

CORRESPONDENCE

This department is provided for the publication of informal communications which are of interest, whether because they are informative or are suggestive and stimulating; to serve as an open forum for discussions of matters brought up by readers.

INFECTIOUSNESS OF NEURAL CASES

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To the EDITOR:

I shall be greatly obliged for an answer to, or a discussion of, the following question: On what grounds are patients suffering from pure nerve leprosy, including the tuberculoid form, believed to be noninfective and therefore not a danger to the community?

Is it only because, as a rule, these patients do not shed acid-fast bacilli? Can we be sure that the granular forms found in the skin lesions of nerve cases are merely noninfective degenerate forms, and not a stage in the life history of the germ which may be as infective as the acid-fast bacillus itself? What about the hypothetical sub-microscopic phase referred to by Wade in his article on lepra reaction in tuberculoid leprosy [this JOURNAL 2 (1934) 291]? Is there no case on record of the communication of the disease from a patient suffering from the pure nerve type to persons who had never been in contact with any other type?

It seems to be the concensus of opinion that neural cases require at least to be kept under observation because they may change to the cutaneous type, which is generally recognized to be relatively highly infectious. Another point with respect to the handling of neural cases is that, according to our observation, those which are neglected and allowed to live in poverty are likely to develop gangrene of the extremities and extensive ulcerations, and to go on to wasting, sapremia and death. The question of what should be done with these cases is one of great importance here because it has been proposed that pure nerve cases be excluded from this asylum, for reasons of economy.

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P. D. STRACHAN, M.D.
Medical Superintendent

Comment by Dr. H. P. Lie, Bergen, Norway:

Regarding the questions of Dr. P. D. Strachan about the infectiousness of neural cases, I should say that a case of *pure* nerve leprosy (i.e., a case without any skin lesion) may be looked upon as "closed" leprosy and noninfectious. On the other hand, from my own experience I hold that neural cases must be considered more or less infectious when there are infiltrations or other active processes in the skin, for the reason that leprosy bacilli are to be found in those lesions and they may be transported through the epidermis to the surface of the skin. Regarding the invisible stage of *Myco. leprae*, I neither know such a stage myself nor believe that the existence of it has been proved by others.

This is the theoretical side of the question. Practically, the campaign against leprosy must always begin with the most dangerous cases, and then when possible be extended to include the less infectious cases, even though these latter are not very infectious. But when it is impossible to care for all infectious cases one treats the most infectious as the most dangerous, taking all circumstances into consideration.

This is a matter on which the experience in Estonia should give some information. I myself know with certainty of only two cases in which infection was derived from a maculo-anesthetic case; these were two sisters infected by their father, and who themselves developed the maculo-anesthetic form. After thorough inquiry it was impossible to state that they had been in contact with any other leper than their father.

Comment by Dr. N. E. Wayson, until recently Director, U. S. Leprosy Investigation Station, Honolulu, Hawaii:

Question.—On what grounds are patients suffering from pure nerve leprosy, including the tuberculoid form, believed to be noninfective? Is it only because, as a rule, these patients do not shed acid-fast bacilli? *Answer.*—If the *Mycobacterium leprae* (Hansen's bacillus) is accepted as the cause of leprosy, there are no grounds for assuming that patients affected with the neural forms of leprosy may be considered noninfectious. It is conclusively established that a large percentage of such patients harbor the bacterium in the upper layers of the nasal mucous membrane, and that they may therefore readily disseminate it to others. Furthermore, it is not uncommon for patients with the neural forms of leprosy to develop cutaneous lepromata. To demonstrate the presence of the organism in the nasal mucous membrane in the cases referred to, it is often if not usually necessary to repeat the examination a number of times, and to make prolonged searches of the preparations.

Question.—Can we be sure that the granular forms found in the skin lesions of nerve cases are merely noninfective degenerate forms, and not a stage in the life history of the germ which may be as infective as the acid-fast bacillus itself? *Answer.*—The significance of the granular forms of the bacterium has not been determined, but the presence or absence of these forms should not be used as a basis of administrative procedure. It has been our experience that persistent and repeated search of specimens containing granular forms will reveal rod forms.

Question.—What about the hypothetical submicroscopic phase referred to by Wade in his article on lepra reaction in tuberculoid leprosy [this JOURNAL, 2 (1934) 291]? *Answer.*—In our experience there has been no evidence to justify the assumption that there are submicroscopic forms.

Comment by Dr. José Rodríguez, Cebu, Philippine Islands:

With reference to the questions raised by Dr. Strachan, I believe that few leprosy workers would care to affirm at the present time that lepers suffering from pure nerve leprosy are absolutely noninfective. However, there is definite evidence based on epidemiological grounds that the neural type is much less infectious than the nodular form.

Hansen and Looft showed that in certain districts of Norway, where the proportion of neural cases was high, the incidence of new cases within a given period was distinctly lower than in districts where the cutaneous cases predominated. Also, in the Memel epidemic the pure neural cases which were allowed to live in their homes did not give rise to any new infections. Finally, Dehio, using Lohk's data on his survey of Oesel, Estonia, cites the following: "Of 48 nodular cases, 36, or 67 per cent, had in all probability been sources of contagion. Of 13 cases of anesthetic and mixed leprosy, there was not even a suspicion that any one of them might have transmitted the disease to others."

With regard to the granular or nonacid-fast forms of *Myco. leprae*, I personally believe that at least some of the lesions of closed cases of leprosy are produced by such forms, which may represent a stage in the life cycle of the organism. On the other hand, I also believe that we do not as yet possess the least evidence of any kind proving that these nonacid-fast forms transmit the disease to others. Probably this important question cannot be definitely settled until after the leprosy bacillus had been cultivated, the granular, nonacid-fast forms produced, and the latter inoculated to some experimental animal previously proved to be susceptible to the acid-fast forms. Only then will we tell with certainty whether these forms are infective or not.

I know of no instance in which a patient suffering from pure nerve or "tuberculoid" leprosy had definitely communicated the disease to others in absence of other possible sources of contagion, though obviously observations of this kind cannot be free from objection when made in a country where leprosy is endemic. However, though there is ample reason to believe that such cases offer little if any danger of infection, they should be examined for acid-fast bacilli, particularly from the nasal septum, periodically and at short intervals.

Comment by Dr. J. J. du Pre le Roux, Medical Superintendent, West Fort Leprosy Institution, Pretoria:

Dr. Strachan's inquiry is not quite clear to me, as he includes under "pure nerve leprosy" the "tuberculoid form," and also skin lesions of nerve cases in which the granular form of the bacillus is found. Personally I have not been able to recognize the "tuberculoid form" as a clinical entity, and certainly if we find bacilli of any type in a skin lesion we are no longer dealing with a pure nerve case.

To avoid confusion we must therefore include under the classification "nerve leprosy" only those cases which do not show the presence of bacilli in either skin or mucous membrane. Under these circumstances we can safely assume that the possibility of their shedding acid-fast bacilli is extremely remote, and it is on this assumption that the Public Health Department in 1933 adopted the policy of discharging all "closed" cases from our institutions.

As Dr. Mostert of this institution has recently investigated the probable sources of infection in a series of institution cases, I have taken the opportunity of asking him for his views, which he has set down in the note attached hereto.

Comment by Dr. H. v. R. Mostert, Medical Officer, West Fort Leprosy Institution, Pretoria:

A "pure" neural case I regard as one in which there is leprous infiltration of certain nerves without accompanying active cutaneous manifestations. These nerve lesions, in the early stages, have bacilli, but in the later stages they become bacteriologically inactive fibrous cords. In rare cases the nasal scrapings may be positive.

Dr. Strachan presumably refers to active cutaneous macules when he speaks of "granular forms found in the skin lesions of nerve cases." Such cases I would classify under cutaneous leprosy. I know of no case in which bacilli have been found in a neural macule.

A pure nerve case with negative nose I would regard as a "closed" case, whether there be bacilli in the nerve or not, and as such of no danger to the public. Those cases with positive noses may be a danger. Our knowledge of the transmission of the disease is such that we cannot as yet form a true estimate of the infectivity of these cases. de Langen has shown that the nodular case during an exacerbation of the disease is infectious, but there is the possibility that relatively inactive bacilli (such as those in the nose of a neural case) may gain entry into the body and lie latent until such time as the health is below par and then become actively vegetative. Of 230 cases in this institution in which the source of infection could be traced, 41 per cent contracted the disease from maculo-anesthetic cases, but I regret that I cannot with certainty state whether any of these were "pure" nerve cases.

Comment by Dr. R. G. Cochrane, until recently Medical Secretary, British Empire Leprosy Relief Association.

The question which Dr. Strachan raises is one of great interest and importance.

In administrative matters I feel that we must abide by the general rules, for the administrative problem would become too complicated should we base our findings on hypotheses which have not yet been proved. It is generally believed that leprosy can be acquired only from a case in the open stage, and it is assumed, rightly I feel, that the greater the number of bacilli disseminated either from the skin or the nasal mucous membrane the greater the chance of infection.

Strachan raises the question whether the granular forms which are occasionally found are infective or not. One must assume for these purposes that should leprosy bacilli in any form be discovered, the individual is potentially a source of infection. However, if the conditions under which the patient is living

are such that he is unlikely to come into close contact with children or young adolescents, then the chances of his transmitting the disease are probably nil.

Strachan also raises the question whether there is a submicroscopic phase of the bacillus. A good deal has been written concerning this question, not only in leprosy but also in tuberculosis, but there is no evidence that such a phase, if it exists, is of importance from the public health and preventive viewpoints. I know of no record of infection being transmitted by a case of the pure nerve type, unless such an individual had a positive nasal lesion in addition to the ordinary neural changes. In that event the case would, for administrative purposes, be classified as open, and would therefore come under segregation.

The situation in Basutoland is such that the money expended on leprosy is out of proportion to its importance as an endemic disease, and, further, under the present methods there seems very little likelihood of causing an appreciable difference in the incidence of the disease as the result of measures already taken.

Any ordinance or regulation with regard to leprosy should definitely differentiate between the infectious and noninfectious varieties, and if it is impossible to ensure isolation in a village community, then infectious cases should as far as possible be isolated in an institution. However, better results would ultimately be attained if the headmen and chiefs could be so educated as to look upon certain types of leprosy as dangerous to the community. I have been told that the Basutos themselves differentiate between the cutaneous and neural forms, and if my informant is correct the relatively more virulent cutaneous cases are designated "black leprosy." If this is the case it is an interesting point to take hold of in any general propaganda which might be instituted.

Comment by Dr. E. Muir, Medical Secretary, British Empire Relief Association; until recently Leprosy Research Worker, Calcutta:

The question is asked: "On what grounds are patients suffering from pure nerve leprosy, including the tuberculoid form, believed to be noninfectious and, therefore, not a danger to the community?" Before attempting to answer this question a few explanations are necessary.

What is meant by "pure nerve leprosy"? The obvious answer would be leprosy in which the infection is confined entirely to the nerves and does not directly cause lesions in the skin or elsewhere in the body. Indirect affection of the skin, bones, joints, etc., due to blocking of their neurotrophic supply, should not invalidate the diagnosis of "pure nerve leprosy" provided the actual infection is present only in the nerves. What is meant by "neural leprosy" in the special sense accepted by the Manila Conference is that, clinically, the lesions are principally those of the nerves, although the skin may also be involved to a limited extent.

There are four distinct classes of cases which are often included under the name "nerve" or "neural" leprosy:

1. One class, comparatively rare in North India, consists of cases without any skin lesion but with anesthesia of a limited area of skin, generally the ulnar side of the hand and the little finger. There is usually palpable thickening of the sensory or mixed nerve or nerves supplying the part. On incising the epineurium and scraping the underlying nerve fibres, one may find acid-fast bacilli in

smears. The term "pure nerve leprosy" is particularly applicable to this class, because clinical, histological and bacteriological examinations show no sign of invasion of the skin by the leprosy organism. In these cases the leprolin test tends to be fairly strongly positive.

2. The second class comprises those cases with raised, indurated lesions which vary in size and number. Either the whole lesion may be indurated, raised and red, or only the margin, the center in the latter being flattened and depigmented. As a rule these lesions are anesthetic to light touch, either throughout their whole area or at least centrally. The margin, if the lesion is spreading fairly rapidly, may not be markedly anesthetic. The term "tuberculoid" is applied to these lesions by many workers because of their histological resemblance to certain types of tuberculous changes, viz., dense foci of epithelioid cells in the superficial layers or the corium surrounding the hair follicles and sweat glands and ducts, and marked cases involving the whole thickness of the corium; often there are also large numbers of giant cells. The sensory nerves connected with these skin lesions are frequently palpably thickened, and on section show granulomatous infiltration with giant cells as in the corium. Acid-fast bacilli are few in the skin, as a rule being found, if at all, only after very careful search, but they are much more frequent in the nerves, though even there careful examination may fail to reveal them. In these cases the leprolin test is as a rule strongly positive.

3. The third class consists of the "juvenile" variety of the disease, found in children who have suffered massive infection during their earliest years, when resistance is particularly low. They may show only slight, ill-defined patches with hypopigmentation, erythema or keratosis, the margins of the patches blending imperceptibly with the surrounding skin. Bacteriological examination often fails to show bacilli. Some would classify these cases—I believe wrongly—as belonging to the neural type. Their resistance to leprosy infection is often low, the leprolin test is weak or negative, and abundant infectious lesions may appear suddenly all over the body, especially if for any reason their general health becomes impaired.

4. There is also the class comprising those cases that have formerly been of the cutaneous type (C2 or C3), but that have become bacteriologically negative on repeated examination of both the nose and the skin. There is a tendency for these cases, as they progress toward recovery, to develop nerve lesions. Those in which the cutaneous-type manifestations have subsided, leaving only the neural changes, are the "secondary neural" cases of the Manila Conference classification. Throughout their whole course there may have been a high degree of infection in the nerves, but the presence of bacilli in the nerves failed to produce marked cellular reaction—and therefore clinical neural signs—until the infection in the skin and mucosa became reduced or disappeared. It must always be remembered that in such cases the nerves may still harbor large numbers of bacilli, far more than are likely to be present in early neural cases with only a few lesions of limited size, and these bacilli may possibly again find their way into the skin. In this group the leprolin test is generally weak, probably because of the large numbers of bacilli still present in the nerves and perhaps

in other parts of the body. Graduated doses of potassium iodide will often reveal latent leprosy foci.

Of these four groups the first two may as a rule be allowed to mix freely with others, provided that they remain under medical supervision and treatment. This opinion is based on the fact that there are few bacilli and they are confined almost entirely to one or two nerves. When bacilli are present in the skin they induce strong cellular reaction and become phagocytosed. But in these cases marked lowering of the general health may be accompanied by (a) extension of lesions, the extending margin taking on the characteristics of the skin type, and (b) generalization of the disease; hence the proviso regarding medical supervision.

Regarding what I have called the "juvenile type," care is necessary. Like the secondary neural cases their special resistance to leprosy is as a rule fairly low, as is shown by the course of the disease and by the leprolin reaction. But though they are supposed to be bacteriologically negative, careful and repeated examinations of nasal and skin smears not infrequently reveal leprosy bacilli, even when the clinical signs were noticeable only on very careful examination.

In my experience a negative or only slight reaction to the Hansen-bacillus leprolin, occurring in any of the groups mentioned above, should be considered an indication for repeated bacteriological examination, especially if there is at the same time a comparatively strong reaction to rat-leprosy leprolin standardized to the same strength.

Regarding the fourth group of cases, more care should be exercised than with any of the others. If bacilli are still present in large numbers in the nerves there is danger of their finding their way into the skin or mucous membranes once more. This entrance into the skin would not be accompanied by such strong cellular reaction and phagocytosis as in "tuberculoid" or other resistant cases, and infection might easily increase and spread to a dangerous extent without attracting the notice of the patient or his medical adviser. Special care should of course be exercised regarding their contact with children.

In the course of years of following up clinic cases I have occasionally found one, the only possible source of infection of which appeared to be a bacteriologically negative and resistant case. But when careful inquiries were made at the home of the patient, especially if the home was situated in a rural area with a settled population, I generally obtained a history of contact with a fairly advanced case of the cutaneous type. In our rural investigation center in the Bankura district of Bengal we have found frequent instances of young children who have, for years, been in close contact with adults suffering from lesions of the bacteriologically negative resistant type, but these children have so far failed to develop leprosy.

Summary.—(1) While from the nature of things it is impossible to prove that patients whose lesions are of the bacteriologically negative, resistant type are under no circumstances able to transmit leprosy, available evidence is against their being a source of danger to children, who are usually highly susceptible.

(2) With regard to the juvenile type, the frequency with which such cases suddenly develop widespread, bacteriologically positive lesions makes clear the

necessity of keeping children suffering from this type of the disease under close observation, remembering the danger of their suddenly becoming actively infectious cases.

(3) There is a tendency for advanced cutaneous-type cases to develop nerve lesions in the later stages of the disease. Patients seen at this stage are often classified as neural (properly, "secondary neural"). Routine bacteriological examination may at first fail to show *Mycobacterium leprae*, but repeated examination will often show clumps of acid-fast bacilli in the skin, nose or gums. Patients who have at one time suffered from widespread cutaneous leprosy with bacteriologically positive lesions should, even after the disease has become quiescent and arrested, be kept from close contact with healthy people and especially with children. Such contact should be permitted only when the disease has remained arrested for several years, when the patients have shown no signs of the disease on being subjected to the iodide test, and when all parts of the skin, nasal mucosa, gums, etc., have been carefully examined for bacteria and found negative.

(4) Reference is made to the use of the leprolin test in determining resistance to invasion by *Myco. leprae* and in judging the degree of danger of transmission of disease.

[In view of the importance of this question, readers of the JOURNAL are especially invited to contribute observations that bear on it. Such contributions may be in the form of full original articles, brief reports, or informal correspondence.—EDITOR.]