

Investigations on the Physiopathology of the Nerve in Leprosy

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In 1933, 1956 and 1964, S. N. Chatterjee asserted that in a number of cases the neurologic syndromes in leprosy were due, not to Wallerian degeneration, but to reduced circulation in the nerves. He did not, however, offer evidence to support his concept. This local ischemia has been attributed to concurrent causes (lower temperature, repeated traumatism, etc.) by Wade, Minato, Souza Campos and others. The Argentinian L. Diez, in 1943, was the first to bring forward some positive elements, e.g., elongation of the hypertrophied ulnar nerve producing ischemia (Marnette's sign, 1928), and slow progression of the lipiodol visualized through neurography, formerly used by Chaumet (1921), Saito (1933), Picco (1936), and Dorang and Matske, who showed, in 1961, that, even in a sound nerve, a drop of radioactive product stagnates at the level of the osteo-ligamentous channels. With respect to the leprosy nerve, Mitsuda (1924), Reddy (1957), and Desikan and Job (1968) using necropsies, have shown that *M. leprae* is found spread along the whole nerve in slightly greater amounts at these levels.

In 1965 we resumed study of nerve circulatory disorders by making lymphographies of the limbs. These showed the perineurovascular lymphatic spaces and the lymphatic pedicles responsible for drainage of the nerve. Selective arteriographies of the lower brachial collateral artery showed a circulatory block above the supratrochlear-olecranal tunnel.

In 1966 comparison of these neuro-radiologic examinations with histology (Camain) confirmed the existence of a noninflammatory edema at this level. Since then, we have undertaken further investigations in the neurographic and arterio-

graphic fields on the four nerves most frequently affected by leprosy. The study was based on critical examination of the following:

Sixty-three neuroographies performed by percutaneous injections into the ulnar nerve (4 in the common peroneal nerve did not give interpretable pictures).

Twenty selective neuroographies (using a small incision) which permitted visualization of the common peroneal nerve, the posterior tibial nerve, the median nerve of the wrist, and the deep branch of the ulnar nerve.

Eight dynamic neuroographies to study how a drop of lipiodol would ascend, and the combination of five neuroographies with arteriography and two neuroographies with lymphography (i.e., a total of 98 examinations).

Forty-five selective arteriographies of the trunk and collateral vessels of the ulnar, median, common peroneal and posterior tibial nerves.

Nine lymphographic examinations.

NEUROGRAPHIC DATA ON CONSTRICTION AND SPEED OF ASCENSION OF THE CONTRAST MEDIUM INJECTED

Classic neurography, i.e., percutaneous injection of diodone into the ulnar nerve, shows clearly noticeable thickening under the skin and, on the following days, relative narrowing in the tunnel.

Selective neurography (Carayon, 1965) shows a combination of trunk thickening and narrowing in nerves for which percutaneous injection is hazardous, viz., the median, radial, and posterior tibial nerves, and also some branches (digital nerve of the median nerve, ramus profundus of the ulnar nerve).

This method can reveal dual localizations in the same nerve (e.g., ulnar nerve at the elbow and wrist, and median nerve under

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the biceps process and at the carpal tunnel).

The dynamic neurography of the involved nerve shows stagnation in the usual areas of hypertrophy (fluid lipiodol or radioactive iodine).

In 1965, Cave, using 80 successful percutaneous neurographies, studied the morphologic aspect of trunk hypertrophy, noting normal diameter or mild hypertrophy, simple, harmonious hypertrophy, without contusion alterations, hypertrophy with parietal alteration, and hypertrophy with one or several swellings.

Our study, based on 98 cases, does not restate the morphology already described; however, among our cases, we keep the five per cent proportion of tapered narrowing, which approximates Dowe's figures (from 2

to 3 per cent of nerves bearing caseous abscesses). The degree of hypertrophy is also an interesting element. The study deals with different subject matters as follows:

1. Direction and speed of ascent of the contrast medium. *Direction:* in principle, the medium injected into the trunk migrates toward the limb hilum. When the injection is perineural, it migrates downward (Saito). With the percutaneous method, the product is most frequently injected, using both modalities; the surgical

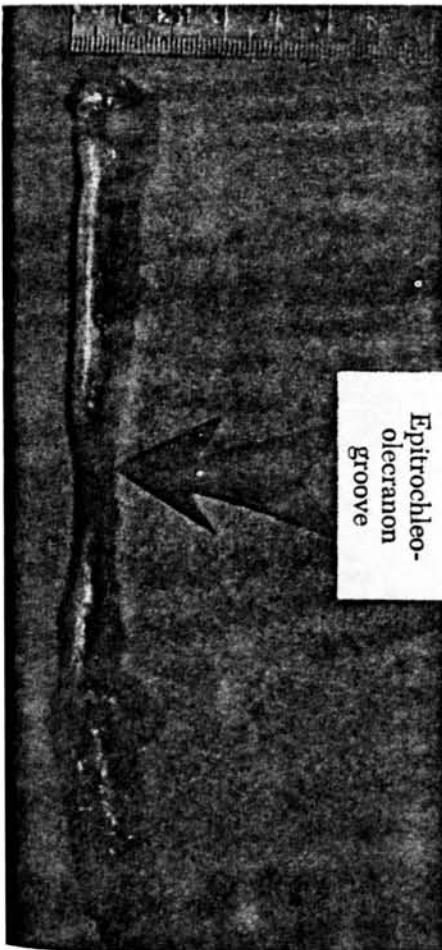


FIG. 1. Ulnar nerve from patient with tubercloid leprosy who died from tetanus.



FIG. 2. Lower limit of stricture visualized by ascending lipiodol in the nerve.

injection is for the nerve only. *Speed of ascension of product injected:* Dynamic neurographies, with a drop of fluid lipiodol, show a slow rise in the ulnar nerve with a block at the level of the supratrochlear-olecranal tunnel. Classic neurographies of the leprosy nerve show an ascension which is five to ten times slower. *Resorption time:* the resorption of a lipiodol neurography in a healthy nerve takes a month normally; the nerve concerned is the ulnar or the posterior tibial. In a leprosy nerve, the resorption time is five to ten times longer. Common peroneal nerve, however, is an exception; resorption is very rapid (24 hours), even when there is a regular hyper-

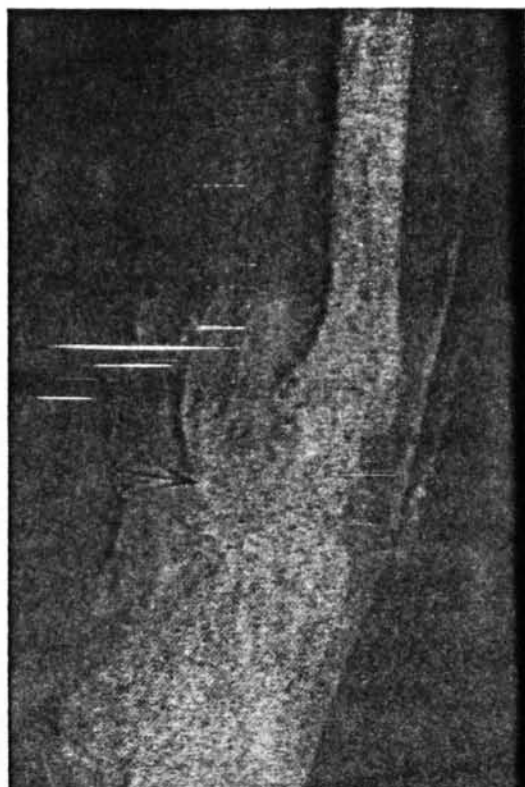


FIG. 3. Stricture of median nerve at level of the carpal tunnel (profile).

trophy in half of the cases. We found, three times only, that the contrast medium had been diffused outside the nerve by way of the peritruncal lymphatic pedicles; the draining pedicles are not well injected, while lymphography carried out in a man with leprous neuritis very often visualizes them.

Stricture site in relation to osteo-ligamentous channels. *Tunnel of the ulnar nerve at the elbow.* The nerve is not constricted in the leprous child, for the apophyses have not yet reached their definitive volume and the ligament is weaker. This can explain the rarity of involvement of the ulnar nerve, especially in the child under 16 years of age.

The degree of constriction of the nerve varies. In the adult it is not found in the case of the ulnar nerve à Ressaut (one case in leprosy, 2 in nonleprous persons) or of flaccidity of the ligament (7 cases). The tendinous ligament of the anterior ulnar muscle can then cause constriction. The

upper level of the stricture lies at the entrance of the tunnel (40% of cases) or at the point of departure from the second half of the groove (60% of cases).

This localization of hypertrophy predisposes to pain from elongation of the nerve on forced flexion of the elbow (Marneffe's sign, described in 1928, and named Lassegue's sign of leprosy). The lower level of the stricture is at the distal part of the epitrochlea.

Carpal tunnel (median nerve). Neurographies show a clear compression of the nerve in all cases, but in four cases out of ten the nerve branches underlying the nerve are also hypertrophied.

Tarsal tunnel (posterior tibial nerve): There is more severe constriction behind the malleolus; the calcaneal tunnel is wide enough (8 cases out of 10).

Peroneal passage (common peroneal nerve): usually this is only slightly constricted in cases of moderate hypertrophy of the nerve.

DATA ON THE ARTERIAL AND VENOUS REPERCUSSIONS OF THE OSTEO-LIGAMENTOUS CHANNELS

Diez, in 1942, was the first to suggest a vascular obstacle (slow progression of the



FIG. 4. Stricture at level of canal at head of fibula.

lipiodol and probability of ischemia due to elongation). Since 1965, we have reported a number of observations.

The venous repercussion has appeared clearly to all operators. It is marked by venous hyperplasia and hypertrophy around trunks affected by a relatively recent neuritis (1 to 2 years). Brand has explained clearly that a venous replacement supply in the circulation is concerned. Sometimes, however, a neural hypertrophy is found above the carpal tunnel separated from the usual hypertrophy by a narrowing, sometimes also between a main tunnel and an accessory one (epitrochlear-olecranal tunnel, and tunnel for the anterior ulnar nerve, and tarsal and calcanean tunnels). The rapid resorption seen in three cases in the common peroneal nerve is probably due to the important venous drainage (proximity of the popliteal vein).

The arterial repercussions have been the subject of our personal studies (selective arteriography) since 1965. Forty-five explorations, made on four types of nerves, have shown an intense spasm of the main artery, associated with venous congestion. The use of the flowmeter to study the arterial flow will indicate accurately the amount of ischemia relative to the limb, the cause of which is clearly perceived during explorations (localized spasm), but is not evident on all arteriographies. Arteriography has yielded the following results, which have been compared with six examinations made on nonleprosy subjects.

Collateral and trunk arteries of the ulnar nerve at the elbow (15 cases). The accessory anastomatic artery is the lower brachial collateral artery, which anastomoses above the elbow joint-line with an anterior branch of the brachial artery, and below the joint-line with the recurrent ulnar branch. The main trunk artery is supplied by three or four arterial pedicles from the collateral artery.

Only one technique has been used in 15 cases, viz., counter-flow arteriography of the brachial artery through an approach which will permit the performance of neurolysis and translocation. Arteriography is carried out before any manipulation on the nerve, i.e., clamp on the lower brachial artery and



FIG. 5. Neuritis of posterior tibial nerve behind the internal malleolus. Neurography shows the passage of lipiodol narrowed by edema, and absence of injection of a plantar nerve.

counter-flow injection. The internal collateral artery is very effectively perfused. In four cases, a combination of arteriography and preliminary neurography has been used with the advantageous result of identifying the trunk artery and its pedicles perfectly.

Two types of result have been obtained: (1) block of the collateral and trunk arteries at the tunnel stricture level. The blood flow is restored after incision of the tunnel; sometimes the blood flow passes into the collateral artery with decreased diameter, but the trunk artery is not visualized on the path of the ulnar nerve in the supratrochlear-olecranal groove. Restoration of the blood flow after tunnel incision. (2) Same procedure before tunnel incision; restoration of blood flow in the collateral artery but not in the trunk artery or else a block in both arteries at a point higher than the upper part of the tunnel. These last pictures indicate either a residual compression by nerve hypertrophy and peritrunkal fibrosis or a thrombosis (infrequent). The

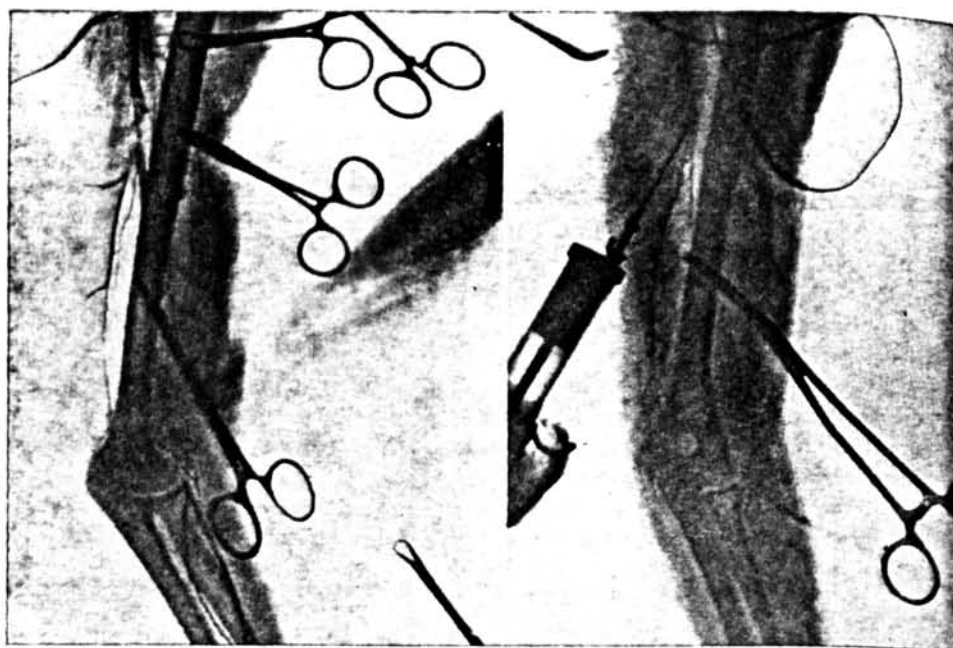


FIG. 6. Before incision of canal; failure of passage to elbow.

FIG. 7. Passage after incision.

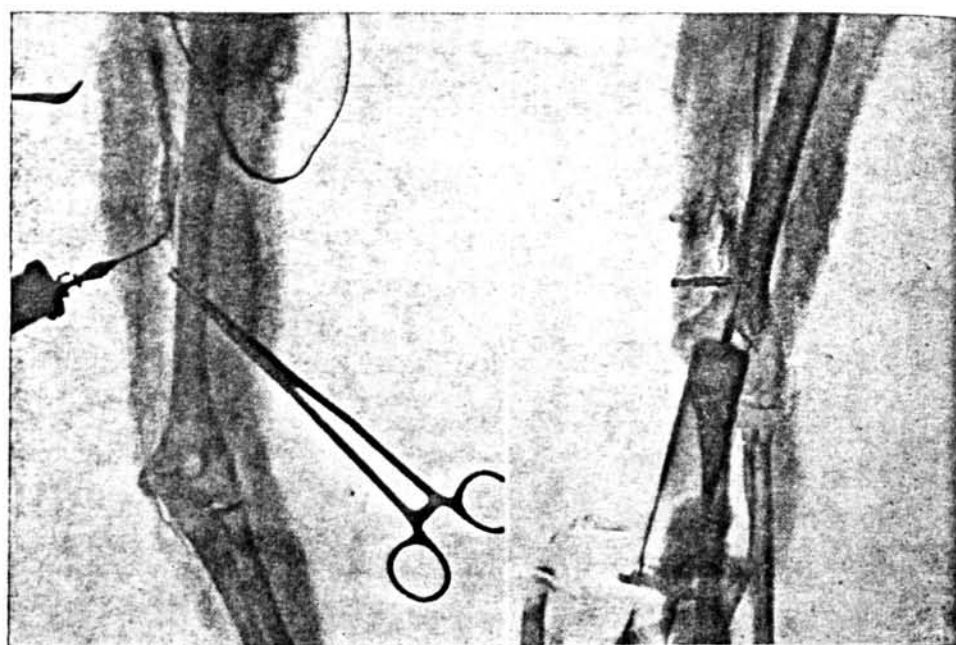


FIG. 8. Late period of passage.

FIG. 9. High arrest of passage, by endoneural stricture and not by the canal.

FIGS. 6-9. Selective arteriography of the collateral arteries and intratruncal supply of ulnar nerve.

latter is most often located in the arterioles and not in the trunk or collateral artery.

Arteries of the median nerve at the wrist (10 examinations). The artery of the median nerve originates in the anterior interosseous artery (collateral artery). In 4.5 per cent of cases only (Dieulafe, MacCormack) the median nerve artery is important. In 45 per cent of cases, it is thin, and in 33 per cent of cases it pierces and passes through the median nerve at the upper third of the forearm, which decreases its flow still more. We may note that a case of thrombosis of this artery has been reported in a syndrome of the carpal tunnel in a nonleprous subject (P. Burnham).

Technique for arteriography of the interosseous artery. We used to make injections into the brachial artery at the point where it divides into two branches, using a clamp below the origin of the radial and ulnar arteries, but we now prefer a simpler technique, viz, injection into the brachial artery at the bend of the elbow, with interruption or reduction of the blood flow in the radial and ulnar arteries through compression of the external and internal edges of the forearm. A combination of neurography of the median nerve and arteriography of the interosseous artery has been used. Previously, a series of separate neurographies had already shown the projection of the median nerve on the skeleton.

Results: The interosseous artery leaves the median nerve at the upper border of the carpal tunnel and ends in an anastomosis with the radial artery. In leprous neuritis the median nerve artery is interrupted at the upper part of the carpal tunnel; if the nerve is healthy, it goes half way down the tunnel. The branches coming from the radial artery through palmar arches then take over. When arteriographies are performed in cases of median nerve neuritis, after tunnel incision the median nerve artery goes a little lower than the upper level of the tunnel, but a normal picture is not seen. We should note this area of vascular dispersion at the level of nerve dispersion with a segment of the median nerve, rather poorly irrigated at this level.

Artery of the common peroneal nerve (5 examinations). This originates in the popliteal artery two fingers' breadth above the knee joint-line, or in a popliteal branch, and follows the nerve a long distance. Below the passage into the external muscle group of the leg, a branch of the anterior tibial artery takes over. Let us bear in mind that the compression against the neck of the fibula affects the truncal artery more when it follows the external side of the nerve (80%) than when it is centro-truncal. The poor vascular supply of this nerve is well known (Sunderland, Fontaine, Imbert, Merle D'Aubigné). The technique used is arteriography of the popliteal area with a tourniquet at the upper part of the calf preliminary to incision of the tunnel in the neck of the fibula.

Results: These are of two different types: (1) the arterial flow is clearly interrupted at the fibula neck (compression by the tunnel), and (2) the artery is perfused only at its point of origin (intra-truncal compression). After tunnel incision and neurolysis, it appears more clearly and goes lower down, though without going beyond the tunnel. In this localization the nerve is poorly supplied through a great part of its length (area of vascular dispersion), and, moreover, its venous drainage is strong and rapid in 50 per cent of cases (neurographic demonstration).

Collateral arteries of the posterior tibial nerve and plantar nerves and trunk arteries (15 examinations). Here the collateral artery of the nerve is the posterior tibial artery, the main artery of the foot in 55 to 65 per cent of cases (Dubreuil-Chambardel). In this instance, the internal and external plantar arteries, which present a classic path, originate in it. When the anterior tibial artery is the main artery of the foot, in 30 to 44 per cent of cases (Dubreuil-Chambardel), the posterior tibial artery ends at the calcaneus and the recurrent branches of the anterior tibial artery take over. Arteriographies of the posterior tibial artery in this anatomic arrangement have possibly suggested obstructions which do not actually exist.

The most logical technique is arteriography of the femoral artery at the Hunter

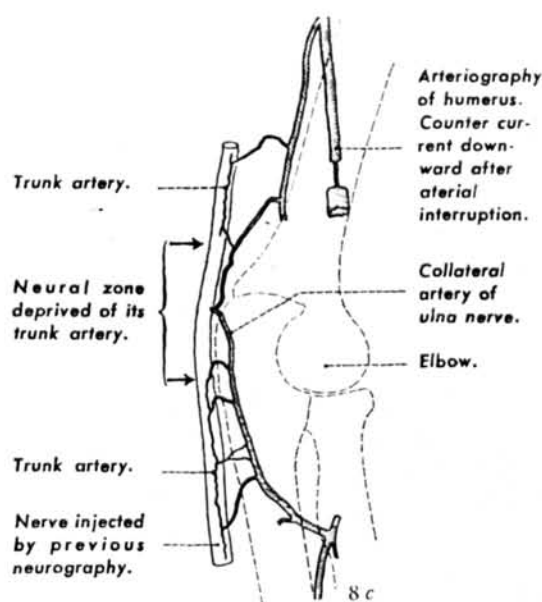


FIG. 10. After incision of the epitrochleo-olecranal canal. The flow passes through the collateral artery and not the trunk artery (radiographic tracing).

canal of the popliteal artery. After a few tentative efforts, we have performed it, using the internal retro-malleolar approach at the upper part of the future neurolysis, avoiding the obstacles pointed out earlier in this paper (anatomic arrangements). (1) Parallel-flow arteriography, performed high enough for the artery of the posterior tibial nerve to be visualized. If it is a case of predominant posterior tibial we perform a second arteriography after tunnel incision and neurolysis. (2) If a predominant anterior tibial type is concerned with the anterior tibial artery branches ending at the heel, we perform a counter-flow arteriography which visualizes the anterior tibial and its branches, without a second operative approach.

Results: The posterior tibial artery is constricted and spasmodic behind the malleolus. Because of the constricting effect of the tarsal ligament, the posterior tibial nerve artery is frequently compressed and not perfused (6 times). Four times, the compressed lateral or internal plantar ar-

tery was not perfused. After tunnel incision, the blood flow is restored in the artery of the posterior tibial nerve and in the internal plantar artery. However, the thin branches to the plantar nerves are not visualized (frequent thrombosis found at operation). In this localization (tarsal and calcaneal tunnels) there is constriction of the vascular supply of the nerve as well as stricture of the main artery of the foot, a possible cause of trophic disorders.

CONTRIBUTION OF LYMPHOGRAPHY TO STUDY OF DISORDERS OF ENDOTRUNCAL HYDRAULICS (9 CASES)

Lymphographies have only succeeded in making evident the lymph relations of the main collector at the lower third of the arm and ulnar nerve. Study of the common peroneal and posterior tibial nerves after lymphography of the external saphenous collectors which pass far from the nerve, or of the plantar collectors, has not yielded valid results.

From the technical point of view, the perfusion must be maintained for two hours. The nine lymphographies performed have shown three types of picture: (1) six times, a subnormal lymphography, with hyperplasia of variable intensity of the supra-trochlear and axillary lymph nodes (slight

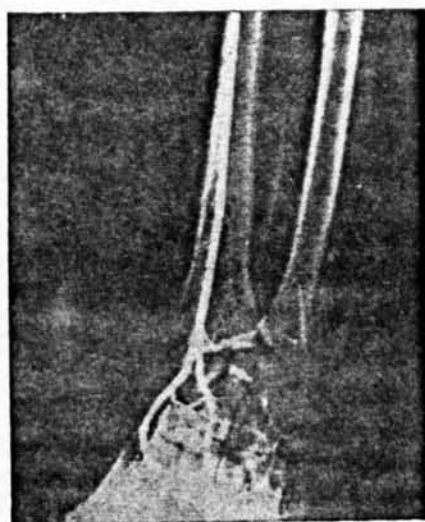


FIG. 11. The artery of the median nerve is blocked at the upper level of the carpal tunnel.

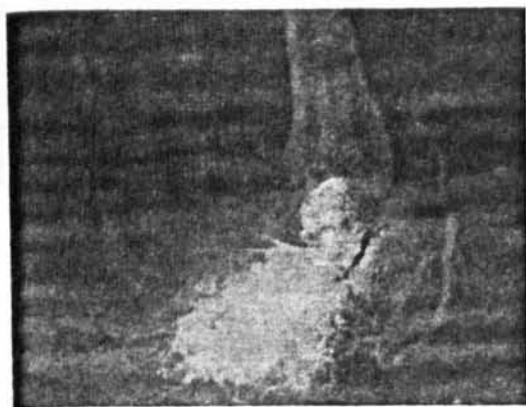


FIG. 12. The posterior tibial artery is narrowed in the internal retromalleolar tunnel.

stasis), (2) twice, a group of dilated lymph vessels surrounding one or two vascular pedicles of the ulnar nerve, with lymph vessels diverted into the perivascular spaces (Wallace type), and (3) once, three pedicles of lymphatic origin which ran into a network of dilated and newly formed lymph vessels with extravasation of the contrast medium. In this case, the lymph vessels in the sheath of the nerve itself became visible after lapse of several days after the injection.

The interpretation of these combined examinations (lymphography and selective arteriography) is made easier by the Starling law, 1895, supplemented by the work of Wolff (1960) and Weale (1968); even a slight increase of the arterial pressure increases plasma filtration through the capillaries. The interfibrillary and interfascicular spaces are poorly drained by the perivascular lymphatic spaces, leading to issue from the sheath around the arterio-venous pedicles. In the nerve trunk a progressive edema is caused, the height of which varies with the number of permeable shunts. If these shunts are blocked, the length of the hypertrophied segment increases. If the permeability is preserved, the lymph vessels of the pedicles can expand and a newly formed and ectatic lymphatic network appears in the connective tissue. The expansion of perivenous lymphatic spaces of the sheath represents an attempt at drainage through the top. Pains can be explained by blocked hypertension in the early stages,

which finds a drainage channel later on.

The histopathology (R. Camain) of six large neural leprous trunks, removed after death in a case of tetanus, and comparison with biopsies of cutaneous filaments taken a short time before, have permitted us to define some points, the importance of which is not recognized, including (1) confirmation, after thorough histopathologic study, that disorders of endotruncal hydraulics do exist, viz., interfascicular, non-inflammatory edema, and expansion of the lymph vessels of the sheath, and (2) confirmation that different levels of intensity of lesion exist. The level of intensity is proportionally higher the more superficial the nerve. It is not possible to extrapolate from a biopsy of a superficial cutaneous nerve (cervical plexus, cutaneous nerve of the arm or the leg) in order to suggest a prognosis of the damaged large trunk. The combination, in the same subject, of extensive lesions of cutaneous nerve filaments



FIG. 13. The lateral plantar artery is not injected (before incision of tibial and calcaneal tunnels).

and less apparent lesions of large trunks was very clear in the six samples.

ANALYSIS OF CIRCULATORY DISORDERS IN LEPROSY NEURITIS

Vascular factors are important and offer multiple modalities, including the following:

1. **Spasmodic state of big arteries** (brachial, femoral, tibial) close to a large nerve trunk affected by leprosy neuritis, which was noted when we inspected the arteries before arteriography. The first measurements, made with a Doppler ultrasonic flow-meter, have shown a moderate reduction of the flow. The phenomenon can be interpreted as a classic consequence of irritation of the sympathetic fibers in the affected nerve. The use of vasodilators or sympathetic infiltrations is in order.

2. **Segmental interruption of arterial circulation in the nerve at the tunnel stricture level**, a factor of localized edema. The presence of quiescent bacilli in Schwann sheaths and slowing of the lymph-flow in the limbs due to glandular hyperplasia at the hilum at first produce a slight, symptom-free, trunk hypertrophy. Some time later the contents (nerve trunk) become too large for the container (osteoligamentous channel) and the vicious circle studied by means of selective arteriography and lymphography is started. The trunk artery is blocked at the level of the nerve segment near a bone canal; frequently the collateral artery and sometimes even the main artery (posterior tibial) are compressed.

The result is an increased arterial pressure at this level. Starling's law (increased filtration) applies and the intraneural drainage is hampered by a general slowing of the lymph flow in the limb and reduced number and diameter of the draining lymph pedicles (perivascular lymph spaces of the pedicles). Edema and trunk hypertrophy are enhanced above the tunnel (on the limb root side) and down the tunnel in the direction of the lymphatic and venous flow. In this way is solved the mystery of this localized hypertrophy, the site of which seems anomalous if one considers the con-

striction only in terms of lymphatic and venous flow. The efferent vessels (veins and lymph vessels) find sufficient anastomoses above the tunnel; the venous hyperplasia and hypertrophy observed are evidence of this. This hydraulics disruption can occur in nerves which are not or only slightly altered, or which have suffered irreversible localized damage. The difficulties encountered in assessing the amount and seriousness of intraneural disorders make the prognosis uncertain.

3. **Segmental ischemia of the nerve, a factor of interruption of nerve conduction.** Intratruncal hypertension compresses the internal arterial system, which is all the more sensitive as the arteries make hair-pin loops. On the other hand, selective arteriographies have shown, in the areas of nerve dispersion which are usually affected, an arterial scarcity peculiar to the common peroneal nerve and localized on a short segment of the median nerve in the carpal tunnel. The ulnar nerve is anatomically more favored, though microtraumas are liable to produce a circulatory by-pass at the expense of its collateral artery (Langeron). The posterior tibial nerve and its branches are less dependent on this mechanism; here the dual tunnel stricture and the amount of intratruncal arterial hypertension brought about by the tunnel compression of the main artery of the foot are the principal factors. Another important effect consists in localized disintegration of myelin.

4. **Nonspecific reactional endovasculitis** (Carayon and Camain, 1965). This seldom affects the collateral arteries or the main artery (posterior tibial), but mainly involves the thin arterioles which enter the trunk and occasionally the trunk artery. These arteriolar obstructions may be incomplete or recover their permeability later on. It is obvious that the confluence of these obstructions may result in an irreversible lesion, but this seldom occurs in the early stages.

5. **Part played by circulatory disorders in the bacillus-induced lesions.** We know there is a slight lymph stasis at the osteoligamentous tunnel, that bacilli evenly distributed in the remaining part of the nerve



FIG. 14. The artery is injected after incision of the tunnel.

are somewhat more numerous there, and that the mild edema of the leprosy nerve is more marked at these sites. The nutritional state of *M. leprae* due to circulatory disorders is different at this level, hypoxia, altered pH, and compression all bringing about death of the bacillus, which lives in a hibernating state in other parts of the nerve. Also, severe reactional states of the nerve are always encountered at these sites (caseous abscesses of tuberculoid leprosy, infrequent acute abscesses in the lepromatous form, and reactional arteriolitis). Thus, in a number of cases, destructive lesions are added to vascular disorders reversible by application of therapy. Therefore, the selection of cases where decompression is recommended will be of great importance.

6. Differences of circulatory disorders depending on the injured nerves. This study allows us to evaluate the importance of the following factors in relation to the nerve involved: (a) importance of tunnel constriction in the hypertrophied nerve, (b) re-

peated traumatism of the thickened nerve (mainly elongation), (c) dispersion areas, (d) arterial insufficiency of the nerve with preferential ischemia and (e) simultaneous compression of the main artery of the limb. Results may be summarized as follows:

- (a) Importance of tunnel constriction in the hypertrophied nerve

Ulnar +++ Median +
Posterior tibial ++ Common peroneal +

- (b) Repeated traumatism due to elongation. These cause pain as well as ischemia induced by circulatory shunts.

Ulnar +++ Median +
Posterior tibial ++ Common peroneal 0

- (c) Dispersion areas: unfavorable because the multiple dividing walls predispose to constriction, which, in these sites, is more endoneural than external.

Median +++ Posterior tibial +
Common peroneal +++ Ulnar ±

- (d) Poor vascularization: This additional slighter factor results in paralysis by arterial deprivation.

Common peroneal +++
Median +
Neural and posterior tibial 0

- (3) Concomitant construction of the main artery.

Posterior tibial ++



FIG. 15. Block of posterior tibial artery in posterior part of the foot. Arterio-venous shunts.

TABLE 1. Factors concerned in disorder of various nerves.

	Ulnar	Posterior tibial	Common peroneal	Median
Tunnel constriction	+++	++	+	+
Traumatism from elongation	+++	+	0	±
Dispersion areas	±	+	+++	+++
Arterial insufficiency	0	0	+++	±
Constriction of the main artery of the limb	0	++	0	0

Table 1 shows the importance of factors depending on the nerve involved.

Circulatory disorders differ with the nerve affected. *Ulnar nerve*: importance of intratruncal hypertension and of compression; relative ischemia caused by elbow flexion and circulatory by-pass. *Posterior tibial nerve*: importance of intratruncal hypertension and of compression; relative ischemia in the limb extremity. *Common peroneal nerve*: predominant ischemia of the nerve. *Median nerve*: predominant compression; relative ischemia caused by circulatory by-pass along a short segment.

THERAPEUTIC INFERENCES

General Indications

Edema and hypertension localized above the tunnels favor the development of destructive lesions of nerves of tuberculoid character or reactional lepromatous lesions which occur only at the sites. Breaking the vicious circle by the simplest means, i.e., incision of a large infraclinal nerve, will thus be a procedure of minor importance, but a rewarding one, for it prevents the development of severe lesions. We come gradually to prophylactic intervention (Callaway, Fite and Riordan). General administration or endoneural injection of alpha-chymotrypsin and hyaluronidase is palliative and often disappointing; thalidomide, requiring care in its use, has given promising results, but has failed on some occasions.

Elongation of a thickened ulnar nerve is a determining factor in the continuance of pain. Rather than immobilization in plaster in a relaxed posture (120° flexion), incision of the tunnel and rerouting of the nerve are

to be preferred. Translocation of the ulnar nerve, avoiding painful elongation of the nerve (Marneffe maneuver) is, therefore, more justified.

Against arterial spasms and nerve ischemia, sympathectomy infiltrations will be used.

Special Indications

Ulnar nerve: the degree of constriction at the lower part of the tunnel and of a two cm. elongation every time there is a forced flexion, show that early incision and translocation are indicated.

Posterior tibial nerve: early incision has a neural and vascular action (arteriolysis of the posterior tibial artery) on trophic disorders.

Common peroneal nerve: early incision will prevent addition of a new cause of ischemia; infiltrations into the lumbar sympathetic system are indicated.

Median nerve: classic incision of the carpal tunnel.

Circulatory disorders due to the conflict of a hypertrophied nerve and a narrowed osteo-ligamentous passage are not only in themselves the cause of neurologic deficiencies but they also create a favorable terrain for nerve destructive lesions around the bacillus so that the hibernating life conditions of the latter are changed. Therefore, we must begin early to combat them (thalidomide and sulfonamides and incision of tunnels).

GENERAL ANALYSIS OF THE MECHANISM OF LEPROUS NEURITIS

Leprous neuritis is induced by an exciting factor, *M. leprae*, but above all is due to

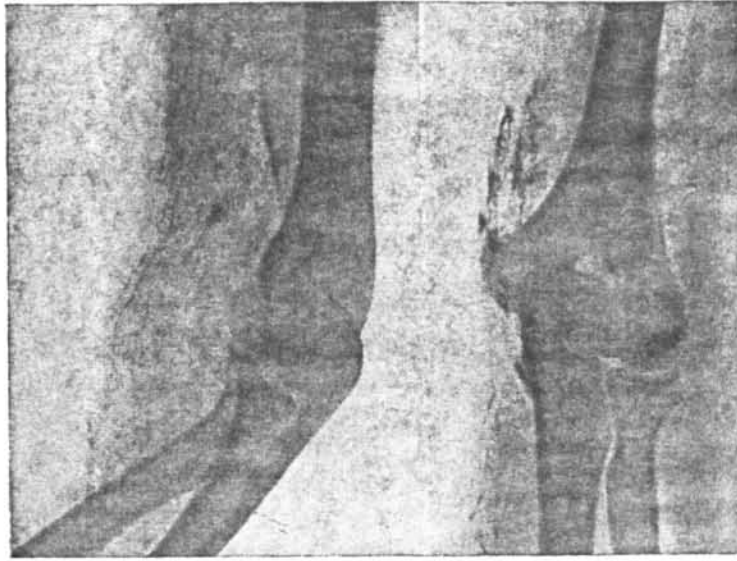


FIG. 16. Lymphography. Pedicle of lymphatic origin running from ulnar nerve to brachial collectors.

chain reactions. The bacillus, to use Cochrane's excellent comparison again, is like the cigarette thrown on twigs in a coniferous forest. The twigs are the precipitating causes; the forest fires represent the chain reactions. The bacillus can live in nerve fibers, and especially in Schwann cells, without altering the nerve impulse conduction. This kind of hibernation produces a slight thickening of the nerve without symptoms of deficiency.

The nerve may suffer from a pathologic phenomenon called "leprous reaction". For us, the expression "leprous reaction" refers to a general mechanism and depends on immunologic phenomena developing from dead bacilli and myelinic disintegration products; it produces a set of component disorders: cell proliferation and infiltration, tissue changes, hydraulic alterations of lymphatic origin, and vascular obstructions.

This reaction appears sometimes in very early stages (lepomatous form treated with sulfones, tuberculoid form with prevailing nerve lesion). Sometimes it occurs late (lepomatous relapses, delayed tuberculoid reactions).

Vascular disorders are integrated in the general picture of leprosy. These include:
1. *Cellular components which differ with the type of leprosy, inflammatory in lepoma-*

tous forms and composite in tuberculoid forms (attenuated inflammatory and auto-immunologic). In lepomatous forms, there are multiform infiltrations predominating in histiocytes with a tendency toward Virchow morphology of the latter cells. Conversion of Schwann cells into phagocytes has been suggested. In tuberculoid forms there is histiocyte infiltration with a tendency toward epithelioid and giant cell formation. In intermediate or undifferentiated forms there is more distinct lymphoplasmacyte infiltration.

In tuberculoid neuritis, the skin branches most frequently show important destructive lesions; at the level of the large trunks the less intense lesions are either of the pure edematous type (rare) or of the localized destructive type associated with interfibrillar edema. In lepomatous and paralepomatous neuritis, the lesions are located in the connective tissue between nerve fibers and fasciculi. The intensity of lesions, which are more dramatic at the level of the skin branches and less destructive at that of the large trunks, must be attributed to the lower temperature (Brand), either because the bacillus finds better conditions for becoming pathogenic or because the relative cold is favorable to immunologic phenomena.

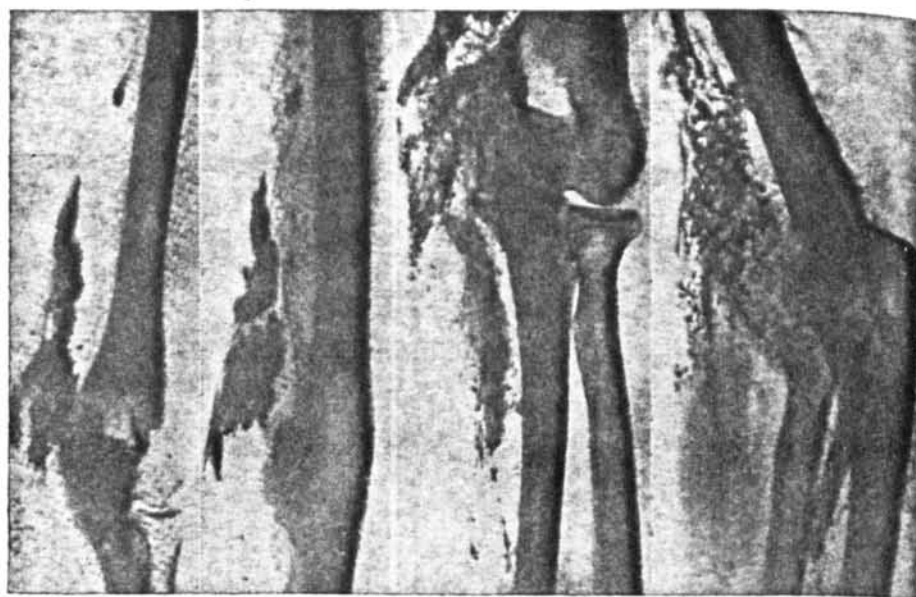


FIG. 17. *a.* Newformed lymphatics between the nerve trunk and the principal lymphatic path. Two pedicles of lymphatic derivation from the ulnar nerve are readily visible in the lower quarter of the arm. *b.* Comparison of lymphography and neurography. The derivative pedicles are readily visible.

Cellular infiltrations and inflammatory reactions in a not very extensible trunk sheath bring about a compression of axons, then a destruction of axons in the preserved Schwann sheath (axonotmesis), and finally connective tissue hyperplasia.

In the "inter-polar" forms (paratuberculoid, dimorphous, borderline) we have observed a common type of lesion with prevailing edema associated with moderate cellular infiltration (Carayon and Camain, 1966). The arterial reactions are of the vasculitis obliterans type and affect a few vasa nervorum.

In paralepromatous forms, in the early stages, the axon is merely inhibited (neurapraxia) or more simply in a state of axonotmesis. It is usually thought that tuberculoid regression is a beneficial phenomenon; unfortunately, it is in no way true for the nerve.

A few parts of the nerves only have been affected by deterioration of the nerve fibers, Schwann sheath included (Zachary's neurotmesis). For the remaining part, an endotruncal decompression, combined with a nonaggressive medical treatment for the

invaded Schwann cells, ought to be effective.

The concept that damage to tuberculoid and interpolar nerves is irreversible from the start is, therefore, a mistake. So is the alleged mildness of lepromatous and paralepromatous neuritis: Iyer and Thangarag show in successive histologic studies that from one reactivation to another the nerve is ultimately destroyed. The decompression of a large painful nerve, as yet only slightly paralysed, is, consequently, rewarding in the long run.

2. *Vascular components.* We may class these as mechanical circulatory disorders in which interruption of arterial flow generates localized edema at the level of the tunnels. In the first stage (Starling law, 1895-1896) the exchange of fluids between capillaries and interstitial tissues is controlled by the filtration pressure which involves osmotic and hydrostatic pressures (stasis of venous capillaries) or arteriolo-capillary hypertension, which increases capillary pore diameter. Arterial block increases the pressure by a factor of 150-300 per cent (Weale). Starling thought that the

capillary vessel is permeable only to water and electrolytes, and not to proteins, which, held up in the blood vessels, increase the osmotic pressure. Drinker (1941-1946), Clark (1947), Patterson (1958), Mac Person (1961), and Calnan (1967), by isotopic methods, have shown that capillaries lose proteins and that protein concentration in interstitial tissues is maintained by an effective return flow of the lymph. In the nerves, there are only lymph spaces, poorly drained by the perivascular spaces of vasculo-neural pedicles. Both pressures, the osmotic and the hydrostatic, have an unfavorable action in this case.

The second stage creates an endoneural compression with an increase of venule resistance and then an ischemia which gradually reduces the arteriole flow. The flow reduction and the appearance of a replacement supply circulation in the veins contribute afterward to the stabilization of nerve hypertrophy.

Vascular reaction through autonomic-reflex: the spasmodic arterial state, which reduces the diameter and diminishes the beats, has always been clearer during our 45 surgical approaches of arteries than

in the arteriographic pictures. It has always been present in the brachial artery at the upper third of the arm and in the lower popliteal artery and posterior tibial artery, near an affected nerve (ulnar nerve, common peroneal nerve, posterior tibial nerve). The flow decrease is moderate (flowmeter).

The diffused sympathetic stimulation offers an explanation. The plantar arteries, when the fibers of the posterior tibial nerve are disintegrating, undergo a noncontractile vasodilation (through acute paralysis of the destroyed vascular nerve filaments) due to their distal situation (scantier sympathetic anastomoses). The opening of shunts visualized by angiography is also made easier. There is an important reduction of the flow in the posterior tibial arteries associated with this vasodilation and these shunts; this combination (reduction of blood flow and early leakage) brings about osteolysis through a reduced supply and an important escape of calcium released by the local mutations produced by traumatism. The trophic disorders of the skin induced by relative ischemia do not allow an effective closing of wounds.

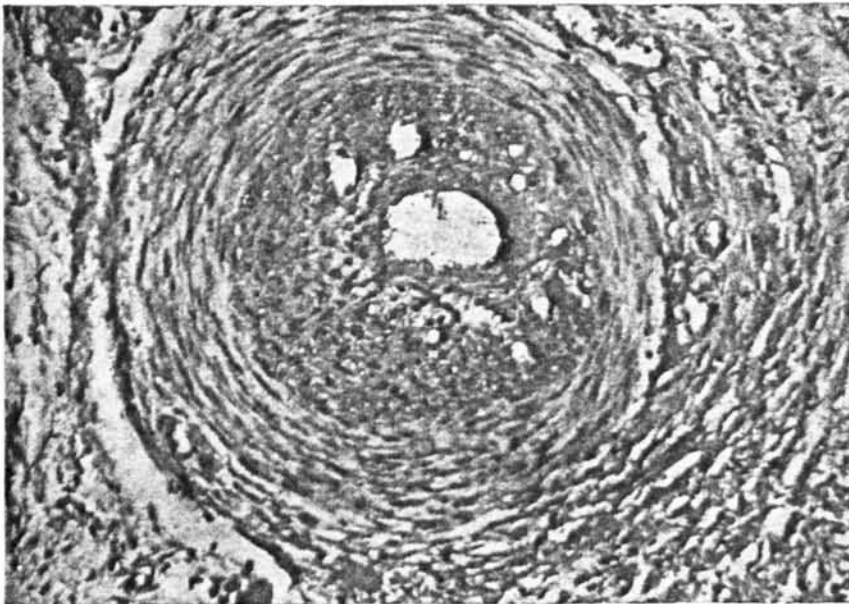


FIG. 18. Endarteritis in a muscular artery of the epineurium. Subtotal obstruction of partially reopened vascular lumen. (Case of tuberculoid leprosy. Edema and endarteritis, but no specific leprosy lesion).

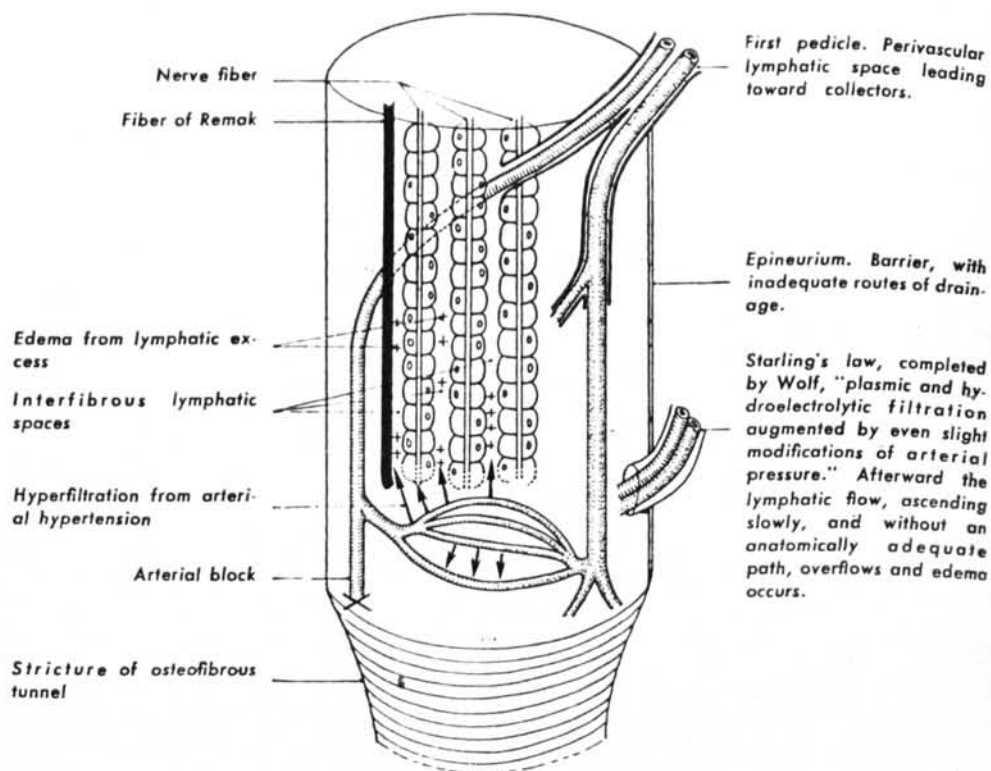


FIG. 19. Scheme showing mechanism of active edema below the canal (down-stream in venous-lymphatic current).

In the hand, when the median nerve is affected by a partial lesion, the flow is slightly reduced. If the median nerve is destroyed at the wrist, besides the overlying arterial spasm or associated lesion of the ulnar nerve, there may be a noncontractile vasodilation and opening of shunts evidenced by angiography.

Proliferating and obliterating vascular reaction: this "endovasculitis", most frequently nonspecific, facilitated by sustained vasomotor reflex, is more probably of auto-immunologic origin (true leprous reaction).

3. *Secondary reactional auto-immunologic component*: This is an immunologic reaction which disturbs the balance of the quiescent bacilli in Schwann cells. The first reaction triggers off the process with increase of edema, constriction in the tunnel, considerable hypertrophy of the nerve above the tunnel, and "endarteriolitis." A secondary reaction may occur, de-

veloping from the products of truncal (injured nerve) or microbial (dead bacillus) desintegration, and reach other nerve trunks in the manner of the Guillain-Barré syndrome (delayed hypersensitivity). An example occurred in a patient suffering from a recent tuberculoid leprosy, who presented classic lesions of the ulnar nerve at the elbow and of the median nerve at the wrist, but also "multineuritic" lesions of the radial and median nerve at the elbow without edema or tunnel constriction (neuroparaxia with segmental demyelination as in diabetes).

4. This study is of considerable importance because *metabolic disorders* (mainly myelinic), generated by ischemia and segmental constriction, are indeed the factors which create a favorable terrain for attack against the nerve by *M. leprae*. Outside these areas the bacillus has a hibernating life.

SUMMARY

Over a period of five years personal studies have been made on circulatory changes in leprosy neuritis. These show that the theoretic concepts of Chatterjee (1933) and Louis Diez (1943) were prophetic.

Documents. Five kinds of examination have been undertaken: dynamic neurographies, selective angiographies of nerve vessels, lymphographies, flowmetries and histopathology.

Neurography: 98 examinations are presented. The nerve stricture and vicious circle created by progressive neural hypertrophy in a narrow canal, variable for each nerve passing into several nerves (ulnar, median, common peroneal, and posterior tibial) is visualized. The stricture begins with the definitive shape of bone prominences. Slowing of speed of ascension of the contrast material (5 to 10 times) and lengthening of resorption time are emphasized.

Angiography: 45 selective examinations of collateral artery and intraneural supply were performed by personal technique. A spastic condition of main arteries near leprosy nerves, reducing the blood flow, was seen before injection of the contrast material. The following were noted with respect to individual nerves.

Ulnar nerve: Flow interruption of collateral artery and of intraneural supply. After incision of the epitrochlear-olecranon tunnel there were several responses, viz., discharge of blood flow in the two arterial channels, or discharge of the collateral artery flow, but not of the intraneural supply, or high interruption in the forearm. After the fascicular neurolysis of the author, discharge (intraneural compression) or persistence (arteriolitis) occurred.

Median nerve: Poor supply at the wrist, aggravated by carpal tunnel stricture.

Common peroneal nerve: Poor supply along the trunk, aggravated by the stricture.

Posterior tibial nerve: Compression of the main artery of the foot, and some-

times interruption of a branch and arteriolitis of rami.

After a time the venous step of angiography shows hypertrophy and hyperplasia, which are able to restore the return circulation. Sometimes there is precocious venous return (common peroneal nerve) or shunts (posterior tibial nerve).

Lymphography: With this procedure three types of result occurred, viz., subnormal, with little stasis and hyperplasia of axillary and epitrochlear nodes (6 times); dilated channels around the vascular pedicles of the ulnar nerve (twice); three pedicles of lymph derivation with a network of dilated channels and extravasation (once).

Flowmetry: Slight reduction of flow in brachial and popliteal arteries; more important for the posterior tibial artery.

Histopathology: Examination of six nerves from a leprosy patient dead from tetanus showed an acellular interfascicular edema.

Synthesis. Many vascular components were evident, as follows:

(a) slight reduction of the blood flow through the main arteries in the vicinity of leprosy nerves (brachial and popliteal arteries), and marked reduction for the posterior tibial artery.

(b) Segmental block of the neural blood supply at the level of the osteoligamentous channels. Consecutive increase of arteriolar pressure (150 to 300%) produced an increased filtration of hydroelectrolytic plasmic and even cellular elements (Starling law, 1896). Intraneural venous and lymphatic drainage was impaired and trunk edema and hypertrophy appeared toward the head of the tunnel. Thus is explained the paradoxical focus of hypertrophy of main nerves in leprosy. In a second phase venous drainage was increased and the process was stabilized.

(c) Segmental ischemia of nerves, a factor of interruption of neural conduction. The inhibition was favored by the hairpin shape of the intraneural arteries.

(d) Nonspecific reactional endovasculitis.

(e) Interrelation of circulatory changes and bacillary lesions. Caseous abscesses,

acute abscesses, and arteriolitis are produced by dead *M. leprae*, and promoted by poor vitality in the regions where they occur.

Conclusions. Changes in circulation are responsible for edematous hypertrophy of nerves and of lesions secondarily produced by the death of bacilli.

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1. CARAYON, A. Chirurgie directe des gros troncs nerveux dans la lèpre. J. Chir. (Paris) 99 (1970) 235-274. This article lists pertinent references to Carayon's papers and those of others. The illustrations in the article here presented are reproduced from the paper cited with the permission of its publishers, Masson et Cie.