groups, intradermal injection consistently gave higher post-vaccination tuberculin reactions than vaccination by bifurcated needle. (This was found by both tuberculin testers.) The overall difference was 2.62 ± 0.38 mm (95% confidence limits).[a]

In the children under 1 year of age who were given half the dose (volume) by the intradermal method but the full dose by bifurcated needle, the difference was 2.22 ± 0.88 mm. Statistically this is not significantly different from the difference observed in the older children (2.68 ± 0.44 mm).

From Fig. 1 it may also be seen that the reactions of the children vaccinated by bifurcated needle do not seem to conform to a normal distribution. This suggests that the bifurcated needle technique is less uniform than intradermal injection.

Pre-existing tuberculin sensitivity. Children who had tuberculin sensitivity before vaccination were not excluded. Thus, depending on their proportion in the study population, the difference in BCG-induced tuberculin sensitivity may have been masked (the observed difference reduced) to a certain extent. To clarify this matter, the tuberculin reactions in children that had neither a sign of smallpox vaccination nor of BCG vaccination are shown in Fig. 2. It is seen that in both study areas the proportion of children with a high level of tuberculin sensitivity is very small. If these children can be assumed to be representative of the study population, it is obvious that pre-existing tuberculin sensitivity cannot have had much influence on the observed distributions and certainly not on the comparision of the two vaccination techniques.

Vaccination lesions

The numbers of BCG vaccination lesions (predominantly scars) observed in each cluster are shown in Appendix Table 2. They were very similar in boys and girls. The results irrespective of sex are shown in Fig. 3. For both techniques the lesions

[a] This difference is similar to that found in quality control tests carried out in Danish schoolchildren (see Appendix Table 1).

observed in the first trial area were significantly larger than in the second trial area. In fact this difference was larger than that observed between the vaccination techniques, which overall was 0.40 mm. For both techniques, and in both trial areas, the lesions observed in the children under 1 year of age were slightly smaller than those in the older children. Large BCG lesions were extremely rare: of the total of 8163 children seen, one child had a BCG reaction of 20 mm, one a reaction of 25 mm, and one a reaction of 35 mm. The smallpox vaccination lesions were considerably larger

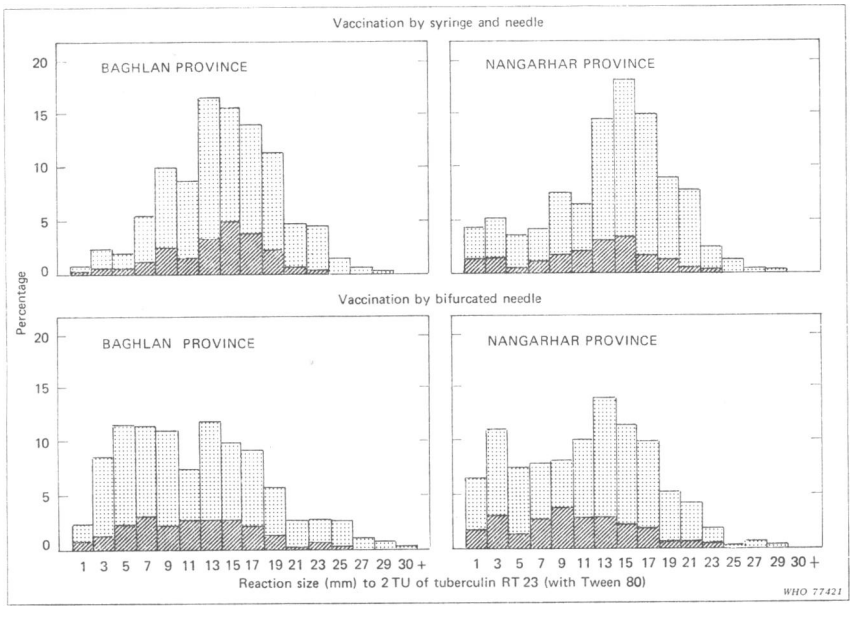

Fig. 1. Tuberculin reactions, 10 weeks after vaccination, by trial area and vaccination technique, in children with a fresh smallpox vaccination lesion at the time of registration. Lighter columns: all ages up to 5 years; darker columns: children aged <1 year.

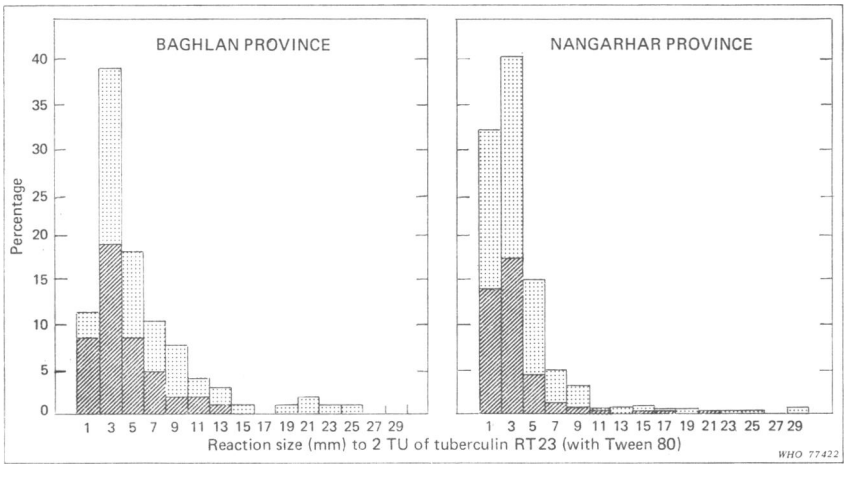

Fig. 2. Distribution of tuberculin reactions in children without fresh or late smallpox vaccination or BCG vaccination lesions. Lighter columns: all ages up to 5 years; darker columns: children aged <1 year (No. of children: Baghlan Province, 104; Nangarhar Province, 494).

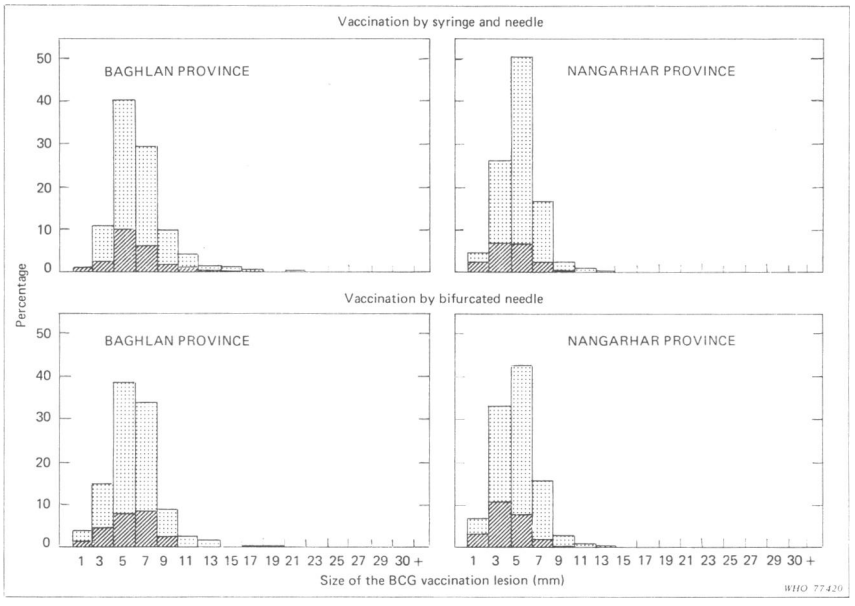

Fig. 3. BCG vaccination lesions, 10 weeks after vaccination, by trial area and vaccination technique, in children with a fresh smallpox vaccination lesion at the time of registration. Lighter columns: all ages up to 5 years; darker columns: children aged < 1 year.

(mean 8 mm) than the BCG lesions (mean: 4–6 mm, according to vaccination area and technique, see Fig. 3), and large reactions were slightly more frequent: 12 children had a reaction of 20 mm or more, the largest one being 32 mm.

Complaints

Complaints at the time of post-vaccination testing were investigated and recorded. Altogether 45 complaints (see Table 6) were reported by the parents to the evaluation team.

Table 6. Complaints reported 10 weeks after vaccination, in 8163 children examined, according to side of vaccination and technique used

Complaint	Left	Right	
	Smallpox	BCG, intradermal	BCG, bifurcated needle
Lymph gland swelling	2	3	1
Fistula	2	5	2
Unpleasant lesion	—	22	8

Lymph node swelling was rarely reported, but 7 cases of perforated axillary lymphadenitis were observed at the right (BCG) side, of which 5 were in intradermally vaccinated children and 2 in children vaccinated by bifurcated needle. There were also 2 cases at the left (smallpox vaccination) side. The etiology of these was not determined. All cases of perforated lymphadenitis occurred in children over 1 year of age.

Complaints about the vaccination lesions were more frequent for those vaccinated by syringe than for those vaccinated by bifurcated needle, but the lesions were not found to be excessively large: only 6 were larger than 10 mm, the largest one was 15 mm.

Cost of the vaccinations

The vaccination programme (not including the evaluation) involved the following expenses:

	US$
Overheads (salaries senior staff, accommodation, etc.)	2 668
Running costs for 4 teams (salaries, per diem, petrol, etc.)	6 816
Cars (2 motor vehicle years) estimated	4 000
Total	$13 484

Furthermore the following supplies and equipment were used [a]

	BCG, intradermal	*BCG, bifurcated needle*
Steel needles	960 = $ 41.60	
Syringes	288 = $313.92	
Bifurcated needles		5120 = $49.56
Containers		307 = $10.45
Alcohol	80 litres = $ 80.00	
Total	$435.52	$60.01

[a] The following prices have been applied: steel needles: $ 0.52 per dozen; syringes: $1.09 each; bifurcated needles: $9.68 per 1000; containers: $4.90 per gross; alcohol: $1.00 per litre.

Considering the numbers of vaccinations (see Table 2), and also that half the staff was engaged in smallpox vaccination and the other half in BCG vaccination, the average cost per BCG vaccination (not including the vaccine) was: intradermal $0.0541; bifurcated needle $0.0437. The cost of the vaccine has not been included since reasonably priced concentrated vaccine is not available on the market. However, from the cost per vaccination as shown above, the number of ampoules of concentrated vaccine used (1500), the cost of shipment of vaccine (Copenhagen-Kabul: $350 per 1000 ampoules, including reconstituting fluid), and the cost of the intradermal vaccine (estimated at $2000 for 2400 5-ml ampoules), it may be calculated that one vaccination by bifurcated needle would have been cheaper than one intradermal vaccination provided that the cost of an ampoule of concentrated vaccine did not exceed $2.35. Compared with the 10-ml ampoules of intradermal BCG vaccine commonly used in mass vaccination programmes (1500 ampoules at $1.18 each), the break-even point is at a price of $1.85 per ampoule of concentrated vaccine.

DISCUSSION

The practical question that this study was intended to solve was whether trained smallpox (bifurcated needle) vaccinators when used for mass BCG vaccination should employ the bifurcated needle technique or the intradermal technique (after brief training). The answer obtained appears to be unambiguous.

The results of vaccination by bifurcated needle observed were very similar to those obtained in controlled studies (*1*, *2*): whereas vaccination by bifurcated needle with a concentrated vaccine induces an appreciable level of tuberculin sensitivity, this level was significantly lower than that after intradermal injection of a far more dilute vaccine prepared from the same strain. Thus it seems that if field conditions have an unfavourable effect on the quality of intradermal vaccination, this applies equally to the bifurcated needle technique. In young infants the difference in tuberculin sensitivity induced by the two techniques was not significantly smaller than in older children. This was rather surprising because by injection the young infants had only been given half the dose. Although the difference of about 2–3 mm in the mean tuberculin reactions may appear to be relatively small, it indicates that the amount of vaccine effectively introduced by the bifurcated needle was some 10–20% of that injected by syringe.[a] The crucial question is of course what such a difference means in terms of protection. Empirical information on this matter is scarce. In a controlled trial in American Indians (*4*), a poor culture medium had been used for some time. The vaccine prepared from cultures grown on this medium resulted in a conversion rate of 16.1%, against 46.1% observed in the population given the same dose of vaccine prepared from cultures grown on a different medium. Five years later the protection observed with the former vaccine was 53%, against 80% with the latter in the total vaccinated population (*5*). In a controlled trial in England, adolescents vaccinated with batches containing 20–29 million viable units per milligram had a mean post-vaccination reaction of 9.6 mm (to 3 TU of O.T.), whilst those vaccinated with batches containing 30–39 million viable units per milligram had a mean reaction of 9.9 mm. The levels of protection, observed ten years later, were respectively 73% and 86% (*6*). Thus a small difference in vaccine dose (and induced tuberculin sensitivity) could correspond to an important difference in protection afforded, and the difference observed in the study should give reason for caution.

Although the lesions after intradermal injection were on the average larger than after vaccination by bifurcated needle, they were perfectly acceptable to the population, and complications were rare. The vaccination coverage was the same for both techniques.

In the mass vaccination programme studied, the practical advantages of the bifurcated needle technique did not result in a noteworthy increase of the

[a] For the dose–response relationship in BCG vaccination, see Edwards et al. (*3*).

vaccination output. Moreover, under the circumstances in Afghanistan, where the cost of staff is relatively low, an increase in the vaccination output would not reduce the cost per vaccination very much, as the latter largely depends on the price of the vaccine. In fact there is no concentrated vaccine available at a price that would render vaccination by bifurcated needle cheaper than intradermal vaccination in the current programme in Afghanistan.

It must be pointed out that the conditions of the Afghanistan programme seem to have been to the disadvantage of the bifurcated needle technique. In a different type of programme in a country where the cost of staff is relatively high or in a population where a low dose of vaccine is used, the bifurcated needle technique might well be a profitable substitute for the current procedure, e.g., for the vaccination of young infants, provided that (intradermal) revaccination is ensured at school age.

The method of evaluation used in this study, including the selection of the samples, appeared to be expedient and may be used for the evaluation of routine vaccination programmes. It should be noted that counting the BCG lesions (scars) gave an underestimate of the vaccination coverage of some 3–5%, according to the vaccination technique, but in comparative evaluation this is scarcely a drawback. Many vaccinated children who have no distinct vaccination lesion (scar) are probably poorly vaccinated, and for practical purposes are best considered as not vaccinated. Post-vaccination tuberculin reactions in the 0–5 year age group were hardly influenced by pre-existing tuberculin sensitivity. Evaluating BCG-induced tuberculin sensitivity in this age-group will probably prove satisfactory in most countries.

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RÉSUMÉ

ADMINISTRATION DE BCG AVEC UNE AIGUILLE BIFURQUÉE DANS UN PROGRAMME PILOTE DE VACCINATION

La technique vaccinale au moyen de l'aiguille bifurquée, qui a été extrêmement utile dans les campagnes de vaccination antivariolique, a donné dans un certain nombre d'essais sur le terrain de vaccination par le BCG de moins bons résultats que la technique d'injection intradermique classique; mais il est possible que, dans un programme de vaccination systématique, la différence entre les deux techniques soit moins marquée et qu'une légère réduction de l'efficacité soit peut-être compensée par des avantages opérationnels, à savoir un moindre coût unitaire. C'est pourquoi les deux techniques ont été confrontées dans un programme de vaccination systématique BCG/variole.

Les performances de quatre équipes ont été évaluées sur deux périodes de huit semaines chacune dans deux aires différentes. Les équipes qui avaient une longue expérience de la vaccination (antivariolique) au moyen de l'aiguille bifurquée ont suivi un stage d'instruction préliminaire sur les injections intradermiques. Chaque équipe a utilisé les deux techniques en alternance pendant quatre semaines. Les vaccins BCG pour injection et pour usage percutané avaient été préparés tout spécialement à partir du lot de semences 1173 P_2S et étaient lyophilisés. Le vaccin intradermique a été utilisé à la concentration de 0,75 mg/ml, le vaccin percutané à la concentration de 325 mg/ml. L'équipement et les techniques habituels ont été employés.

Le programme a été évalué, conformément à une méthode recommandée par l'OMS, dans une grappe de population choisie aléatoirement d'après un plan

équilibré. Il a été tenu compte du nombre de vaccinations (rapportées), de la couverture vaccinale, de la dimension des lésions vaccinales, des taux de complication et du niveau de la sensibilité tuberculinique induite par le BCG. On a également évalué le coût des vaccinations.

Un total de 70 390 vaccinations intradermiques et de 78 572 vaccinations percutanées a été signalé; mais les écarts de productivité ont été importants entre les équipes et d'une région à l'autre et la différence observée n'est pas statistiquement significative. Dans l'échantillon examiné, on a constaté que 1846 enfants avaient été vaccinés par la seringue et 1852 au moyen de l'aiguille bifurquée. La couverture vaccinale pour les deux techniques était sensiblement la même.

Les lésions vaccinales observées après l'administration percutanée au moyen de l'aiguille bifurquée étaient un peu plus petites que les lésions consécutives à l'injection intradermique; la différence entre les techniques était faible comparée aux différences entre les équipes et les aires de vaccination (pour les deux techniques). Les lésions BCG étaient beaucoup plus petites que les lésions consécutives à la vaccination antivariolique. Les lésions de dimension disgracieuse étaient très rares.

Pour 8163 enfants examinés, on a enregistré 45 complications: deux cas de lymphadénite perforée du côté gauche (vaccination antivariolique) et 7 du côté droit (BCG); dans 5 cas, les enfants avaient été vaccinés au moyen de la seringue.

La sensibilité tuberculinique consécutive à la vaccination au moyen de l'aiguille bifurquée a constamment été inférieure à la sensibilité induite par injection intradermique. La différence était de l'ordre de 2 à 3 mm, tant pour les enfants de moins d'un an (auxquels on avait injecté la moitié de la dose) que pour les enfants plus âgés. Ceci indique que la quantité de vaccin effectivement introduite dans la peau par l'aiguille bifurquée représente environ 10% à 20% de la quantité injectée par la seringue, ce qui peut entraîner une différence importante de la protection conférée.

Dans les conditions régnant en Afghanistan, le coût de la vaccination dépend essentiellement de celui du vaccin. Pour que la vaccination au moyen de l'aiguille bifurquée revienne moins cher que l'injection intradermique, il aurait fallu que le coût d'une ampoule de vaccin concentré (80 mg) soit inférieur à $2,35 contre $0,83 pour une ampoule de 5 ml de vaccin intradermique (3,75 mg).

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Appendix Table 1. Extract from the results of the quality control examinations of the batches of BCG vaccine used

	Batch No.				
	F 12	F 13		F 14	F 15
Vaccine concentration	320 mg/ml	0.75 mg/ml	320 mg/ml	320 mg/ml	320 mg/ml
Sterility (liquid as well as freeze-dried)	No sign of microbial contamination				
Safety	No macroscopic signs of tuberculosis in guinea pigs (6 for each batch) at autopsy 6 weeks after vaccination with 5 mg (each) of the liquid bulk				
Oxygen consumption per 120 mg/hour					
Liquid vaccine	166 µl	184 µl	184 µl	156 µl	138 µl
Freeze-dried vaccine (reconstituted)	119 µl	67 µl	133 µl	115 µl	130 µl
Number of culturable particles (millions per mg)					
Liquid vaccine	12.0–13.8	18.3–19.9	18.3–19.9	14.9–16.3	20.9–25.3
Freeze-dried, immediately after preparation	3.2–3.9	3.7–4.7–4.8	3.8–3.8	3.2–3.5	5.4–5.3
stored one month at 2–4°C	3.6	5.3	5.6	2.2	6.1
stored one month at 37°C	0.7	1.5	0.5	0.5	1.3
Germination rate (%) after 48 hours					
Liquid vaccine	90–95	90–95	90–95	95	90–95
Freeze-dried, immediately after preparation	50	25–50	50–75	50	50
stored one month at 2–4°C	50	50	50–75	25–50	50
stored on month at 37°C	10	10–25	10–25	5–10	10–25

Tests in Danish schoolchildren

	Intradermal		Bifurcated needle			
Tuberculin reactions (2 TU of RT23 + Tween)	Reference	Batch F 13	Batch F 12	Batch F 13	Batch F 14	Batch F 15
No. tested	92	100	50	23	49	49
Mean size (mm)	17.8	17.4	15.9	15.0	16.9	15.9
Standard deviation (mm)	2.6	3.3	4.8	3.9	3.5	4.4
Vaccination lesions (after 2 months)						
No. examined	103	104	52	26	51	53
Mean size (mm)	6.5	6.4	6.2	5.2	5.1	5.8
Standard deviation (mm)	1.3	1.4	1.8	2.3	1.7	2.2

Appendix Table 2. Tuberculin reactions and BCG vaccination lesions, 10 weeks after vaccination, by age, sex, and cluster (technique) in children with a fresh smallpox vaccination lesion at the time of registration

Cluster No. (technique) [b]	Post-vaccination tuberculin reactions [a]												BCG vaccination lesions											
	Age < 1 year						Age 1-5 years						Age < 1 year						Age 1-5 years					
	M			F			M			F			M			F			M			F		
	n	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD	*n*	$\bar{x}$	SD
1 (i)	46	11.7	3.8	34	13.9	5.4	132	13.8	4.6	122	13.4	5.0	45	7.2	3.3	34	7.0	3.4	132	6.9	3.7	120	6.5	3.1
2 (b. n.)	27	9.6	5.6	41	10.3	5.9	78	9.6	6.2	98	9.0	6.6	29	6.0	3.2	42	5.8	1.5	78	6.0	2.8	102	5.7	2.5
3 (i)	28	12.5	5.2	26	11.6	5.3	80	14.2	5.4	69	13.7	5.3	29	4.4	2.0	28	4.3	1.6	81	4.9	1.8	69	5.1	1.8
4 (b. n.)	19	9.7	4.7	26	9.9	4.8	93	10.5	6.6	84	11.1	6.6	19	3.6	1.4	26	4.0	1.8	96	4.6	1.6	84	4.5	1.6
5 (b. n.)	12	11.6	5.5	12	12.8	5.1	44	13.3	8.1	40	15.6	6.7	12	3.8	2.1	12	5.3	2.3	44	5.3	1.9	40	5.6	1.9
6 (i)	22	14.8	4.5	18	16.1	4.3	74	15.2	4.7	47	16.0	5.7	22	5.1	2.3	18	5.2	1.6	76	6.0	2.2	48	5.7	1.6
7 (b. n.)	20	11.3	5.6	22	10.7	5.1	90	12.1	6.2	98	12.2	5.6	20	5.3	1.7	22	5.0	2.0	90	5.4	1.7	98	5.6	2.0
8 (i)	7	11.7	4.9	3	13.7	6.5	32	13.8	6.0	24	13.6	6.8	7	5.2	2.1	3	5.7	2.1	32	5.4	1.3	24	5.1	1.8
9 (b. n.)	22	11.9	4.5	16	11.6	6.6	81	9.3	6.2	88	11.0	6.5	22	4.9	1.7	16	4.7	1.5	81	4.9	2.2	90	4.9	2.2
10 (i)	30	11.4	5.6	30	13.1	4.9	139	14.5	6.1	151	14.6	6.0	31	3.9	2.2	30	3.8	1.7	145	4.9	1.8	159	4.7	1.7
11 (b. n.)	24	7.5	5.1	22	8.7	5.2	107	9.4	6.7	86	11.3	7.1	23	2.7	1.9	23	3.2	1.3	108	4.7	1.5	93	4.7	1.4
12 (i)	18	9.8	5.6	10	8.4	5.5	81	12.2	6.2	70	13.1	5.9	18	3.9	2.4	10	3.1	2.4	85	4.4	1.6	74	4.9	1.6
13 (i)	26	9.7	5.5	22	10.6	6.5	130	12.1	5.9	120	14.0	5.2	26	3.2	1.7	22	3.5	1.7	136	4.2	1.5	122	4.2	1.5
14 (b. n.)	74	10.1	4.9	45	8.4	5.6	146	11.1	5.7	154	11.8	6.0	75	3.2	1.5	45	3.0	1.6	146	3.9	1.5	155	4.0	1.6
15 (i)	29	10.4	4.8	30	11.5	5.1	89	13.0	4.5	105	13.3	5.4	29	2.9	1.6	30	3.8	1.5	92	4.2	1.3	106	3.9	1.2
16 (b. n.)	19	6.8	4.3	21	8.0	5.5	79	10.6	6.3	60	12.7	5.7	20	2.3	1.6	21	2.7	2.1	82	3.2	1.5	63	3.4	1.5

[a] Tuberculin reactions to 2 TU of RT23 + Tween; M = male; F = female; *n* = number; $\bar{x}$ = arithmetic mean; SD = standard deviation: the last two values are given in mm.

[b] i = intradermal (syringe); b. n. = bifurcated needle.