POSITIVE BACILLARY FINDINGS IN THE SKIN OF CONTACTS OF LEPROSY PATIENTS [1]

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INTRODUCTION

Early in the course of work in the treatment and investigation of patients at the clinic of the Acworth Leper Home, the need for some system of follow-up of patients was acutely felt, as an appreciable number of patients ceased attending and observation of the results of treatment was frequently interrupted. It was practically impossible to carry out an examination of contacts of the patients who attended the clinic. Such examinations could only be made on some of those who accompanied the patients on their first visit.

A system of home visits by health visitors, specially trained for the purpose late in 1942, was therefore introduced as described elsewhere (3). The follow-up of patients through health visitors led not only to an extended knowledge of the disease in patients generally, but also brought accurate data on the examination of contacts within easy reach.

In addition to detection of early cases of leprosy among the contacts, a close study revealed positive bacillary findings repeatedly in 25 contacts, who surprisingly enough exhibited no signs of the disease.

The first of these cases was from among the few contacts examined before the system of home visits was introduced. This patient was under observation for 7 years and was treated with hydnocreol for the first 2 years of this period. Positive findings, however, continued to be obtained throughout the succeeding 5 years.

The other 24 cases were discovered after a large number of examinations of contacts was made possible through the efforts of the health visitors. Six of these were treated with daily intravenous injections of glucose, 25 per cent in doses of 25 cc. for 3 to 4 months. At the end of this period all were negative for acid-

[1] Reprinted, on recommendation of Dr. R. G. Cochrane, from the *Indian Journal of Medical Sciences* **3** (1949) 253-265, somewhat condensed and with the elimination of one lengthy table.

fast bacilli, but in 2 of them positive findings were again obtained after a negative period of 1 and 1½ years. The remaining 18 positive contacts were not given any treatment, but were observed for periods varying from 1 week to 12 months.

EXAMINATION OF CONTACTS

The health visitors endeavour to persuade as many contacts as possible to submit to clinical and bacteriological examination at the clinic. However, 50 per cent of the contacts are not in a position to do so, either on account of lack of time or because of the inability to grasp the importance of such examination. The following table gives the number of patients, their contacts, and the results of investigation:

TABLE 1 [2]

1.	Patients whose contacts were examined	217	
2.	Contacts in the homes of these patients	1,049	
3.	Contacts examined	573	(54.6%)
4.	Examined contacts found clinically suspicious	319	(55.7%)
5.	Suspects presenting clinical and bacteriological evidence of leprosy (and the proportion of the suspects which they represent)	171	(53.6%)
6.	Examined contacts without clinical evidence of leprosy (cf item 4 above)	254	(44.3%)
7.	Contacts without clinical manifestations found bacteriologically positive	25	(9.8%)

It will be seen that of 319 contacts with suspicious signs, 171 were found to be suffering from leprosy. Of the 254 contacts who did not exhibit any suspicious signs, 25 were found positive for acid-fast bacilli in smears made from snips taken from the earlobe or the skin of the back or both. We find that the skin of the back in the middle line on either side of the spine gives positive results more frequently than any other site and is more convenient for both patient and doctor.

METHOD OF EXAMINATION

The examination of contacts involves three main lines of investigation:

(1) *Clinical*: Contacts are stripped and observed in bright sunlight. This is essential for detecting erythema, loss of hair, and slight variations in pigment and texture of the skin. Tests for sensory changes are carried out as follows: (*a*) tactile, with a wisp of cotton; (*b*) thermal, with two test tubes, one with tap water and the other with water heated to 50° to

[2] Condensed from the original, with the substitution of "suspects" for descriptive phrases.—EDITOR.

60°C.; (*c*) pain, with a pin. The 25 positive contacts showed no abnormalities and complained of no symptoms referable to leprosy.

(2) *Bacteriological:* Lowe (5), writing on tuberculoid leprosy, stated that increased care in the examinations, studying not one but if necessary six or eight sections, increased the positive findings from perhaps 10 per cent to about 60 per cent. This observation is also true of the examination of smears from snips of skin lesions of neural cases, and our positive findings have increased from 20 per cent to 43 per cent. It was found that at least half an hour was necessary for a thorough examination of a slide showing 4 or 5 bacilli in 100 fields. The same care was exercised in the examination of contacts.

The procedure of making smears from snips of the skin and earlobe of contacts is as follows: The surface is washed with 5 per cent carbolic lotion and wiped with a swab of rectified spirit. Instruments—scalpels, forceps, etc.—are sterilized by boiling and passing them through the Bunsen flame a few seconds. A small piece of skin, 2 to 3 mm. deep, is taken and pressed on an unused, cleaned slide, and a smear is made. Scrapings from the cut surface of the skin are also added to the smear, which is carefully fixed with heat. To stain, carbol-fuchsin is filtered on the slide and allowed to remain for 20 minutes. The slide is then washed in running water, decolourised for a few seconds with a solution containing 5 parts of concentrated hydrochloric acid, 75 of rectified spirit and 20 of distilled water, washed again, and counterstained with Loffler's methylene blue for one minute. Smears of nasal scrapings taken from the septum are stained similarly.

In this manner smears from snips of the skin of the back and earlobe and nasal scrapings were taken and examined on 2 occasions in 5, on 3 occasions in 7, and 4 to 10 times in 13 of the 25 positive contacts during a period of from 1 week to 7 years.

(3) *Immunological:* Cochrane (1) is of the opinion that the lepromin reaction can be positive only in the presence of a primary focus, and is therefore analogous to the Mantoux test. His opinion is based on his observation that a positive lepromin test in a monkey is not obtained without previously inoculating the animal with a nodule from a patient with leprosy.

The lepromin test was done in 9 of the 25 positive contacts, and all 9 gave positive results. The refined lepromin of Dharmendra was used to avoid any reaction produced by extraneous tissue material. Of these positive reactions, 7 were contacts of lepromatous patients, 1 of a positive neural, and 1 of a negative neural case.

RESULTS OF EXAMINATION

The examinations of the 25 positive contacts revealed from 4 to 25 bacilli in 100 microscopic fields in the skin alone of 5, and in both skin and earlobe of 20. Smears from the nasal scrapings taken at the same time gave negative results in all.

The bacilli were acid- and alcohol-fast, slightly curved rods, with rounded ends and uniformly stained, giving a beaded or fragmented appearance with pale connecting links. Figs. 1 and 2 show the bacilli found in the skin of the back in 2 of the 25 positive contacts.

In four of these positive contacts, lesions developed later during the period of observation. These cases are described below:

(1) D. B., female, aged 30 years. Husband an Na_2s_2 case (positive neural). No clinical lesion. Bacteriological examination made on December 12, 1939, positive in the skin of the back and earlobe. This examination repeated on 9 occasions at intervals of 1 to 32 months gave the same results on all occasions, 5 to 16 bacilli being detected in 100 fields. Nasal scrapings were negative throughout. One and one-half years after the first examination, small hypopigmented macules appearing on the neck, and later on the legs. No sensory changes could be detected. One of the lesions on the neck was positive for bacilli, the skin and earlobe also being positive at the same time.

(2) A. M., male aged 19 years. Father an L_2N_2 case. No clinical lesion. Bacteriological examination, August 31, 1946, positive in the skin of the back. Repeated on 4 occasions at intervals of 3 weeks to 4 months, with positive results in the skin on the first repetition and in both skin and earlobe on the next 2 occasions, 5 to 8 bacilli being found in 100 fields. The last examination was negative. Nasal scrapings were negative throughout. Seven months after the first examination, a hypopigmented, raised, circular macule, 1 inch in diameter, was observed on the right forearm. There was no sensory change at first, but after 3½ months tactile and thermal sensory disturbances were demonstrable. Bacteriological examination of the lesion gave negative results, and the nose, the skin of the back, and earlobe were also negative. Lepromin, 1½ months after the first examination, positive.

(3) R. B., female, aged 40 years. Husband an Na_2s_2 case (positive neural). No clinical lesion. Bacteriological examination, March 20, 1946, positive in the skin. Repeated 5 times at intervals of 1 week to 4 months, with similar positive results on all occasions except the last, 4 to 8 bacilli being found in 100 fields. The earlobes and nose were negative throughout. Five small hypopigmented macules with disturbances of tactile and thermal sensations were observed 12 months after the first examination on the lower extremities. Examination of one of the lesions showed 6 bacilli, but the skin of the back, the earlobe and nasal scrapings were negative. Lepromin, 7 months after the first examination, positive.

(4) E. D., male, aged 50 years. Wife an L_2 case. No clinical lesion. Bacteriological examination, March 11, 1946, positive in the skin and earlobe. Repeated on 5 occasions at intervals of 1 week to 3 months, with similar findings every time except the last, 5 to 11 bacilli being found in 100 fields. Nasal scrapings were negative throughout. Eight months after the first examination, 2 hypopigmented flat macules, each about 1 inch in diameter, were observed on the left arm and the back. Tactile and thermal sensations impaired. Bacteriological examination of the lesions gave nega-

tive results, as did nasal scrapings and snips of the skin of the back and earlobe. Lepromin, 5½ months after the first examination, positive.[3]

DISCUSSION

Certain phases of leprosy which might be confused with the 25 contacts in whom the positive bacillary findings were made are the "hazy" patches of Chiyuto and Rodriguez (1), the "juvenile leprosy" of Muir (6), termed "pre-lepromatous maculae or incipient lesions of childhood" (and occasionally of adults) by Cochrane (1), and the earlier stages of diffuse lepromatous leprosy.

In the pre-lepromatous or incipient lesions of childhood, the main characteristics as described by Cochrane are: small multiple, hypopigmented patches with the appearance and distribution of lepromatous rather than neural leprosy. That is, the lesions are slightly shiny, indicating some erythema, with the periphery fading imperceptibility into the surrounding normal skin. There is no nerve enlargement or anaesthesia of the extremities, and the lesions are negative to standard methods of examination. Lepromin is also negative.

Cases of diffuse lepromatous leprosy in the early stages are very difficult to detect because no actual lesions are demonstrable (1). Cases with wide-spread infiltration have often escaped clinical detection even under expert examination, and yet bacteriological examination showed massive infection of the skin (6). Constant features of this stage of leprosy are the ease with which fairly large numbers of bacilli are found and the negative reaction to lepromin.

The above stages of the disease and the positive contacts presented in this paper are tabulated for comparison (Table 2). It will be seen that the positive contacts differ from the two stages of leprosy mentioned in two essentials: the number of bacilli, and the result of the lepromin test. What then is the significance of positive bacillary findings in individuals residing wth leprosy patients? Are these persons in a very early stage of the disease? And if so, to what classification do they belong?

The acid-fast bacilli found presented all the morphological and staining characteristics of *M. leprae*. Further, the individuals were all residing with leprosy cases—14 with lepromatous cases, 8 with bacteriologically positive neural cases, 3 with bacteriologically negative neural cases. It is not suggested that the

[3] The original article at this point contains a five-page tabulation of the data of all of the 25 cases found bacteriologically positive.—EDITOR.

TABLE 2.

Type	Clinical findings	Bacteriological findings	Immunological findings
Pre-lepromatous or incipient lesions of childhood.	Definite lesions, visible as hypopigmented areas with ill-defined margins	Negative for acid-fast bacilli by standard methods of examination.	Negative to lepromin.
Early diffuse lepromatous leprosy.	No clinical lesions demonstrable.	Fairly large numbers of acid-fast bacilli.	Negative to lepromin.
Positive contacts.	No clinical lesions demonstrable.	Very small number of acid-fast bacilli.	Positive to lepromin (9 out of 9).

3 negative neural cases were responsible for infecting their contacts. There was probably some lepromatous patient responsible for this damage to the contacts, and some such source must be presumed to explain the causation of the disease in the neural cases, but we have not personally been able to trace such sources. Only those patients residing with the contacts have been seen.

The development of clinical lesions in four of the positive contacts is not without its significance. The lesions could have been caused only by the presence of *M. leprae* in the skin, and that the acid-fast bacilli found in the skin are the *M. leprae* concerned is therefore the logical conclusion.

Further, lepromin gave positive reactions in all 9 of the positive contacts tested, and in the opinion of Cochrane "a lepromin reaction (excluding the reaction produced by extraneous tissue material) can only be positive in the presence of a primary focus, and is therefore analogous to the Mantoux test."

Sorel (7) and Leboeuf (4) have found *M. leprae* in the lymph glands of apparently normal individuals living in close association with persons suffering from leprosy.

It is the hypothesis of Cochrane (1) that:

> . . . when infection takes place one of three things may happen: (1) The person may never develop leprosy and thus no indication of a previous infection is available. (2) The person may develop leprosy which shows itself in clinical lesions which may remain stationary or disappear entirely either by themselves or as a result of the development of tissue immunity. (3) The lesions may progress and the person become an advanced case of leprosy.

The above is based on the theory:

> . . . that wandering cells of the body are probably able to deal by phagocytosis with considerable numbers of bacilli, if introduced into the body; but if this is impossible because of the numbers of bacilli introduced by the

original inoculation or inoculations or for some other as yet unknown reason, then the bacilli pass to the skin and clinical lesions make their appearance.

It is therefore not unlikely that bacilli exist in the skin for some time before clinical lesions develop, and hence the presence of *M. leprae* in the skin is not incompatible in the absence of clinical lesions. The 25 contacts described in this paper may therefore be classed as group (2) above, with the difference that they have developed leprosy which shows itself, not in clinical lesions, but as a bacillary invasion of the skin, a stage earlier than any described so far. The 229 contacts examined and found negative may be grouped under (1) above, for these persons must have received inoculations of bacilli during their residence with the infecting patients, and yet "no indication of an infection is available."

There does not appear to be any informed opinion on the bacteriological examination of healthy looking contacts of leprosy cases, nor do we know whether such examinations are carried out as a routine procedure anywhere. We believe that if a careful bacteriological examination of all contacts of leprosy patients in households is systematically carried out, many cases of the type described in this paper will be brought to light.

SUMMARY

(1) A description is given of 25 contacts of leprosy cases presenting no clinical lesions of leprosy, but showing evidence of acid-fast bacilli in the skin. (2) The significance of the presence of acid-fast bacilli in the skin of the 25 contacts is discussed. (3) It is shown that these 25 contacts were not in any of the known stages of leprosy, but were probably in a phase of the disease earlier than any that has so far been described.

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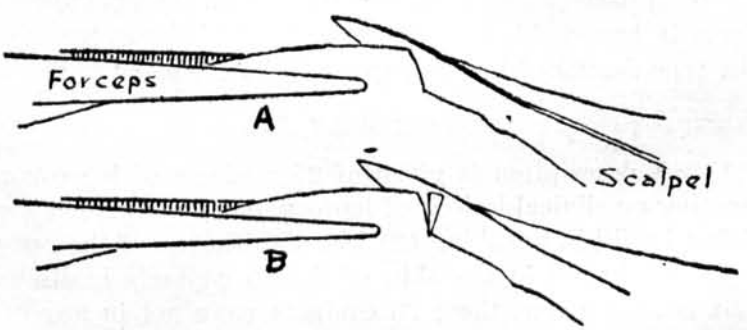
ADDENDUM

TECHNIQUE OF MAKING SMEARS EMPLOYED

The skin of the back a little to one side of the spine has usually been the site examined, but recently we have found the anterior surface of the forearm also to give positive results. The surface is washed throughly with soap and water and swabbed off with absolute alcohol. The whole skin is pinched up between the forefinger and the thumb, and held pinched with sterile forceps. A deep incision is then made at an angle to the surface with a sharp sterile scalpel, so as to reach the subcutaneous tissue (Text-fig. 1, A). Another, similar incision is made about 2.5 mm. from the first, angled to meet it in the subcutis (Text-fig. 1, B). The elongated wedge-shaped piece so excised, including some of the subcutaneous fat, is then lifted out with another sterile forceps. Before relaxing pressure of the forceps on the pinched skin the cut surface is scraped, and the material so obtained is spread on a new, clean slide. The piece of the skin with its raw surface downwards is then pressed on the same slide until all the serous substance is expressed. The whole substance is then spread evenly to make a smear about an inch long and three-quarters of an inch broad. It gives an evenly stained surface for the examination of hundreds of microscopic fields, which is essential for a thorough examination since the bacilli are very scanty.



TEXT-FIG. 1. Demonstrating the technique employed in obtaining material for the bacteriological examination of contacts.

DESCRIPTION OF PLATE

PLATE 6.

FIG. 1. Photomicrograph of smear from skin of a positive contact showing two bacilli, one uniformly stained, the other fragmented in appearance.

FIG. 2. Photomicrograph of smear from skin of a positive contact showing two uniformly stained bacilli.

(Photomicrographs made by Dr. V. R. Khanolkar.)

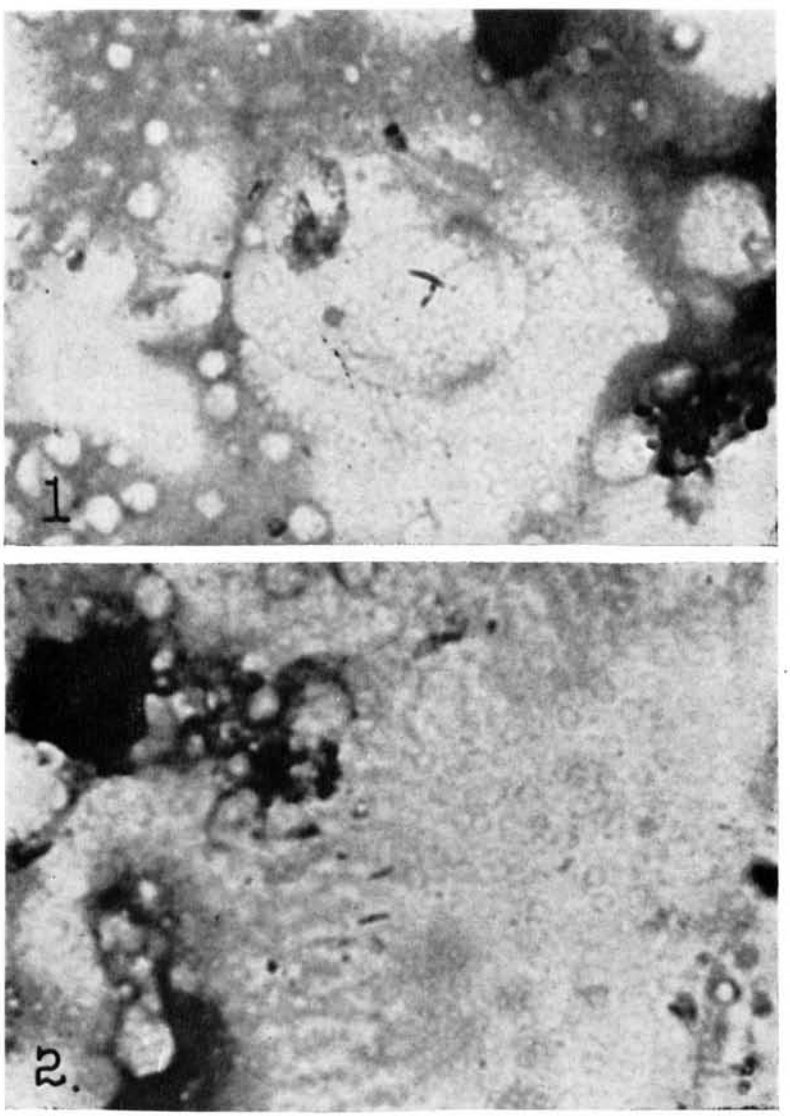


PLATE 6.