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Abstracts

1. **BGG Vaccination of Children against Leprosy: First Results of a Trial in Uganda,** by J. A. KINNEAR BROWN, and M. M. STONE, with an appendix by DR IAN SUTHERLAND. *Brit. Med. Journ.* 1966, **1**, 7–13.

A controlled trial of BCG vaccine in the prevention of leprosy started in the Teso district of Eastern Uganda in September 1960. By September 1962, 17,397 children, more than 80% of whom were aged under 10 years, had been included. All were relatives or contacts of known leprosy patients.

Those with negative reactions to an initial Heaf tuberculin test, or with Grade I or Grade II positive reactions, were allocated alternately to an unvaccinated group (8152 children) and a BCG-vaccinated group (8149 children). Those with Grade III or Grade IV reactions (1096 children) were all left unvaccinated, as were children who already had skin lesions due to leprosy.

In the course of the first follow-up of all the participants, between May 1963 and May 1964, more than 94% of the children were seen and examined for leprosy. A total of 116 cases of leprosy had developed during this period of about two years since intake. The incidence in the unvaccinated children was 11·0 per 1000, and in the vaccinated children 2·2 per 1000, which is one-fifth of the incidence in the absence of vaccination. Among those positive in Grade III or IV and left unvaccinated the incidence was 8.3 per 1000. The reduction in leprosy incidence in the vaccinated group did not appear to depend on the grade of initial tuberculin sensitivity (negative, Grade I or Grade II) nor on the age of the child at intake.

The results so far establish that BCG vaccination has conferred substantial protection against early forms of leprosy in Uganda for a period of about two years. Since these early forms may resolve spontaneously, it is of particular inportance to follow the trial population for some years to see how these lesions evolve, as well as to study the further incidence of the disease. About 8% of leprosy patients in Eastern Uganda have lepromatous leprosy, and it would be unwise to conclude that the present results will necessarily apply in other parts of the world, where the proportion of patients with lepromatous leprosy may be as high as 70%.

The Appendix by Dr IAN SUTHERLAND reports as follows:

By the end of 1961 information on the prevalence of leprosy at intake had been obtained from a total of 4542 child relatives and contacts of leprosy cases. (Children examined in the eitelas in which the intake appeared to have been loaded with unrelated patients were not included in this total). The information was used in the following manner to estimate the expected incidence of leprosy in the course of the trial.

Table A gives the findings in these 4542 children according to age, and shows the general tendency for the prevalence to rise until the age of 15. A straight line was 'fitted' to the prevalence rates to describe their upward trend, the standard statistical technique of weighted regression being used; this straight line provided an adequate fit to the data and there was no indication of curvature. The figures were therefore consistent with a steady increase in the prevalence rate of leprosy from zero at birth to a figure of over 60 per 1000 at the age of 15 years, the increase amounting to 4·62 per 1000 for each year of age.

TABLE A

Prevalence of Leprosy among 4542 Children at Intake Examination, according to Age

		Cases of Leprosy	
Age (Years)	*Total examined*	*No.*	*Prevalence per 1000*
0	633	0	0
2	810	2	2
4	934	13	14
6	749	16	21
8	546	30	55
10	345	17	49
12	309	13	42
14	165	10	61
16 or more	51	2	39
All ages	4542	103	23

If it is assumed that the population of child contacts is 'stationary'—that is, not changing in total size or age distribution—and that the risk that they will contract leprosy is also not changing, then the increase in the *prevalence* of leprosy from one year of age to the next may be taken as a minimum estimate of the annual *incidence* of the disease. (The true annual incidence of leprosy is likely to exceed this estimate, since a proportion of the cases, having developed, will from past experience resolve spontaneously and so not contribute to the prevalence at the next year of age). Subject to those assumptions, therefore, the estimated annual incidence of leprosy is this population of child contacts, in the absence of vaccination, was 4·62 per 1000 children per year.

At the time when this estimate was made a total of 4263 children (all in Grade 0, 1, or 2 initially) had been admitted to the unvaccinated group. According to the estimate 98 cases of leprosy would be expected to develop among them during a period of follow-up of five years. It was not known whether the population of child contacts was stationary, but it was suspected that, as a result of the treatment of known cases, the risk of contracting leprosy might be falling. In addition it was uncertain how effectively the participants could be traced for follow-up examinations, and whether it would be possible to continue these for as long as five years. In the circumstances it was safer to assume that perhaps only about half of the above total of 98 cases would develop and be detected in the course of the trial. If, say, 50 cases were found in the unvaccinated group, then it would not be permissible to

claim a clear benefit from BCG vaccination unless 25 or fewer cases were found in a randomly allocated vaccinated group of equal size (any lesser difference could be attributed to chance). Since it was important to be able to detect a reduction in leprosy incidence due to BCG vaccination, if it occurred, which was less than 50%, it was decided to increase the number of participants in the trial, and the intake was continued.

The final total of children in the unvaccinated group (Grade 0–II) was 8152. According to the same estimate of incidence a total of 75 cases of leprosy would have been expected to develop among these children during an average period of follow-up of two years. This may be compared with the total of 77 cases actually found in this group during the period of the first follow-up (the other 12 of the 89 cases shown in Tables IV and V had suspicious lesions which were not confirmed as leprosy until the second follow-up). Because of the various uncertainties and assumptions associated with the incidence estimate, it is clear that the agreement with reality is very much closer than could reasonably have been expected. It suggests, however, that the approach described in this appendix was not unrealistic, and represented a useful method of assessing when the intake to a trial of a prophylactic measure for a chronic disease was sufficiently large, from information obtained in the course of the intake. The approach has been placed on record in the hope that it may be useful to other workers in similar circumstances.

2. **Leprosy and Heredity** by AMADO SAUL and MANUEL DIAZ, *Dermatologia*, June 1965, Vol. 9, No. 2, pp. 157–169.

The authors presented a study in heredity in leprosy at the 2nd Mexican Congress of Dermatology held at Guadalajara, Jalisco, Mexico, April 1963. They said that leprosy is infectious and transmissible but is not considered a hereditary disease. Its attack index is very low and it is essentially familial with intra-domiciliary acquisition. A hereditary factor exists which determines whether a person, living under conditions favourable to infection, will or will not acquire the disease, and if he does, which type will develop. It is thought that an irregularly dominant factor P exists which neutralizes natural resistance and leads to the acquisition of lepromatous leprosy whereas it may be said that a person exposed to the infection, in whose family there have been no previous cases of the disease, will either show a positive Mitsuda or acquire the tuberculoid form.

The authors studied 1000 subjects, family relations in 10, and the problem of conjugal leprosy. The results seem to confirm the hereditary factor but further observations are essential.

3. **The epidermic melanocyte, tactile neurone** by A. R. AMORETTI. *Dermatologia*, June 1963, **9**, 2, pp. 197–209.

The author presents the hypothesis that the epidermal melanocyte is the prime tactile neurone. Denuded skin lacks tactile sensation and the tactile sensibility of depigmented areas is proportionate to the abundance of melanocytes. The melanocyte is the tactile cell of Merck composed of dendrites ready for stimuli. Its cellular body elaborates the stimuli and the efferent axon transmits the sensation to the second neurone which then crosses the spinal ganglia to penetrate into the posterior roots of the medulla. The temperature and pain sensations are subepidermal. In the first phases of neuritis of leprosy alterations of pain and temperature sensibilities are observed but not tactile changes. It seems that during these early phases the efferent fibres are less vulnerable than the afferent (dendrites of temperature and pain).

4. **Maintenance of cytopathic activity of Mycobacterium leprae in Eagle's medium supplemented by Mycobacterial extracts**, by A. L. OLITZKI and ZIPPORA GERSHON of the Department of Clinical Microbiology, Hadassah University Hospital and Department of Bacteriology, Hebrew University Hadassah Medical School, Jerusalem, a preliminary communication in *Israel J. of Med. Sci.* **1**, (5), 1965.

The authors point out HANK's explanation of the failure to obtain growth *in vitro* of *Mycobacterium leprae* as being due to its inability to obtain energy from the carbon sources ordinarily used. Failure has followed attempts at culture *in vitro* in human and simian cultures, and in cell-free media under symbiotic conditions with other micro organisms and an anaerobic yeast-glycerol medium. The authors tried to maintain the viability of *M. leprae* on a cell-free medium enriched by the products of saphrophytic mycobacteria (as was done in cultures of Johne's bacillus) and achieved some success with an extract of one mycobacterial strain, and succeeded in preserving the biological activity of *M. leprae* for a period of at least 5 months.

The separation of *M. leprae* from the host tissues was achieved as follows:

A nodule of 500 mg. was taken from an untreated patient, triturated with glass powder in a mortar and suspended in 10 ml. of phosphate-saline solution of pH 7.2. The cell debris was removed by centrifugation at 1000 r.p.m. for 5 min. and the bacteria were collected from the supernatant fluid by refrigerated centrifugation at 10,000 r.p.m. for 20 min. This procedure was repeated and the resultant final suspension contained acid-fast bacilli which failed to grow on Loewenstein medium.

The extracts of a typical mycobacteria were prepared as follows: three strains of atypical mycobacteria were transferred to fresh Loewenstein medium and harvested after a suitable period of incubation in 5 ml. of saline/slope. After a treatment for 3 min. in MSE-ultrasonic power unit at 150 v. the bacterial residues were removed by 2 subsequent filtrations through 3 Sl Seitz filters. The filtrates were aoutclaved and tested for sterility on Loewenstein medium.

The authors give 2 Tables and 2 illustrative figures and 2 summaries, 1 in French and 1 in Spanish' It would be useful to translate these.

'The biological activities of *Mycobacterium leprae* have been observed, and used as indicators of their viability *in vitro* (1) The production of a cytopathic substance which acts on the cultures of murine monocytes. (2) The production of an increasing turbidity in the Eagle medium enriched by a sonic extract of a saphrophytic mycobacterium.

After 4 consecutive passages in this medium, which extended over a period of 5 months after the separation of the bacteria from the tissues of the host, the biological activities still persist.

Note. The reference to murine monocyte cultures is referred to in Fig. 2).