

CORRESPONDENCE

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NERVE BIOPSY; A SYMPOSIUM

In the symposium on classification which appeared in the fourth issue of THE JOURNAL last year [20 (1952) 521-534] several of the contributors spoke of nerve biopsy as if it were a simple and commonly practiced procedure. By certain of them it was held to be often essential in the classification of "primary polyneuritic" cases, since they were not classed in a single group but were divided as tuberculoid, indeterminate or lepromatous according to their histopathology.

The question of how often, and under what circumstances, biopsy of the peripheral nerve trunks is actually performed by different leprologists in their practical work seemed an interesting one, and a questionnaire on the subject was sent out to all who had contributed to the symposium. The questions asked were essentially as follows:

1. Is it or has it been your practice, or that of your associates, to biopsy peripheral trunk nerves for diagnosis, whether of the disease or of the type?
2. If the answer is "yes," do you recommend the procedure as a routine one in all cases in which the information to be gained thereby would be useful?
3. Or, on the other hand, do you recommend that it be done only in exceptional cases?
4. What is the approximate number of cases in which you have made this examination, or in which it has been made in your service or by associated workers?
5. What are the nerves which have been so biopsied?
6. Have you seen bad after-effects from the operation?
7. Have the results of the examination justified the procedure?

The questions were set up for simple "yes" or "no" answers, but supplementary notes were invited, and many of those who responded contributed such notes. For use here the replies have all been worked over, but it has not always been possible to arrive at uniformity with respect to the information conveyed.

The questions referred to peripheral nerve trunks (i.e., mixed nerves like the ulnar and peroneal), which might pos-

sibly suffer harmful motor or trophic effects from the excision of biopsy specimens. Several of the responses, however, deal with or include superficial cutaneous (sensory) nerves, removal of which is a relatively simple procedure without possible after-effects of any consequence. Although the term "biopsy" signifies excision of tissue for examination, commonly histological, certain of the contributors refer to or include simple exposure and scraping of nerves for bacteriological examination in the diagnosis of the disease.

The inquiry was indicated as having arisen in connection with the problems of classification, but to get a broader idea of practices the first question referred to biopsy for "diagnosis, whether of the disease or of the type." Certain of the contributors tell of examinations made in special investigations, not primarily for purposes of diagnosis in either sense. The replies, taken together, are therefore somewhat varied, but there is much of interest in them.—EDITOR.

Dr. Harry L. Arnold, Jr., Honolulu, T.H.: We have biopsied peripheral trunk nerves in a very few cases, but recommend it only for exceptional cases, in which the nerve lesion strongly suggests active disease and positive evidence for diagnosis and classification cannot be obtained from the skin alone—either because there is no skin lesion or because what is found does not yield the necessary evidence. We have biopsied, in 3 or 4 patients, enlarged and relatively distal branches of the peroneal and sural nerves. Usually we have removed only a shaving which reduced the transverse diameter of the nerve by no more than one-fourth or one-third. No ill effects have been seen.

We have biopsied the greater auricular nerve more often than others, about 5 times in all. Total removal of that nerve was done in 1 case in which it was wholly destroyed, and in 2 others in which it was only badly damaged. In only 1 of these cases was there residual anesthesia, and then only on the posterior aspect of the ear.

In all of our biopsy specimens active tuberculoid disease was found, except in one instance in which there was only a fibrous cord, no longer identifiable as nerve. In every instance except the latter it was possible to identify bacilli. Suspected leprosy in these cases was positively diagnosed only in this way, cutaneous evidence having been either entirely lacking or wholly inadequate for diagnosis.

Drs. Guillermo Basombrio, Buenos Aires, and José M. M. Fernandez, Rosario, Argentina: It has been our practice and that of our associates to biopsy peripheral nerves for diagnosis, but only in very special cases and in the way described below. We do not recommend this procedure as a routine measure, but only for the rare cases with only neuritis in which it is practically the only way of making a sure diagnosis. This examination has been made by one of us (G.B.), first with Professor Baliña and afterwards with his own collaborators, in about 50 cases. It has been made by the other of us (J.M.M.F.) in about 6 cases. The nerves examined have been mostly the ulnar, the superficial peroneal, and the collaterals of the

fingers; also the auricular branches in the neck. No bad after-effects have been seen from the method used. The results have justified the procedure, for often the diagnosis of the disease has been arrived at, and in most of the cases also diagnosis of the type.

In this operation we have been very prudent with the mixed nerves, taking only very small portions of the sheath. Sometimes—but only of sensory nerves such as the auriculars—we have removed a section of the branch. In that event total loss of sensibility has been the immediate consequence, but after a few weeks normal sensibility was completely restored without further treatment.

When, however, the diagnosis of leprosy is well-established we resort to other and simpler methods, including the lepromin test, to establish the type of the disease, and hardly ever use nerve biopsy. In one instance, in which bacilli were found in the nerve, lepromatous patches began to appear in the skin some days after the operation. Two reports on the biopsy of the ulnar nerve in the diagnosis of leprosy have been published in the *Revista argentina de Dermatología*, one by Baliña and Basombrio [16 (1932) 541-546] and the other—a report of three new cases—by Baliña, Basombrio and Bosq [*ibid.* pp. 547-556].

Dr. R. Chaussinand, Paris, France: Personally, I have never made biopsies of peripheral nerves, and as yet I have not had any case in which that examination was necessary. In cases of pure primary polyneuritic nature I base the classification on the clinical features of the affected nerves, and on the results of the Mitsuda test and especially the intensity of the reaction. Cases of the regressive, secondary polyneuritic kind are classified according to the history of the case and the perceptible stigmata of previous lesions, with the aid of the Mitsuda reaction. I believe that it is neither possible nor practicable to recommend the biopsy of nerves as a routine examination.

Dr. Robert G. Cochrane, London, England: It is not my practice to make biopsies of peripheral nerve trunks, and I do not recommend it as a routine procedure, only when there is some doubt as to the diagnosis. Altogether I have done it in only about one-half dozen cases, the nerves so examined being the ulnar and peroneal. I have seen one case of dropfoot resulting from the operation, but that was in a service with which I was not connected. The results of the examinations which I have made have justified the procedure. It might be useful to biopsy subcutaneous nerves connected with anesthetic areas.

Nerve biopsy is very useful for research purposes. We still have only a vague idea of the differences in the histopathology of polyneuritic tuberculoid and polyneuritic lepromatous lesions, and therefore workers who are interested in detailed histopathology studies will find biopsy of nerve trunks a useful procedure. I intend to continue making such examinations in suitable cases, in order to elucidate further the histopathological picture in these conditions. The operation should be performed only by surgeons familiar with the proper technique. There is sometimes some difficulty in persuading the surgeon to perform this operation.

Drs. Felix Contreras and J. Gay Prieto, Madrid, Spain: It is not our practice to do nerve biopsy for diagnosis and except in unusual cases do not recommend it for that purpose. We have done it approximately 6 to 10 times, on the cubital and radial nerves, in exceptional cases only, and can

recommend it only for such cases. We have seen bad after-effects. The cicatrices have always been painful, the disturbance persisting for years or indefinitely; and in one instance the operation on the cubital, although done by an excellent surgeon, was followed by permanent functional incapacity. The results of the examination have not justified the procedure.

Drs. Dharmendra and S. N. Chatterjee, Calcutta, India: We do not do, and do not recommend, biopsy of nerve trunks for diagnosis of the disease or of the type. We regard surgical intervention to obtain smears for diagnostic purposes, as in the case related below, to be justified in rare instances when there are signs suggestive of nerve involvement but neither the clinical evidence (sensory changes) nor the nerve thickening is definite, and routine smears are negative. We have done this for diagnosis only in the one case referred to. In such a case actual biopsy of a superficial (sensory) nerve may be justified, but not of a mixed nerve trunk. We have made smears from nerve trunks in several cases for special investigations, not for diagnosis, and have taken biopsy specimens from cutaneous nerves in several instances for similar purposes. Biopsy of nerve trunks has not been practiced, nor is it recommended. No bad effects have been seen after cutting such nerves open and taking smears, or after removing biopsy specimens from cutaneous nerves.

The case referred to was seen in this department several years ago and reported by one of us (S.N.C.) in *Leprosy in India* [6 (1934) 132-135, Case (b)]. The patient came with slight deformity of the left little and ring fingers of very short duration. He could not adduct or abduct the affected fingers, but there was no anesthesia or analgesia, and the ulnar nerve was only very slightly thickened. A cervical rib was suspected, but x-ray examination did not confirm that diagnosis. The ulnar was then exposed and a smear taken from its sheath, not a biopsy specimen. A half-dozen acid-fast bacilli were found in the smear, permitting the diagnosis of leprosy to be made.

Dr. F. A. Johansen, Carville, Louisiana: We do not practice or advise biopsy of peripheral nerve trunks.

Prof. Kanehiko Kitamura, Department of Dermatology, University of Tokyo, Japan: Biopsy of nerve trunks such as the N. ulnaris is not done in our clinic because of the possibility of functional injuries. On the other hand, we often excise the N. auricularis magnus for histological examination. The late Dr. Sato, a pupil of the late Dr. Ota, published in 1941 a very detailed article on the histopathological changes found in this nerve (*Japanese J. Dermat. & Vener.* 49 (1941) 461, in Japanese, with abstract in German).

Dr. Casimiro B. Lara, Cullion, Philippines: We have not performed biopsies of peripheral nerve trunks, and I would recommend it only in exceptional cases, where after repeated clinical examination, and despite previous biopsy of other lesions, the leprous nature of the case cannot be ascertained.

Dr. John Lowe, Uzuakoli, Nigeria: Biopsy of nerve trunks, in the sense of excising a portion for histological examination, I have never done. I cannot conceive the circumstances in which this would be justified. The following remarks refer to exposure of the nerve, naked eye inspection, and scraping to obtain material for the examination for lepra bacilli. With that understanding, my answers to the questionnaire are as follows:

I have made this examination in only a few cases, about 12, and do not do it or recommend it as a routine procedure. The peripheral trunk nerves which I have examined in the way described are the ulnar above the elbow, the median at the wrist, and the peroneal below the knee or at the ankle. No bad after-effects have been seen. The results have justified the procedure in some cases, not in all.

The same examination has also been made of cutaneous nerves in various situations. Excision of such nerves supplying skin lesions, for histological examination, I have done in many dozens of cases. This is a most useful procedure in diagnosis and in classification of doubtful cases. The apparently normal nerves showing leprosy bacilli in the lepromatous case contrast strongly with the markedly infiltrated nerves of the tuberculoid case, with bacilli present but few. Nevertheless, there are many cases in which, while the diagnosis is certain, the classification is uncertain because the findings are equivocal.

In conclusion I would say that study of the nerves in leprosy is of great interest and importance to those who really strive to understand the disease; that biopsy of nerve trunks is never justified, although exposure and scraping may be; and that a study of terminal cutaneous branches often yields useful information, but there is no need to make it a routine procedure.

Dr. E. Muir, London, England: It has been my practice to biopsy peripheral nerve trunks, but I recommend it only for exceptional cases, chiefly early ones in which the diagnosis is doubtful and after all other possible methods of examination have failed. In that event biopsy of small branches or the larger nerve trunks is useful. It would be difficult for me to say in how many cases I have made this examination—perhaps a dozen or more. The nerves involved were the ulnar, median and peroneal, but many of them have been of small branches; I have also biopsied the auricular nerve. No harm has been seen, and the results have justified the procedure.

The circumstances under which I think biopsy is justifiable may be illustrated by the following cases: (1) A patient came with bent ring and little fingers, and a feeling of heaviness in the hand; no anesthesia could be elicited; there was doubtful thickening of the ulnar nerve above the elbow. Slitting the capsule of the nerve and scraping out a few fibers, 2 or 3 acid-fast bacilli were found. The result of this biopsy was not only a definite diagnosis, but also amelioration of the condition: the symptoms cleared up within a few days and remained absent for as long as I was able to check up. (2) A Chinese patient presented a red patch on the cheek and a thickened ulnar nerve. There was no doubt about the diagnosis at the time, but no bacilli could be obtained from the cheek lesion. However, on slitting the nerve capsule and taking a scraping, a fair number of bacilli were found. (3) A patient had a small anesthetic patch on the back of the hand, about one-half inch in diameter, with no other sign of leprosy except doubtful thickening of the small nerve branch supplying the area. I excised a piece of this nerve and found 1 or 2 acid-fast bacilli. The anesthesia cleared up, and so far as I know did not return.

Drs. V. Pardo-Castelló, Francisco R. Tiant and Raul Piñeyro (pathologist), Havana, Cuba: It has not been our practice to biopsy peripheral trunk nerves to determine the type of the disease. Type can usually be

determined without difficulty from clinical manifestations, the bacteriology, the lepromin reaction, and the pathology of skin lesions when present. Therefore, we do not recommend this procedure as a routine performance. We believe, however, that it should be done in exceptional cases when the diagnosis of leprosy is in doubt and neural lesions are predominant. Such cases are very unusual.

Not counting 36 cubital nerves obtained at necropsy, we have performed approximately 75 histological examinations of peripheral nerves and their branches in cases of leprosy. Many of these biopsies were of enlarged subcutaneous branches of the nerves of the arm (median, radial and ulnar) or of the lower extremities, and 3 specimens were of the auricular branch of the cervical plexus while 1 was of a branch of the superficial brachial plexus. Some, however, were of the ulnar and popliteal trunks, and 2 were of abscesses of the ulnar. Of these specimens, 31 were of the lepromatous type, 9 were of the tuberculoid type, and several were of the fibrotic terminal stage (residual neural leprosy), practically all of them late lepromatous. These examinations, of both postmortem material and specimens from patients, were in large part for our special study of nerve changes in leprosy, reported in the *Archives of Dermatology and Syphilology* 55 (1947) 783-792 and at the Havana congress.

We have never seen any bad after-effects from operation on trunk nerves. Most of the patients concerned already had atrophy of the hands and retraction of the fingers. The results of the examinations have justified the procedure occasionally. In our experience it has been vital in proving that, in the cases we have biopsied, those of the so-called pure neural leprosy were always of the tuberculoid type.

Dr. José N. Rodriguez, Manila, Philippines: We have not made such biopsies, and do not recommend the procedure.

Dr. Salomon Schujman, Rosario, Argentina: I regard biopsy of the nerve, especially of the nerve trunks, as the last resort in the diagnosis of leprosy, when there are no skin lesions and when the other diagnostic elements (thickening of the nerves, the state of sensibility, the lepromin reaction and nerve puncture) do not suffice to establish the diagnosis of the disease. As for the diagnosis of type, I am more inclined to depend on the lepromin test. Because nerve biopsy is not a very practicable procedure, involving as it does a wholly surgical intervention, we have used it to clarify the diagnosis only in very exceptional cases of responsibility, when we have had to make an official report, as for example when legal questions were involved. I have made approximately 30 nerve biopsies, but most of them were made in cases where transposition of the cubital nerve was done for therapeutic purposes, advantage being taken of the opportunity to make the biopsy; thus the great majority of my specimens have been of that nerve. No ill effects have been observed, and the results have justified the procedure.

Dr. H. C. de Souza-Araujo, Rio de Janeiro, Brazil: I have had no personal experience with biopsies of peripheral nerve trunks, and would recommend that it be done only in exceptional cases.

Dr. Nelson de Souza Campos, Goiania, Goiás, Brazil: We have made biopsies of peripheral nerve trunks, infrequently, but recommend it only in exceptional cases. The number of cases is about 60, more or less. The

nerve examined was usually the ulnar, the sciatic once. No ill effects have been seen when the operation was performed by an expert surgeon.

Dr. Lauro de Souza Lima, São Paulo, Brazil: We have not practiced nerve trunk biopsy for diagnosis or classification. The information obtained would be very useful, but it would be practically impossible to apply the procedure as a routine measure. It should be done in special cases, but it would be very difficult to lay down specific recommendations. For one thing, among our patients of interest in this connection the nerves are usually not enlarged. The number of cases in which nerve biopsy has been made is somewhat over 40, but no records of what nerves were so examined are available. Harmful effects have never been seen. The examinations have yielded interesting information.

[The reply of this contributor refers to the monograph *Leprosia Tuberculóide* by himself and Nelson de Souza Campos, published in São Paulo in 1947, specifically to the section on the nature of the nerve lesions (p. 33 *et seq.*). There, among other things, are discussed the difficulties of getting study material, which involves arranging for the necessary participation of a surgeon and obtaining the agreement of the patients. In many cases the lack of nerve thickening and of neuritic pain does not seem to justify surgical intervention, in spite of the degree and seriousness of the consequences of the nerve involvement. Thus it is that the documentation of the structural changes in the nerves of simple macular (*incarcaterístico*) cases is scarce. A tabulation of the findings in 44 cases classified according to the Cairo scheme (the nerves biopsied not stated) shows that in all of the lepromatous and tuberculoid cases (16 of each) the findings in the nerves were in agreement with the clinical designations. Of 6 simple macular neural cases, however, only 1 showed nonspecific changes; 1 nerve was lepromatous, while 4 were tuberculoid with caseation. Of 6 anesthetic neural cases, without skin lesions, the specimen from 1 showed nonspecific changes with fibrosis, 2 showed tuberculoid changes (1 with caseation), while 3 were lepromatous. Nothing is said to suggest the possibility that the simple macular cases with caseation may previously have been frank tuberculoid, and that the simple anesthetic cases with lepromatous findings may previously have had skin lesions of that nature—i.e., that these cases may have been of recessive or residual nature and reclassified on that account.—EDITOR.]

Drs. Martín Vegas and Jacinto Convit, Caracas, Venezuela: In our practice the few nerve biopsies done have been almost exclusively for diagnosis of type in cases of primary polyneuritis, and only once for diagnosis of the disease. We do not believe that nerve biopsy should be done as a routine procedure. It is difficult to expose some of the nerves, and the operation in 6 of our 9 cases were performed by our surgeon. Furthermore, the results obtained are sometimes not conclusive and do not justify the effort involved.

Few primary polyneuritic cases are seen in Venezuela, and probably for that reason the proportion of them which we have biopsied is high. We believe that in countries where there are many such cases the procedure would be inapplicable as a routine measure.

The number of trunk nerves biopsied is 8, of which 4 were ulnar and 4 were radial. The great auricular has also been biopsied in 1 case. No bad after-effects have been observed. In the one case examined for diag-

nosis of the disease the results did not justify the procedure, only nerve degeneration being found histologically; we are inclined to believe that the specimen was not taken from the lesion focus.

Dr. Xavier Vilanova, Barcelona, Spain: It has been our practice to biopsy nerve trunks for diagnostic purposes, not as a routine procedure, nor on the other hand only in exceptional cases. It seems to us that there is an intermediate position between those two extremes which is more correct. We have usually biopsied the cubital nerve, less often the posterior tibial, in subjects which clinically we have suspected of having lepra fibrosa. (For our concept of this condition, see my contribution to the symposium on classification, *THE JOURNAL* 20 (1952) 532).

Approximately 40 patients have been biopsied, including those in which only cutaneous nerves were examined. Biopsy of mixed nerves is done surgically, exposing the nerve and removing only a small peripheral portion of shallow depth but of much greater length. No bad after-effects have been seen. The patients were already suffering from a considerable deficiency of innervation—claw hand, perforating plantar ulcer, etc.—and the extirpation of the few altered nerve fibers which are removed did not cause any later harm. On the contrary, some patients have improved after the operation, perhaps because the incision of the fibrous casing which contained what remained of the undamaged nerve fibers saved them from destruction. The results have justified the procedure, and the findings have permitted the characterization of a new form of leprosy, lepra fibrosa.

A part of our material, as said, has been obtained from thickened cutaneous nerves, when the macular skin lesions have shown an indeterminate structure but the clinical findings indicated lepra reactiva (tuberculoid). Such nerves have been on the dorsum of the hand, the foot, the cervical region, etc. Complete section of these sensory nerve branches has not been followed by disagreeable effects.