AN ACCOUNT OF 2,500 INFANT B.C.G. VACCINATIONS

BY

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The subject of this paper is the personal experience of 2,500 cases of infant vaccination with B.C.G. The material has been drawn from babies born in the Royal Maternity Hospital, Belfast, and the Malone Place Maternity Hospital, Belfast, and has been carried out under the auspices of the Northern Ireland Hospitals Authority and the Department of Child Health, Queen's University of Belfast.

Compared with the recent literature on vaccination against tuberculosis in older age groups, there is little information about infant B.C.G. vaccinations. This is largely due to the fact that vaccination of the infant age group has not been included in the mass vaccination campaigns sponsored by the World Health Organization. In Great Britain, also, vaccination in the younger age groups has hitherto not been extensive.

Selection of Cases

The cases quoted in this study were all vaccinated personally between March, 1952, and March, 1953. Vaccination is offered to every mother for her baby during the lying-in period. The vaccination is optional, but the medical and nursing staffs use their helpful influence, and explanatory literature is freely available. A personal interview is given to any mother who desires it, and to almost every case in which there is a family history of tuberculosis or liability to exposure. Isolation is provided in the hospitals for the babies from birth and throughout the post-vaccinal period when this is indicated.

The live births in the hospitals for the period in question numbered 2,750, and the vaccinations for the same period 2,500, giving an acceptance rate of 92.59%.

Queries Arising During Course of Investigation

As occurs in most investigations, various small problems arose which had not been anticipated and which necessitated some alterations in the original scheme. For example, it became apparent that many of the premature babies had been one, two, and even three months in hospital before being considered fit for discharge. When this fact was realized pre-vaccinal tuberculin skin-testing was instituted if four or more weeks had elapsed between birth and vaccination, instead of omitting all preliminary testing, as is the usual procedure with infant vaccinations.

In addition, having had doubts aroused about the validity of the current belief in the extreme rarity of congenital tuberculosis, a routine tuberculin test is now done on the infants of all tuberculous mothers. It is hoped, at a later date, to publish a report on congenital tuberculosis as a result of an investigation which is now being carried out in these hospitals.

Technique of Dosage and Administration

With regard to technique, dosage, and administration, the recommendations of Winge and Sigrid Holm, of the Central Tuberculosis Clinic, Copenhagen, and of Tolderlund, of the State Serum Institute of Denmark, have been adhered to throughout the survey (Personal communications). There is a tendency in some centres to reduce the recommended dosage in view of the increased liability of infants to develop regional adenitis and abscess formation following B.C.G. injections. This has not been accepted in the present investigations, for two reasons: in the first place the majority of these infants (93.36%) had no known tuberculous contact at the time of vaccination and are unlikely to meet tuberculosis in the first few years of life; secondly, it is admitted (Gaisford, 1953) that the percentage of cases giving a positive tuberculin reaction one year after vaccination falls off enormously if a smaller initial dose of vaccine is given. In this series, in which more than 350 cases have already had the first annual test, there has been no single case in which the post-vaccinal conversion had not been maintained. It is probable, also, that it will not be possible to ensure annual tuberculin testing on a large proportion of these children who hail from all over Northern Ireland, and with the smaller dose the immunity may lapse very soon, while the parents continue to harbour a feeling of false security.

The observation that adenitis is due to an injection which is too deep rather than to too large a dose of vaccine (Palmer and Edwards, 1953) has been confirmed in the present series. Adenitis is almost always due to failure in technique, and the reason that it is more frequent in the infant age group is that it is technically more difficult to get a true intradermal injection in these subjects.

The infants in this series therefore received 0.1 ml. of vaccine—that is, 0.075 mg. of B.C.G.—intradermally in each deltoid region.

With the exception of premature babies, or some ill babies, or those with birth injuries or congenital abnormalities, all were vaccinated between the first and the eighth day from birth. It is desirable that the infant be removed from its cot for the purpose and that the top part of the trunk and arms should be bared. Before these precautions were taken a few babies were vaccinated too high in the arm, and the adenitis, when it occurred, affected the cervical glands rather than the axillary ones, which is unfortunate for cosmetic reasons and also because these glands are more likely to suppurate through being subjected to frequent nasopharyngeal infective onslaughts.

Post-vaccinal Examination

Post-vaccinal testing is carried out at the Royal Belfast Hospital for Sick Children eight weeks after vaccination, at a special clinic reserved for these babies. The attendance rate at this clinic is about 85% of the original number vaccinated. I am indebted to physicians of the chest clinics throughout Northern Ireland, and most particularly to the health visitors of the Northern Ireland Tuberculosis Authority, for carrying out the tuberculin skin tests on babies whose parents live a great distance from Belfast, and also on the defaulters nearer home.

On the occasion of the visit to the hospital for post-vaccinal testing, mothers are invited to bring older children for preliminary testing if they so desire. The facility is made use of to a considerable extent, and it is interesting to record that a definite, albeit small, proportion of siblings of 3 years and under are Mantoux-positive at this examination. By this means some cases with a definite primary tuberculous complex have been revealed, though in the majority there was no known source of exposure, and the parents and other household inmates were radiologically free from tuberculosis. Two of these cases were from farms, and the children in question had been reared on unboiled milk from untested cows; the infection may therefore well have been bovine in origin.

At the post-vaccinal examination routine questions are asked about neonatal health. In no case has there been reason to suspect any constitutional disturbance as a result of the vaccination, although whooping-cough, bronchopneumonia, gastro-enteritis, operations for congenital pyloric stenosis, and transfusions for erythroblastosis have all been experienced during this period. In spite of advice to the contrary, many of the babies have already had their smallpox vaccination when they return to the clinic, and apparently without adverse effect.

The vaccination sites are examined and a search is made for evidence of regional adenitis. The conversion rate at

the time of post-vaccinal testing is 99.69%. Only seven cases gave a negative result to the tuberculin skin test. In one of these there was no local evidence of vaccination, and it is probable that the child was not vaccinated, but that a card was filled in and filed in error. In the case of the remaining six, four were reported on by local practitioners and two by health visitors; it has not been possible to see the babies in question personally or to repeat the test or confirm the negative findings with a Mantoux 1/100. Table I gives an analysis of the results in this series.

TABLE I.—*Analysis of Findings*

Vaccinations			2,500
Complete:			
With post-vaccinal control		2,331 (93·24%)	
Successful, with positive P.V. test		2,324 (99·69%)	
Unsuccessful, with negative P.V. test		7 (0·31%)	
Incomplete:			
Without post-vaccinal control		169 (6·76%)	
Untraced	145		
Dead	24		

Premature Babies, or Babies with Congenital Illnesses or Abnormalities

Approximately 12% of the vaccinated babies are premature and inhabit the nursery wing of the Royal Maternity Hospital. A birth weight of under 5½ lb. (2.5 kg.) is accepted as the criterion of prematurity. As already stated, some of these babies have been a considerable time in hospital before vaccination. Discharge takes place when they are 5½ lb. if otherwise thriving and the home conditions are reasonably good. Consequently, the premature babies are vaccinated when they are in or about this weight. There has been no difference in the post-vaccinal behaviour of these infants as compared with full-term ones, and no greater incidence of adenitis.

Babies with congenital abnormalities or diseases—for example, spina bifida, hydrocephalus, mongols, cretins, infants with retrolental fibroplasia, or haemolytic disease—are all included in the vaccination programme, provided that the physician in charge considers that they are likely to survive the first few months of life. This perhaps is a mistake from the statistical point of view, as it follows that the overall death rate of these infants will be higher than the average infantile mortality rate; but this is offset by the fact that it impresses on the parent the idea of the vaccination being a normal routine procedure. It also ensures that the handicapped child, if it survives, will not be at any disadvantage compared with its more fortunate brother when and if exposed to tuberculosis.

Table II gives the number and percentage of deaths in our series of cases and the cause when this could be ascertained.

TABLE II.—*Deaths*

Belfast City death rate (1952) under 1 year=44 per 1,000 live births		
Deaths in present series of 2,500		24 (0·96%)
Infanticide	1	
Haemolytic disease	2	
Virus infection	1	
Gastro-enteritis	3	
Bronchopneumonia	2	
Congenital abnormalities	2	
Premature, within two weeks of discharge	2	
Unknown cause; neighbour's report	11	

Tuberculous Contacts

There was either a tuberculous contact in the household or a family history of tuberculosis in 166 (6.64%) out of 2,500 vaccinations. Table III gives a summary of these. Where required isolation was carried out (*a*) by keeping the infant in hospital till tuberculin conversion occurred; (*b*) by keeping the infected relative in hospital or away from the home; or (*c*) by arranging for the baby to be kept, for the post-vaccinal period, in an uninfected household or child hostel. Many of the mothers concerned came from the sanatorium for their confinement, returning there afterwards. They do not handle the baby at any time.

Four infants had contact with active though hitherto unsuspected sources of infection during the post-vaccinal period. These have been the subject of two-monthly review, but no signs of tuberculosis have yet been discovered in any of them, and chest *x*-ray films have all been normal.

TABLE III.—*Contact of Family History*

No. of contacts		166 (6·64%)
Relationship of contact:		
Parent	97 (58·5%)	
Grandparent	17 (10·2%)	
Aunt or uncle	29 (17·4%)	
Sibling	12 (7·2%)	
Other	11 (6·7%)	
Isolation required in 64 (2·56%)		

Regional Adenitis and Abscess Formation

Regional adenitis or abscess occurred in 46 cases (1.84%) of this series of 2,500 infants. This is a minimal estimate, as no doubt there have been other cases which have been treated elsewhere and are not personally known at the clinic. Table IV summarizes the incidence, treatment, and also the bacteriological report where available.

TABLE IV.—*Incidence of Regional Adenitis Among* 2,500 *B.C.G. Vaccinations in Infants*

Cases of regional adenitis		46 (1·84%)
Single	27	
Multiple	19	
Simple adenitis		28 (1·12%)
Adenitis with abscess formation		18 (0·72%)
Spontaneous rupture	3	
Incision required*	15	

*Bacteriology of pus: B.C.G. recovered, 4; other organisms, 4; sterile, 4; no information, 3.

As previously mentioned, it is considered that in most cases this complication occurs as a result of faulty technique, where a greater or less amount of vaccine is injected subcutaneously instead of intradermally, and this is especially apt to occur in babies well endowed with subcutaneous fat.

In qualification of this statement with regard to technical failure, it should be noted that the strength and viability of the organism in the vaccine culture are not as constant as assurances would lead one to believe. In this series covering 13 months, in which 56 weekly batches of vaccine have been used, adenitis occurred in 14 different or consecutive batches of vaccine, whereas without this factor being involved one would expect a more even distribution of the complication.

Experience shows that if abscess formation occurs in the first eight weeks after vaccination it is usually due to secondary infection of the vaccination site; if it occurs within six months B.C.G. organisms are almost invariably recovered from the pus; whereas if it occurs after this period the pus is usually sterile.

Treatment of the adenitis is conservative. If an abscess is red, tense, and points on the skin it is dealt with by simple incision and evacuation, and the application of a sterile dressing. Formerly these abscesses were aspirated as recommended by the Danish authorities, but this practice has been abandoned in favour of incision and would appear now to be more generally acceptable. No abscess has had to be reopened, though a second abscess in the same child at a different site has occasionally required incision. Even in cases with multiple abscesses there has not been any case in which the infant's general health has suffered or in which the hilar glands have been involved. A few cases have been reported at the clinic after spontaneous rupture; these have been treated with ultra-violet light and have dried almost immediately, and healed after half a dozen exposures. In a small proportion of cases in which superficial ulceration at the site of the local lesion has discharged for more than a week it has almost invariably been found that an occlusive elastic dressing has been applied at home. This tends to produce a weeping eczematous area around the vaccination, and should be replaced by a loose piece of sterile gauze or lint. The discharge then ceases and the lesion heals.

Summary and Conclusions

This study presents the findings in 2,500 consecutive cases of infant vaccination against tuberculosis with B.C.G. vaccine. The normal procedure with uncompli-

cated cases is discussed, and also the different procedures involved in contact cases and with premature infants.

The complications of vaccination have been estimated and the methods used for combating them are described. A personal view is submitted regarding the desirability of adhering to the recommended dosage. The infant mortality in this series is compared with the death rate in infants under 1 year for Belfast city.

In conclusion it is shown that since the introduction of infant vaccination with B.C.G. no anxiety has arisen and no major problems have had to be overcome. In addition, it is an admirable and simple way of further propagating information about the prevention of tuberculosis in a population which is already very conscious of the problem. There has been an excellent and increasing response to the introduction of B.C.G. among parents, and it has, in general, been warmly welcomed by practitioners and health authorities alike. It will be for posterity to judge the ultimate value of this preventive measure. A most careful follow-up of these cases is indicated.

I have to thank all my colleagues, obstetrical and paediatric, for their co-operation in this work, and particularly Professor F. M. B. Allen for his unfailing support and encouragement in the use of B.C.G. vaccine in Northern Ireland.

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CHANGES IN SKIN RESPONSE IN ASTHMA

A SKIN-TEST FOLLOW-UP OF ASTHMATICS

BY

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The use of skin-testing as a method of diagnosis in asthmatic patients, while generally accepted and more or less implicitly relied on by specialists in allergic disease, is still a controversial topic among general physicians and general practitioners. The idea of determining the sensitivity of the bronchial mucosa by applying the suspected agent in one way or another to the epidermis is to many somewhat fantastic. It is, of course, now generally recognized that allergic sensitivity is only one of the aetiological factors in the asthmatic reaction, but it seems to be equally widely agreed that it is an important one.

The disagreement comes when an attempt is made to assess just how important it is. The unbiased observer who nevertheless has some experience of the investigation and treatment of asthmatic persons would probably sum up the position by saying that it all depends. In some patients allergic sensitivity is the major cause of the symptoms; in some it is one among several equally important factors; and in others it is of no importance at all. In the present article this view is accepted as probably correct.

The survey and analysis presented are an attempt to contribute towards the answers to two questions: (1) What changes, if any, occur in skin reactions over the years? (2) What is the significance, if any, of such changes (or, alternatively, the absence of any changes) in relation to the clinical progress of a series of asthmatic patients?

From a personal study of the literature, as well as from a careful search kindly made for me by the Library of the Royal Society of Medicine, it seemed that such a combined follow-up of a series of cases had not, so far, been carried out.

For some years I have conducted a special out-patient session, to which I can refer those persons suffering from bronchial asthma who attend my general out-patient morning session. This originated from experience of the chaos caused in a general out-patient clinic by an attempt to investigate and advise the asthmatic patient on the spot. Inevitably clinical material accumulates in such circumstances, and one is faced with the obligation to analyse it.

Skin-test Method

An early problem confronting anyone who attempts to do more than pacify the asthmatic and his relatives is the skin-test method. How important is it? What does it mean? At first I took the view that it probably had a place in the confirmation of allergic sensitivities suggested by the history of the case. I was warned that most people would show reactions, and that I would either be deceived or merely confused by the high proportion of positive results. It was therefore with some surprise that I found my difficulty to be the large number of negative results in patients with strongly "positive" histories. The potency of the solutions used seemed to be proved by the intensity of the reactions when they did occur.

Confidence in the method as a valuable aid to diagnosis naturally declined, and for a number of years relatively few patients were investigated in this way. However, clinical experience forced one to the conclusion that allergic sensitivity was a most variable quality, appearing, disappearing, and varying in an inconsequential manner, for which the skin-testing method could not be blamed; and it seemed worth while to see if this was clearly shown in the records of those cases which were available. About six years ago, therefore, a number of energetic skin testers, armed with a battery of syringes, were assembled, and those patients previously tested were summoned. The response was so poor that the survey did not yield any significant results.

It was therefore determined to carry out a minimum routine number of skin tests on every adult patient attending, and to repeat the follow-up testing on a larger series at a later date. This has just been done, and the results, though not as numerically valuable as was originally hoped, are interesting enough to warrant publication.

The actual testing was carried out by two independent observers, who also noted the patient's own assessment of his symptoms over the intervening years since the previous testing. I did not see the patients at all when they attended for this special purpose, and the observers who did see and test them took no part whatever in the original assessment, the original testing, or in the analysis.

The tests carried out in this series were group mixtures for the most part, including the common inhalant allergens (household dusts, clothing materials, pollen dusts, etc.), but excluding foodstuffs. Friedewald (1952), in a study of 1,900 cases, came to the convincing conclusion that skin-testing with solutions or other preparations of foods was so much waste of time. No apology is therefore made for the policy adopted in this connexion, nor is it thought necessary to go into all the arguments for and against the testing of foods by any method other than that of dieting.

The survey comprises only a small proportion of the total number of cases attending the special out-patient session, and indeed not many of those in whom skin tests had been