conditions of our experiments, the inactive representatives did not. This association suggests that the mechanism of the chemotherapeutic action and that of the depression of sensitivity may have some common factor. Nevertheless, it must be admitted that there is at present little evidence in favour of the closer relationship of cause and effect—i.e., that the antituberculous effect is in fact due to desensitization. For although the many previous attempts to desensitize tuberculous guinea-pigs have had to be made with tuberculin, the results, taken as a whole, suggest little, if any, advantage to the host. Moreover, the present surface-active agents are equally effective in mouse and guinea-pig tuberculosis, in spite of the very different levels of allergy in these two species. Thus a tuberculin skin reaction cannot be elicited in the tuberculous mouse; and, although this animal can manifest a systemic reaction when tuberculin is given intravenously, much larger doses are required than in the guinea-pig (Smith, 1928; Rees and Hart, 1952). The influence on experimental tuberculosis of a number of other substances that depress tuberculin sensitivity, such as N-acetyl-sphingosine (Fisher *et al.*, 1951), dehydroascorbic acid and alloxan (Long *et al.*, 1951c), will be investigated. If these anti-allergic substances should also prove antituberculous, the hypothesis of a causal connexion between desensitization and chemotherapeutic activity would be strengthened.

Summary

The development of experimental tuberculosis in guinea-pigs is markedly inhibited by injection of certain surface-active polyoxyethylene ethers. Using the response to intracutaneous tuberculin as a measure of allergic hypersensitivity in albino guinea-pigs infected with B.C.G., we find that:

- (1) Single subcutaneous or intravenous injections of these drugs diminish sensitivity to a degree comparable to that of cortisone.
- (2) The chemotherapeutically active representatives of the series diminish tuberculin sensitivity, whereas the inactive members fail to do so.
- (3) Their mode of action differs from that of cortisone, since it is independent of dietary factors and of thyroid activity.
- (4) Neither D2a, a chemotherapeutically active detergent, nor cortisone, in heavy continual dosage, depressed skin sensitivity to diphtheria toxin, or antitoxin levels, in guinea-pigs immunized with diphtheria toxoid (in this experiment the animals were sensitized with dead tubercle bacilli). Both drugs depressed tuberculin sensitivity.
- (5) The possible mode of action of these surface-active agents is discussed.

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TUBERCULOSIS IN FAMILIES WITH B.C.G.-VACCINATED AND NON- VACCINATED CHILDREN*

BY

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Since the introduction of B.C.G. vaccination 25 years ago much has been written to prove or disprove its value. In the Scandinavian countries, in particular, investigators gradually became convinced that the Calmette-Guérin vaccine had a very important part to play in the prevention of primary tuberculosis in both children and adults.

Many workers all over the world have reported surveys demonstrating the protective value of the vaccine. Others found little evidence to support this view. The problem of carrying out controlled investigations to cover all possible variables has made it very difficult to assess its true value. The report of an outbreak of tuberculosis in a school in Denmark in 1943, investigated by Hyge (1947), fulfilled many of the conditions necessary for a true analysis of the protective value of B.C.G. vaccination. The reports of Heimbeck (1929, 1932), Rosenthal, Blahd, and Leslie (1945), and Aronson (1948) are examples of investigations with different types of control groups.

Another approach to the problem is to examine those families in whom some children have been vaccinated and others not. The number of reports of such families in the literature are few. In France, Bertoye (1936) described a family of four children. The second child was vaccinated at birth because it was customary to vaccinate all infants at the maternity hospital where the child was born. In June, 1935, a domestic servant had an unexpected haemoptysis. She was immediately removed to hospital and the diagnosis of tuberculosis confirmed. The following month the three non-vaccinated children (aged 8, 5, and 1½ years) each developed a fever with hilar adenitis and a positive tuberculin reaction. The youngest child later died of tuberculous meningitis. The vaccinated child (aged 6 years) remained quite well.

Selection of Families

A search was made in the records of the Norrtull's Hospital, the Samariten Hospital, and the Central Tuberculosis Dispensary, Stockholm, for families satisfying all the following conditions:

1. That some children in the family had been vaccinated with B.C.G. and some not.
2. That every child said to have been B.C.G.-vaccinated was actually vaccinated and had been negative to 1 mg. of old tuberculin at the time of vaccination. (All B.C.G. vaccinations and the post-vaccinal tests are notified to the Central Tuberculosis Dispensary, and the records were consulted.)
3. That the tuberculin reaction was positive at the time of the check test (at about three months in infants and six weeks in older children).
4. That the tuberculin test had become positive following the vaccination before the time of exposure to an active case of adult tuberculosis.

*This work was carried out at the Paediatric Clinic of the Karolinska Institute, Norrtull's Hospital, Stockholm, during the period of tenure of a Cow and Gate Travelling Scholarship from the Department of Child Health, Queen's University, Belfast.

5. That all the children in the family (and, in this series, in all the families) had been vaccinated with vaccine made in the one laboratory—the Bacteriological Laboratory in Gothenburg.

6. That there was a definite confirmed case of active tuberculosis as the source of infection.

7. That all the children in the family had been in contact with the source of infection.

8. That the duration and time of contact with that case of tuberculosis (the source of infection) was the same for all the children.

In general, it may be stated that all families with B.C.G.-vaccinated and non-vaccinated children exposed to a known source of infection, and irrespective of whether or not there was any case of tuberculosis among the children, are included.

Family 1 (4 Children, 2 Adults)

One of twins, a girl aged 2 years, developed erythema nodosum in July, 1946. She was found to have x-ray evidence of primary tuberculosis, and a tuberculin-jelly test was positive. She was known to have been tuberculin-negative in February, 1946. She had not been vaccinated with B.C.G. When the family was called for a check-up it was found that the other twin, a boy, had an active hilar adenitis and was tuberculin-positive. He also had never been B.C.G.-vaccinated, but was known to have been tuberculin-negative in November, 1945.

The other two children had been B.C.G.-vaccinated—the 17-year-old girl in April, 1944, and the 16-year-old girl a year later. When examined on September 2, 1946, both had normal chest x-ray films and were Mantoux-positive. Repeat examinations in September, 1947, and September, 1948, showed normal chest x-ray films and positive Mantoux reactions.

In August, 1946, the mother was Mantoux-positive and had a normal chest x-ray film. Repeat yearly chest x-ray films up to 1951 remained normal. (She was also known to have had a normal chest x-ray film in March, 1934.) In August, 1946, the father was found to have active tuberculosis, with a positive sputum.

Family 2 (3 Children, 2 Adults)

The mother was discovered to have active tuberculosis with a positive sputum in April, 1949. On follow-up the same month the father's chest x-ray film was clear.

The three children were examined early in May, 1949. One, a 7-year-old girl who had not previously been B.C.G.-vaccinated, was discovered to have active primary tuberculosis with a positive tuberculin-jelly reaction. No previous tuberculin tests were known. At the time of examination she was found to have a pyrexia, which lasted two weeks. This was considered to be the initial fever.

The other two children had been B.C.G.-vaccinated—the 8-year-old boy in November, 1948, and the other boy, aged 10, the previous year. Both had normal chest x-ray films and were positive to tuberculin-jelly tests.

Family 3 (4 Children, 2 Adults)

The mother of this family had pleurisy in 1942 and developed lupus vulgaris in November, 1946. At this time her chest x-ray film showed nothing very definite—there was just a suspicion of a slight interlobar effusion. A year later her chest x-ray film was normal. However, in May, 1948, she was found to have pulmonary tuberculosis. On follow-up the same month (May, 1948) the father's x-ray film was normal, but a 14-year-old boy was found to have a raised temperature (considered the initial fever), persisting for some weeks. His x-ray film showed primary tuberculosis and his Mantoux reaction was positive. There was no knowledge of previous tuberculin tests and he had not been B.C.G.-vaccinated.

Two boys, aged 4 and 5 years, were B.C.G.-vaccinated in 1944 and 1943 respectively. The 15-year-old girl had been

B.C.G.-vaccinated in 1941. These three children had normal chest x-ray films and were positive to tuberculin tests in May, 1948.

Family 4 (3 Children, 2 Adults)

A 4-year-old boy was found to be positive to the tuberculin-jelly test and to have a hilar adenitis in October, 1948. His E.S.R. was 34 mm. in one hour. The previous June he was known to have had a rise in temperature lasting about three weeks. This may have been the initial fever. There was no knowledge of previous tuberculin tests and he had never been B.C.G.-vaccinated.

At a follow-up examination in November, 1948, a second boy, aged 6 years, was found to have primary tuberculosis. His tuberculin-jelly reaction was positive and his E.S.R. 41 mm. in one hour. Tubercle bacilli were isolated from his gastric washings. This boy also had a history of a rise in temperature in June, 1948. Again there were no known tuberculin tests, and he had not been B.C.G.-vaccinated.

The third child, a boy aged 14, had been vaccinated with B.C.G. in November, 1945. On follow-up examination in December, 1948, he was positive to tuberculin jelly and his chest x-ray film was normal.

The parents were examined in December, 1948. The father's chest x-ray film showed active tuberculosis. He also gave a history of an attack of pneumonia the previous May. At this time the mother's x-ray film showed some suspicious changes, and these progressed to obvious active disease within a year. Her Mantoux reaction was positive.

Family 5 (2 Children, 2 Adults)

A 2-year-old boy was negative to the tuberculin-jelly test in May, 1946. In June, 1946, this test was strongly positive, and he was found to have an active hilar adenitis. He ran a high temperature—the initial fever—for a fortnight. He had not been B.C.G.-vaccinated.

At a follow-up examination in June, 1946, his 5-year-old brother, who had been vaccinated with B.C.G. in the autumn of 1945, had a positive tuberculin-jelly reaction and a normal chest x-ray film.

The mother was examined the same month. She was tuberculin-positive and an x-ray film of her chest was normal. Yearly repeat examinations for the next four years were clear. The father was examined in July, 1946. His chest x-ray film showed active tuberculosis and his sputum contained tubercle bacilli.

Family 6 (4 Children, 2 Adults)

On Christmas Eve, 1947, three of the children (girls aged 3, 4, and 6 years) developed erythema nodosum. All were positive to tuberculin-jelly tests and suffering from primary tuberculosis. There were no known previous tuberculin tests, and none of them had been vaccinated with B.C.G.

At a follow-up examination the 2-year-old girl, who had been B.C.G.-vaccinated shortly after birth in November, 1945, was found to have some suspicious enlargement of the hilar glands and to be tuberculin-positive. She had a history of having just recovered from whooping-cough. Her hilar shadows were considered to be within normal limits in three months and again a year later.

The follow-up examination showed that chest x-ray films of both parents were normal. It was then found that an uncle had arrived on November 21, 1947, and stayed with them for three weeks; during this time he had become ill. He was admitted to a sanatorium on January 4, 1948, with cavitation and a positive sputum.

Family 7 (3 Children, 2 Adults)

A boy aged 4 years was first seen in October, 1949, and there was a history of his "not being well" since the previous July, when he was known to have had a rise in temperature for some weeks. He was found to be positive to tuberculin jelly and had a primary complex. On looking

back it was thought that his initial fever may have occurred in July. He had never been vaccinated with B.C.G. and he was not known to have had any previous tuberculin tests.

At a follow-up examination in October, 1949, the 11-year-old boy was also found to have a positive tuberculin reaction. At first his chest x-ray film was suspicious. His E.S.R. was 7 mm. in one hour. Further x-ray films did not show any change and there was little evidence of active disease at any time. He had not been B.C.G.-vaccinated and he was not known to have had any previous tuberculin tests.

The 8-year-old girl, who had been vaccinated with B.C.G. the previous year, had a normal chest x-ray film and was Mantoux-positive (1 mg.).

Both parents were examined in October, 1949. Their chest x-ray films were normal and both were positive to 0.05 mg. of old tuberculin.

It was then found that the three children had been staying with their grandmother during the summer. She was examined in the local tuberculosis clinic in October, 1949, and evidence of old changes was found on the chest x-ray film. During this investigation a suspicion arose that a friend of the family with whom the children had been in contact might be the source. He was called for examination and was found to be Mantoux-positive (0.05 mg.). His chest x-ray film showed active tuberculosis, and tubercle bacilli were isolated from his sputum during the first week of November, 1949.

Family 8 (2 Children, 2 Adults)

The mother's sister was found to have tuberculosis in 1947. Tubercle bacilli were present in her sputum, and she died two years later. She was known to have had a chest lesion in 1941.

At a follow-up examination in April, 1947, the 6-year-old boy was found to be positive to the tuberculin-jelly test and to show radiological evidence of primary tuberculosis. Besides the recent contact with his aunt, he had lived with her for a period in 1943. However, his chest x-ray films were normal in October, 1945, and June, 1946. He had not been vaccinated with B.C.G.

His 5-year-old sister was B.C.G.-vaccinated in 1941. There is some doubt about the post-vaccinal tuberculin test. The case records showed her to have been positive then, but the mother could not recall it. She was now tuberculin-positive. She had normal x-ray films between January, 1945, and April, 1947. In November, 1947, there was some degree of hilar enlargement, but an x-ray film six weeks later was normal. Her E.S.R. in April and December, 1947, was 5 mm. in one hour, and in March, 1948, 10 mm. in one hour.

A third child*, a boy, was born in September, 1946, and vaccinated with B.C.G. a short time after birth. He was kept in a children's home for his first year of life and never had any contact with his tuberculous aunt. Six x-ray films between November, 1947, and January, 1951, were normal. Yearly tuberculin tests up to January, 1951, remained positive.

The parents' x-ray films did not show any evidence of tuberculosis, but the mother did have a lesion in 1942. She never had any tubercle bacilli in her sputum.

Family 9 (2 Children, 2 Adults)

The father of this family was found to have active tuberculosis in November, 1948, and a positive sputum. His Mantoux reaction (0.05 mg.) was positive. His wife had been B.C.G.-vaccinated in November, 1947. On follow-up she was still Mantoux-positive (0.05 mg.) and had a normal chest x-ray film.

*This child is excluded from the investigation as he had no contact with the source of infection. The other two children had three possible times of infection—from the aunt in 1941, their mother in 1942, and again their aunt in 1947. In view of the x-ray findings it seems likely that these children were infected just before the aunt was discovered, in April, 1947, to have become active again.

The 2-year-old girl was examined in the first week of January, 1949. She was positive to the tuberculin-jelly test and had an active hilar adenitis. A few weeks later her E.S.R. was 40 mm. in one hour. There was also a history of a rise in temperature just before Christmas, 1948, and it was thought possible that this may have been the initial fever. She had not been vaccinated with B.C.G., and there were no known previous tuberculin tests.

An 11-months-old boy had been B.C.G.-vaccinated at birth. His chest x-ray film was normal and a tuberculin-jelly test was positive.

Family 10 (2 Children, 2 Adults)

An uncle of these children was known to have had tuberculosis in 1944 and to be Mantoux-positive. The two children were in contact with him off and on from the spring of 1946 to the beginning of 1947. He was then discovered to have tubercle bacilli in his sputum.

At a follow-up examination in March, 1947, the 4½-year-old girl was positive to the tuberculin-jelly test and had active primary tuberculosis. She had not been vaccinated with B.C.G., but was known to have been tuberculin-negative three months before.

The 15-year-old boy had been B.C.G.-vaccinated in 1944. His Mantoux (0.05 mg.) was positive and his chest x-ray film normal.

Both parents, when examined in March, 1947, were Mantoux-positive (0.05 mg.) and their chest x-ray films normal.

Family 11 (4 Children, 2 Adults)

A 4-year-old girl was found to be positive to the tuberculin-jelly test in the second week of January, 1950, and to have primary tuberculosis. No previous tuberculin tests were known, and she had not been B.C.G.-vaccinated.

At a follow-up examination the same month the 7-year-old boy was found to be positive to the tuberculin-jelly test and to have active hilar adenitis. It was considered that a rise in temperature he had had in December, 1949, may have been the initial fever. There were no known previous tuberculin tests and he had not been vaccinated with B.C.G.

The 1-year-old boy had been B.C.G.-vaccinated at birth and the 11-year-old boy over two years previously. Both were tuberculin-positive and had normal chest x-ray films.

When the father was examined he was found to have evidence of active tuberculosis. There was no record of the mother having been x-rayed.

Family 12 (2 Children, 2 Adults)

After the discovery of active pulmonary tuberculosis in their aunt this family was investigated in October, 1944. This aunt had also had tuberculosis of a foot bone and erythema nodosum twice. No tubercle bacilli had ever been found in her sputum.

The 3-year-old boy was tuberculin-positive and had an active hilar adenitis. There was no knowledge of previous tuberculin tests and he had not been B.C.G.-vaccinated.

The 9-months-old boy had been B.C.G.-vaccinated at birth. His chest x-ray film was normal and he was tuberculin-positive.

The mother's chest x-ray film was clear and she was Mantoux-positive (1 mg.). The father was never traced, as he had deserted the family.

Family 13 (2 Children, 2 Adults)

The 3-year-old boy developed phlyctenular conjunctivitis in October, 1947. He was Mantoux-positive (0.05 mg.) and had active hilar adenitis. There were no known previous tuberculin tests and he had not been vaccinated with B.C.G.

At a follow-up examination in November, 1947, the 2-year-old boy, who had been B.C.G.-vaccinated at birth, was found to be positive to the tuberculin-jelly test and to have a normal chest x-ray film.

The parents were also examined in November, 1947. The mother was Mantoux-positive (0.05 mg.) and had a clear chest x-ray film. The father was also Mantoux-positive (0.05 mg.), but he had a positive sputum, and a tuberculous cavity was shown on the chest x-ray film.

Family 14 (2 Children, 2 Adults)

A 1½-year-old boy was admitted to hospital with erythema nodosum at the end of October, 1945. His tuberculin-jelly test was positive and he had an active primary tuberculosis. There were no known previous tuberculin tests and he had not been vaccinated with B.C.G.

The 4-year-old boy had been B.C.G.-vaccinated in November, 1942. In November, 1945, he was tuberculin-positive and his chest x-ray film was clear.

Both parents were Mantoux-positive and had clear x-ray films. An aunt with whom the children had been in contact was now suspected. She had a positive sputum, and multiple cavities were shown on an x-ray film. She died seven months later.

Family 15 (2 Children, 2 Adults)

A 2½-year-old boy was found on routine examination to be positive to a tuberculin-jelly test in April, 1948, and to have a hilar adenitis. There were no known previous tuberculin tests and he had not been vaccinated with B.C.G.

The 4½-year-old boy had been B.C.G.-vaccinated in April, 1946. His tuberculin-jelly test was positive and his chest x-ray film clear on follow-up examination in April, 1948.

The mother's chest x-ray film was clear and she was Mantoux-positive (0.05 mg.). The father was known to have had tuberculosis in 1940. He was examined twice yearly from then on, but was never regarded as infectious. He was at work all this time. Their maid, who was found to have active bilateral tuberculosis towards the end of 1947, was considered the source of infection.

Family 16 (3 Children, 2 Adults)

A 6-year-old boy developed chicken-pox in 1948. He did not quite recover, but remained "out of sorts." During the first few days of January, 1949, he was found to be tuberculin-positive and to have primary tuberculosis. There was no knowledge of previous tuberculin tests and he had not been vaccinated with B.C.G.

Twin girls aged 1½ years had been B.C.G.-vaccinated in July, 1947. They were both tuberculin-positive (jelly and 0.05 mg. old tuberculin) and both had normal chest x-ray films.

Both parents were also Mantoux-positive (0.05 mg.) in January, 1945, and their chest x-ray films were clear.

It was then discovered that the family had visited their grandfather between October and Christmas, 1948. (Their grandmother had died 25 years previously with tuberculosis.) The grandfather was examined in February, 1949. He was found to be tuberculin-positive and to have active tuberculosis.

Comment on Cases

The diagnosis of primary tuberculosis was confirmed by the head of each hospital. (Families 1-10 by Professor A. Wallgren at Norrtull's Hospital and families 13-16 by Professor N. M. Malmberg at the Samariten Hospital. In family 11, one child was admitted to Norrtull's and the other to the Samariten. Family 12 was seen only at the Central Tuberculosis Dispensary.) All the children not admitted to hospital, the parents, and other relatives, etc., were examined by tuberculosis medical officers in the Central Dispensary, except those, sometimes the sources of infection, living in country districts, who were examined by local tuberculosis officers and admitted to local sanatoria.

Tubercle bacilli were isolated from the gastric washings of some of the children with primary tuberculosis, but no gastric washings were carried out in the vaccinated children. Hence this part of the investigation is of no value.

Discussion

In all there were 16 families, with 22 vaccinated and 22 non-vaccinated children, and each family satisfied all the given conditions. There is therefore a group of children some of whom act as controls and the others as tests of the protective value of their B.C.G. vaccination. The source of infection for all the children, while not the same, is at least similar. Within each family the familial susceptibility to tuberculosis is probably the same, although the resistance may be influenced by the age composition of the family.

When the source of infection lies in the home, it may be assumed that each child was exposed to the maximum possible risk. The social conditions, especially overcrowding, will vary between each family, but the children in each individual family will live under the same conditions and their standard of nutrition will tend to be the same.

Why some children should have been vaccinated and others not is not very clear. It seems most likely that the mother was offered vaccination for some of the children on one particular occasion—for example, at a school medical examination, at a child welfare centre, or at a maternity hospital—but did not trouble to have the remaining children vaccinated.

One criticism might be that the non-vaccinated children were left because they were known to be tuberculin-positive. In most of the non-vaccinated children there were no known previous tuberculin tests. This, coupled with the presence of active primary disease, would make it unlikely that they had been tuberculin-positive when the other children were vaccinated with B.C.G. One possible exception might be the boy aged 11 in family 7.

There is no reason to believe that any form of selection (such as not vaccinating a child with a chronic illness) occurred among either group of children. It is often said that only the most careful and intelligent mothers will have their children vaccinated, and that this in itself is a great source of selection when using non-vaccinated children in other families as controls. This does not apply to the present series.

The question of race does not arise so far as comparison between each group is concerned, as all the children were Swedish. The possibility of an occupational risk has to be considered in the older children. All the non-vaccinated were 14 years or under (20 of the 22 were under 9 years). There can be no question of an occupational risk in this group. Four of the vaccinated children were 15 years or over; three of them were girls. Despite the known increased risk at puberty and during adolescence, especially in females, and despite a known intimate contact with a source of infection, all these four children (and a 14-year-old boy) were completely protected. Indeed, it must be expected that these older children will have a greater circle of acquaintances outside the immediate family circle and will have the added risk of a casual infection.

It is very unlikely that the question of sex is important before puberty. Age, however, is most important. It is generally accepted that children under 5 years have a much more severe reaction to a primary tuberculous infection than older children. Two of the B.C.G.-vaccinated children had suspicious x-ray films at first (families 6 and 8). Both were under 5 years old, and were the youngest in the family. This probably occurred by chance, because suspicious lesions may occur in B.C.G.-vaccinated children at any age. It is worth noting that the mother of family 6 volunteered the information that, of all her children, the youngest (aged 2) had played continuously with the source of infection for days before his tuberculosis was suspected. In neither of the cases did definite primary tuberculosis develop. On the other hand, a non-vaccinated boy aged 11 (family 7) was under suspicion at first, while his younger brother, aged 4, had a typical infection and his sister, aged 8, who was vaccinated with B.C.G., was completely protected.

Table I shows the classification of the children into four age groups, according to whether they were B.C.G.-vaccinated or not. It is seen that, in general, the vaccinated children

TABLE I

Age	Non-vaccinated			Vaccinated		
	Obvious Primary Tuberculous Complex	Suspect Primary Tuberculous Complex	Total	No Evidence of Primary Tuberculous Complex	Suspect Primary Tuberculous Complex	Total
0- ..	14	0	14	9	1	10
5- ..	6	0	6	4	1	5
10- ..	1	1	2	3	0	3
15+ ..	0	0	0	4	0	4
	21	1	22	20	2	22

were in the minority in the two lowest groups and in the majority in the highest. This is of importance, as it is likely that the young children were more at home than the older children and therefore more exposed to any source of infection within the family. It is of interest, however, to look separately at the different age groups. One child among the vaccinated in each of the two lower age groups had some clinical evidence of primary infection—that is, one of the 10 B.C.G.-vaccinated children under the age of 5 years had some evidence of primary infection, whereas all 14 of the non-vaccinated became clinically ill. Similarly, only one of the five vaccinated children between 5 and 10 years developed some evidence of primary disease, compared with obvious infection in the six non-vaccinated. The other two groups are too small for any conclusions to be drawn.

Family 1 contains two adolescent girls protected, and twins aged 2 years who developed erythema nodosum and primary tuberculosis. In family 16, twins aged 1½ years were protected and a boy of 6 years was infected. Family 3 shows a 14-year-old boy infected and a girl of 15 years and two boys aged 4 and 5 years protected. Families 9 and 12 have two children under 1 year protected, while the other children were infected. In family 11, the two protected children were aged 1 year and 11 years and the two infected children were in between (aged 4 and 7 years). Even in such a small group, then, there is evidence of protection at all ages of childhood. No cases of tuberculous meningitis or miliary tuberculosis occurred in either group.

Table II shows the distribution of the children, by families, in each group and the source of infection. In 8 of the 16 families the source was either the father or the mother; in 5 an aunt or an uncle; and in the rest a grandfather, a maid, and a friend of relatives whom that family had visited. The mother of family 8 had had tuberculosis five years before, but was not considered likely to be in-

TABLE II.—Distribution of the Children in Each Group According to Families with Source of Infection

Family	Non-vaccinated Primary Tuberculosis	B.C.G. vaccinated Tuberculin-positive but no Evidence of Active Tuberculous Infection	Source of Infection
1	2	2	Father
2	1	2	Mother
3	1	3	"
4	2	1	Father
5	1	1	"
6	3	1†	Uncle
7	2*	1	Friend of relatives
8	1	1†	Aunt
9	1	1	Father
10	1	1	Uncle
11	2	2	Father
12	1	1	Aunt
13	1	1	Father
14	1	1	Aunt
15	1	1	Maid
16	1	2	Grandfather

* One boy with no definite clinical disease.

† Each child had a suspicious x-ray film at first.

fectious at the time. The children had, however, been in contact with an aunt who was found to have active tuberculosis and who died two years later.

B.C.G. vaccination offers a relative rather than a complete protection against primary tuberculosis—that is, it raises the resistance to a subsequent superinfection with virulent organisms. It is most likely that all the vaccinated children in this series were superinfected, but only two showed a possible hilar reaction of short duration.

The incidence of tuberculosis in vaccinated and non-vaccinated children admitted to Norrtull's Hospital between 1945 and 1949 inclusive is interesting. Of 625 cases of primary tuberculosis, 26 had been vaccinated with B.C.G. (excluding 9 who had been vaccinated during the incubation period); 12 of these 26 cases were mild and 14 more or less typical, but some of the latter had been vaccinated so long before that it is very likely the immunity had disappeared. In addition, there were 137 cases with spontaneous positive tuberculin reactions. During this five-year period 1,352 vaccinated children were admitted and 7,279 non-vaccinated; and 26 (1.9%) of the vaccinated children had tuberculosis, compared with 599 (8.2%) cases among the non-vaccinated children. There were 28 cases of tuberculous meningitis and/or miliary tuberculosis in the non-vaccinated group and none in the vaccinated group. These figures are not representative of the children of Stockholm, and apply only to the hospital admissions.

The difference in the number of vaccinated and non-vaccinated is surprisingly great. This is partly explained by the fact that in the non-vaccinated group are included infants under 3 months who were vaccinated at birth but were not yet tuberculin-positive, and partly because there has been a very great increase in the number of vaccinations in recent years, so that the proportions for 1949 are quite different from those of 1945. Parallel with this rise in the number of vaccinated children there has been a fall in the number of cases of primary tuberculosis—from 183 admissions in 1945 to 88 in 1949, with an average of 123 in the intervening years.

Summary

A description is given of 16 families in which some children were vaccinated with B.C.G. and others not, and in which all had been exposed to a known source of infection. Reasons are put forward for considering the two groups comparable. Among the 22 children in the non-vaccinated group 21 developed primary tuberculosis. In the B.C.G.-vaccinated group, two at most showed some evidence of superinfection.

The protective value of B.C.G. vaccination is striking, both when the source of infection is within the family (with the maximum risk for each child) and when it is outside.

The difference in the incidence of tuberculosis in the vaccinated and non-vaccinated children admitted to Norrtull's Hospital is recorded and a brief description of the fall in the number of cases of primary tuberculosis from 1945 on is given. The absence of tuberculous meningitis and miliary tuberculosis in the vaccinated group is noted.

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