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Venous Involvement in Leprosy: A Venographic and Histopathological Correlation[1]

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Leprosy is a chronic mycobacterial disease caused by *Mycobacterium leprae* having special predeliction for skin, peripheral nerves, and the mucosa of the upper respiratory tract. While lesions are confined to skin and peripheral nerves in tuberculoid leprosy, there is multisystem involvement in lepromatous disease associated with continuous bacillemia in these patients. There are conflicting reports regarding vascular involvement in leprosy. Some workers have demonstrated normal vessels ([9]), while others have found involvement of blood vessels ([1, 3, 13, 15]). Studies of vessels by angiography alone ([1, 19, 23]) and with radiological and histological techniques combined ([7, 22]) have revealed frequent involvement of small- and medium-sized peripheral arteries. Leprous phlebitis has been mentioned in early studies of vascular lesions of leprosy ([3, 4, 10, 20]), but only a few reports of definite vein involvement are available in the current literature ([11, 12]).

The present study is an attempt to elucidate the extent of venous involvement in leprosy and its correlation with functional impairment by venographic and histopathological techniques.

MATERIALS AND METHODS

Twenty patients with bacillary-positive borderline lepromatous to lepromatous (BL-LL) leprosy and ten patients with paucibacillary tuberculoid to borderline tuberculoid (TT-BT) leprosy were selected at random from the leprosy clinic of the Postgraduate Institute of Medical Education and Research, Chandigarh, India. The patients were classified according to Ridley and Jopling ([16]). There were ten borderline lepromatous (BL) and ten lepromatous (LL) patients. The paucibacillary group had one tuberculoid (TT) and nine borderline tuberculoid (BT) patients.

A majority of the patients (25) were males; there were five females. Ages ranged from 18–60 years with a mean of 34.9 years. The duration of the disease varied from 6 months to 10 years with a mean duration of 4 years in the bacillary-positive group. In the paucibacillary group, the duration ranged from 3 months to 4 years, with a mean of 1.7 years.

In the multibacillary group, four patients were partially treated with multidrug therapy (MDT) with dapsone 100 mg daily; clofazimine, 100 mg on alternate days, 300 mg once a month; and rifampin 600 mg once a month. One patient had completed 2 years of therapy, and the remaining were untreated. In the paucibacillary group, two patients were partially treated with dapsone 100 mg daily and rifampin 600 mg once a month. One had completed 6 months of therapy, and the remaining were fresh, untreated cases.

Patients with normal-looking hands and feet and without trophic ulcerations and mutilations were selected in order to avoid secondary changes in the vascular system. One BL patient presented clinical evidence of leprous phlebitis in the form of palpable cord-like veins of the lower extremities. Two bacillary-positive patients had prominent lower limb veins. The remaining 27 cases had clinically normal venous networks over the extremities.

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FIG. 1. Normal lower limb venogram in a BT patient.

Two main investigations were carried out: a) venography, and b) lower limb vein biopsy.

Venography. Venography was performed with the patient in a semi-upright (30°–45°) position, with the injected leg non-weight bearing and completely relaxed. Conray 280 was injected through a 23 G needle placed in the superficial dorsal metatarsal vein. About 60 ml of contrast was injected in each limb by hand injection at 0.5–1.0 ml/sec. The entire study was carried out under fluoroscopic control, and spot films were taken. Antero-posterior and lateral views of the ankle, leg, and knee were taken. Only one antero-posterior view of the thigh was taken.

TABLE 1. *Venographic changes in patients with leprosy.*

Venographic abnormality	% Patients showing abnormality
Irregularity of lumen	80
Collaterals	74
Tortuosity	55
Narrowing	44
Occlusion	40
Dilatation (post-stenotic)	37
Incomplete filling	37

Vein biopsy. A lower limb vein biopsy was taken from any superficial vein suspected to be involved or from a preselected segment of vein (i.e., any superficial vein twig from the calf region). An upper limb vein biopsy was also taken in two patients (one BL and one LL) for comparison. A 1.5 cm-long segment of the vein was excised after ligating both ends. The tissues were fixed in Formalin (25%) and processed in an automatic processor. The sections were stained with hematoxylin and eosin (H&E), Fite-Faraco, and Verhoeff van Gieson's stains.

RESULTS

In spite of no clinical evidence of venous involvement of the lower limb (except one BL patient who had clinical evidence of leprous phlebitis in the form of palpable cord-like veins), some form of venographic abnormality was seen in 96.3% of the leprosy patients included in the study. Venographic abnormalities consisted of occulsion, narrowing, tortuosity, dilatation, irregularity, formation of collaterals, and incomplete filling of the lumen by the contrast medium (Figs. 1–4). The venous abnormality was graded as: mild (1–3 abnormalities), moderate (3–5 abnormalities), and severe (>5

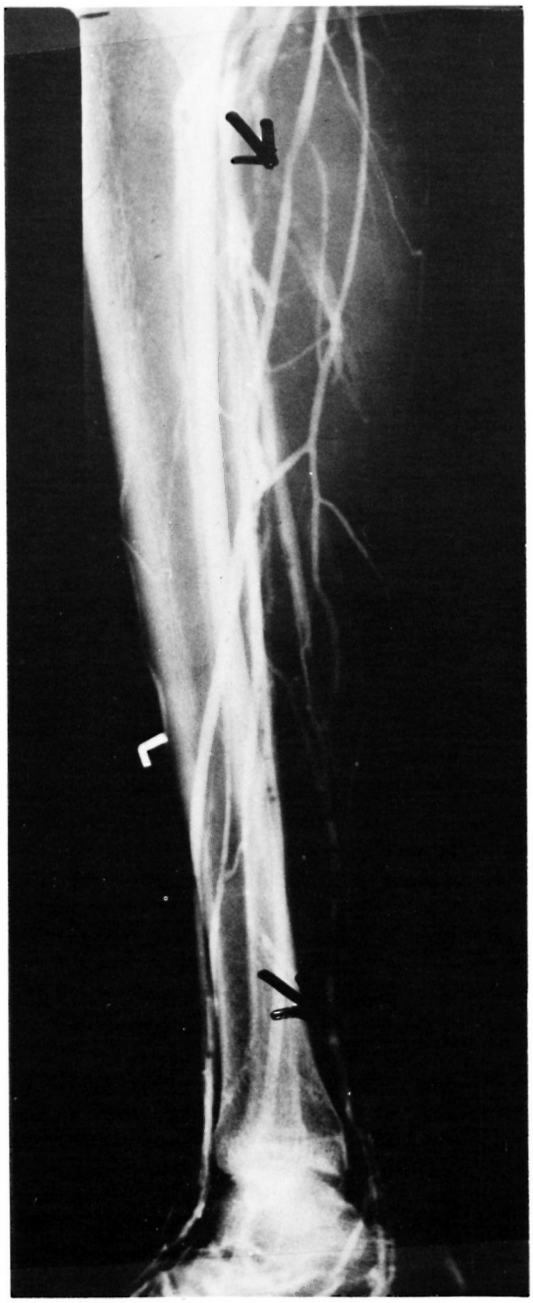

FIG. 2. Lower limb venogram in a BT patient showing mild changes.

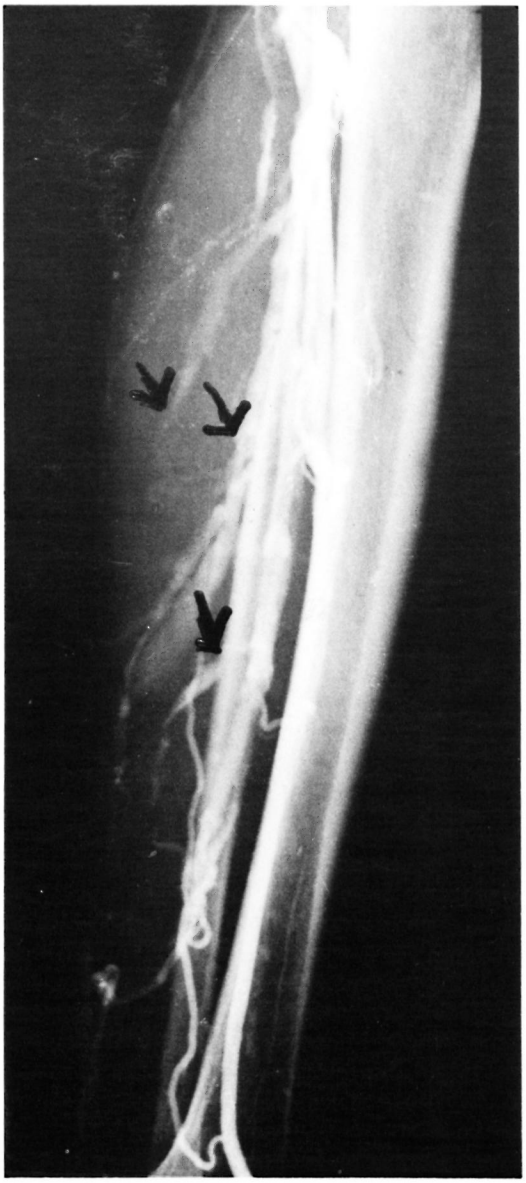

FIG. 3. Lower limb venogram in a BL patient showing moderate changes.

abnormalities). The grading was done according to each individual abnormality noted as a single parameter.

Irregularity of the lumen was seen in 80%, collaterals in 74%, tortuosity in 55%, and narrowing in 44% of the cases. Occlusion was seen in 40%, dilatation (post-stenotic) in 37%, and incomplete filling in 37% of the cases (Table 1). The most common venous abnormalities were irregularity of the lumen and formation of collaterals.

In the paucibacillary spectrum, 90% of the patients showed mild changes while the other 10% were normal. In the multibacillary spectrum, 29.4% of the patients showed mild changes, 41.1% had moderate changes, and the remaining 29.4% showed severe changes (Table 2). The percentage and se-

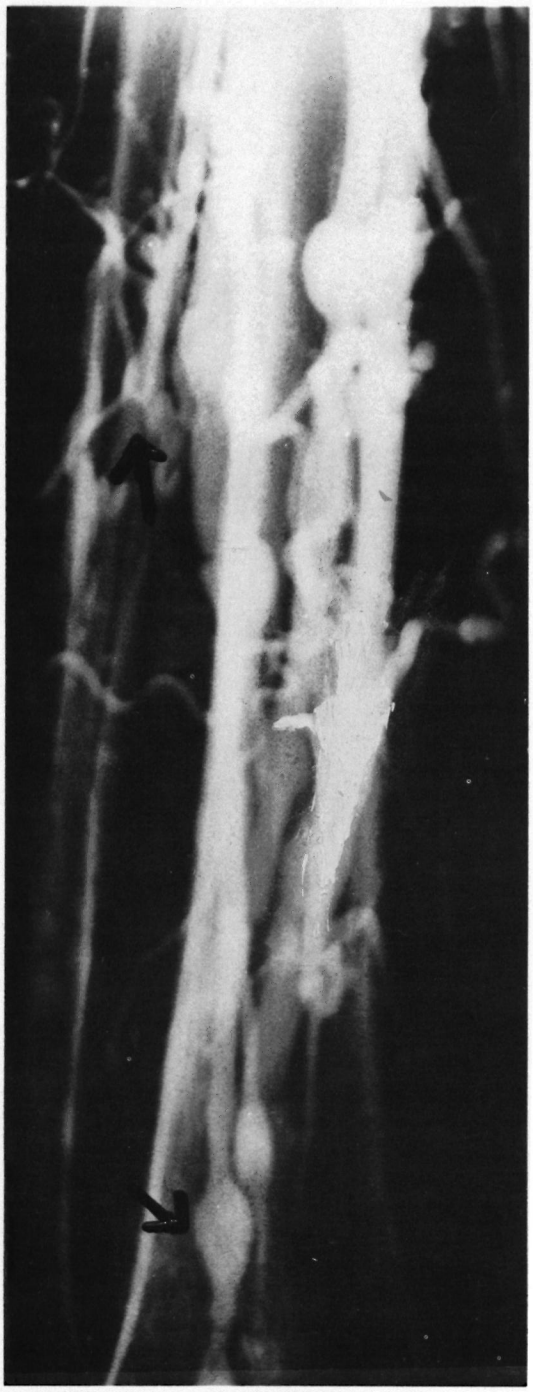

FIG. 4. Lower limb venogram in a LL patient showing severe changes.

verity of venographic abnormality increased from the paucibacillary spectrum to the multibacillary spectrum.

The histopathological changes were evaluated as follows (Figs. 5–8) and expressed as F and C changes in various layers of the vein:

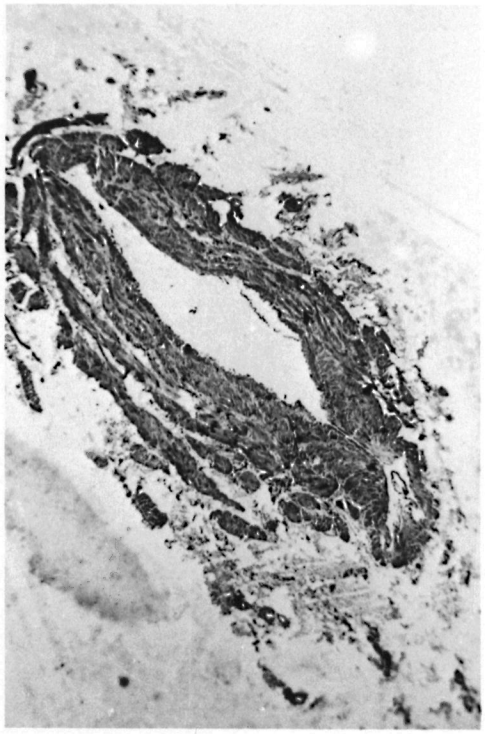

FIG. 5. Section of vein from a BT patient showing normal collapsed vein (H&E ×100).

F = Fibrous ± muscular ± mucopolysaccharide deposits (indicating the granuloma had already been replaced by fibrous or fibro-muscular thickening). Mild = Up to 25% of circumference involved, lumen not compromised; moderate = 25%–75% of circumference involved, lumen narrowed; severe = >75% of circumference involved, lumen severely or totally narrowed.

C = Cellular infiltration (lymphocytes ± histiocytes ± foam cells). Mild = Focal aggregate of cells, either 1 or 2 foci; moderate = >3 focal aggregates but not confluent; severe = diffuse cellular infiltration.

In the paucibacillary spectrum, 50% of the patients showed mild changes, 20% had moderate changes, 10% showed severe changes, and the remaining 20% had normal histology. In the multibacillary spectrum, 25% of the patients showed mild changes, 20% had moderate changes, 35% showed severe changes, and the remaining 25% had normal histology (Table 3).

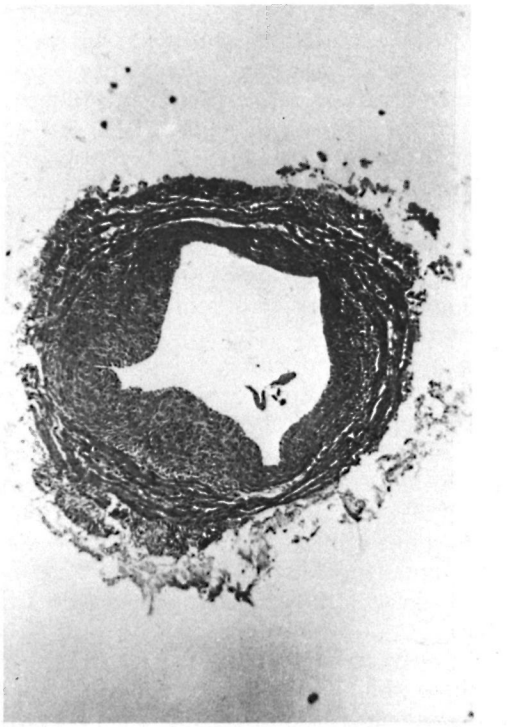

FIG. 6. Section of vein from a BT patient showing moderate fibrous changes in the intima (H&E ×100).

FIG. 7. Section of vein from a LL patient showing severe fibrous and cellular changes in the intima and mild cellular changes in the media (H&E ×100).

Correlation of venographic and histopathological changes. The correlation was evaluated as follows: Perfect = Both radiological and histopathological changes were of same severity, i.e., mild, moderate or severe; good = radiological changes were moderate and histopathological changes were severe or vice versa; no correlation = radiological changes were mild and histopathological changes were severe or vice versa.

In the paucibacillary spectrum, perfect correlation was found in 40% and good correlation in 100% of the cases. In the multibacillary spectrum, perfect correlation was found in 29.4% of the cases, good correlation in 41.3%, and no correlation in 29.4% of the cases (Table 4).

DISCUSSION

Leprous phlebitis was first described by Joelsohn in 1893 ([6]). Since then there have been a number of isolated accounts of venous involvement in the literature ([3, 5, 8, 14, 17, 18, 21]). Mukherjee ([11, 12]) for the first time described definite venous involvement by histopathology in 96% of lepromatous and 4.1% of tuberculoid patients. The results of the present study reveal def-

TABLE 2. *Degree of venous abnormality in leprosy.*

Type of leprosy	% with venographic abnormality			
	Mild	Moderate	Severe	Normal
Paucibacillary	90	—	—	10
Multibacillary	29.4	41.1	29.4	—

TABLE 3. *Degree of histopathological changes in leprosy.*

Type of leprosy	% with histopathological changes			
	Mild	Moderate	Severe	Normal
Paucibacillary	50	20	10	20
Multibacillary	25	20	35	25

FIG. 8. Section of vein from a LL patient showing a foam cell granuloma with globi of acid-fast bacilli (Fite-Faraco ×1000).

inite venous involvement with the percentage and the severity of venous abnormalities increasing from the tuberculoid to the lepromatous spectrum.

In order of frequency, the various abnormalities seen were: irregularity of the lumen (80%), formation of collateral channels (74%), tortuosity (55%), narrowing (44%), occlusion (40%), post-stenotic dilatation (37%), and incomplete filling (37%). About half of the patients (46.6%) had mild changes, a quarter (23.3%) had moderate changes, and the remaining had severe venous wall abnormalities. In 10% of the patients the radiological study was inconclusive. The percentage and severity of vascular abnormalities increased from the tuberculoid to the lepromatous spectrum.

Venography outlines the larger venous channels, and changes in the small vessels may be missed by this method. Histopathological studies are more conclusive of vascular pathology and combined with radiological studies give more complete information.

In the present study, histopathological changes in the veins were seen in 76.6% of the patients. The changes were fibrous or fibromuscular thickening of the vessel wall layers along with cellular infiltration composed of lymphocytes, histiocytes, and foam cells. The cellular changes seen were specific, and were due to leprosy because no other cause for these changes was obtainable.

In the paucibacillary group (TT, BT), 80% of the patients showed changes which were mild and mostly nonspecific. In the multibacillary group (BL, LL) 75% of the patients showed changes comparatively severe in nature. The finding of predominant changes in the intima was in line with the finding earlier reported by Mukherjee ([12]). Acid-fast bacilli were present in 70% of the vein biopsies from the multibacillary group. The bacilli were present within histiocytes, endothelium, and smooth muscle cells. Few free bacilli were seen within the lumen.

In the present study, one BL patient with palpable cord-like veins showed severe histopathological changes. Two other multibacillary disease patients with prominent veins had severe histopathological changes. Mukherjee ([12]) also found histological evidence of leprous phlebitis in 11 out of 12 patients with venous thickening.

TABLE 4. *Correlation of venographic and histopathological changes in leprosy spectrum.*

Type of disease	Venographic changes				Histopathological changes			
	Normal	Mild	Moderate	Severe	Normal	Mild	Moderate	Severe
TT	—	1	—	—	—	1	—	—
BT	1	8	—	—	2	4	2	1
BL	—	4	2	3	3	3	2	2
LL	—	1	5	2	2	2	2	4
Total	1	14	7	5	7	10	6	7

The upper limb vein biopsies taken in two multibacillary patients showed moderate changes in one and severe changes in the other, while lower limb vein biopsies from the same patients showed severe changes. This indicates that the changes were specific and not influenced by gravitational factors.

In the paucibacillary group, perfect correlation of histology and radiology was found in 40% of the patients and good correlation was found in 100%. In the multibacillary spectrum, perfect correlation was found in 29.4% and good correlation in 41.1%; no correlation was found in 29.4% of the patients. The lack of correlation may be due to variable severity of the histopathological changes along the length of the veins.

Considering the many arteriographic changes reported in the literature ([2, 7, 19, 23]), it was only natural to expect venous involvement also. In the present study, venographic and histopathological changes were seen in a large number of patients, and the two correlated well.

No data are available in the English literature to date for comparing the venographic findings in leprosy reported in this study.

In conclusion, peripheral venous system involvement is frequently seen in leprosy patients, the severity and intensity increasing from the tuberculoid to the lepromatous end of the disease spectrum. Specific leprous changes in the veins lead to disturbance in the normal tonicity and blood flow and may contribute to thrombosis at these sites, resulting in ischemia. The frequent vascular changes may be contributing to the mutilations and deformities of the hands and feet which occur in leprosy.

SUMMARY

Venous system involvement was studied by venography and vein histology in 30 leprosy patients irrespective of age, sex, duration of the disease, and treatment. Vascular abnormalities by venography were seen in 96.3% and by histopathological studies in 76.6% of patients. The percentage and severity of radiological and histological changes increased from tuberculoid to lepromatous in the disease spectrum. Perfect correlation of histology and venography was found in 40% of the paucibacillary patients and good correlation was found in 100%. In multibacillary patients perfect correlation was found in 29.4%, good correlation in 41.1%, and no correlation in 29.4% of the patients.

RESUMEN

Se estudió la afección del sistema venoso en 30 pacientes con lepra de diversa duración y variable tratamiento. Por venografía, se observaron anormalidades vasculares en el 96.3% de los pacientes, en tanto que por histopatología solo se observaron alteraciones en el 76.6% de los mismos. Los porcentajes y la severidad de los cambios radiológicos e histológicos aumentaron del extremo tuberculoide al lepromatoso del espectro de la enfermedad. Se encontró una correlación perfecta entre histología y venografía en el 40% de los pacientes paucibacilares y una buena correlación en el 100%. En los pacientes multibacilares se encontró una correlación perfecta en el 29.4% de los casos, una buena correlación en el 41.1%, y ninguna correlación en el 29.4% de los mismos.

RÉSUMÉ

On a étudié l'atteinte du système veineux, par veinographie, et étude histologique des veines, chez 30 malades de la lèpre, sans égard pour l'âge, le sexe, la durée de la maladie, ou le traitement. La veinographie a permis de mettre en évidence des anomalies vasculaires chez 96, 3% des malades, alors que les investigations histopathologiques en ont révélé chez 76, 6%. La proportion des modifications radiologiques et histologiques, de même que leur gravité, augmentaient tout au long du spectre de la maladie, depuis la forme tuberculoïde jusqu'à la forme lépromateuse. On a relevé une corrélation parfaite entre les résultats histologiques et veinographiques chez 40% des malades paucibacillaires, et une corrélation satisfaisante chez 100%. Chez les malades multibacillaires, und corrélation parfaite a été observée chez 29, 4%, une corrélation satisfaisante chez 41, 1%, alors qu'aucune corrélation n'était notée chez 29, 4% d'entre eux.

REFERENCES

1. Basu, S. P., Ghosh, S., Mukerji, N. and Roy, K. P. Angiography in leprosy. Indian J. Radiol. **14** (1960) 180–187.
2. Cochrane, R. G. *Leprosy in Theory and Practice.* Bristol: John Wright & Sons Ltd., 1959, pp. 90, 94, 261.
3. Fite, G. L. The vascular lesions of leprosy. Int. J. Lepr. **9** (1941) 193–202.
4. Gutierrez, F. L. [Leprous phlebitis.] Rev. Bras. Lepr. **29** (1961) 123–126.
5. Herxheimer, G. Ueber die Leprazellen. Virchows Arch. Path. Anat. **245** (1923) 403–447. Cited by Fite in n. 3.

6. JOELSOHN, B. Ueber die Erkankung des Gefässystems bei der lepra. Jurjew, 1893. Cited by Fite in n. 3.
7. KAUR, S., WAHI, P. L., CHAKRAVARTI, R. N., SODHI, J. S., VADHWA, M. B. and KHERA, A. S. Peripheral vascular deficit in leprosy. Int. J. Lepr. **44** (1976) 332–339.
8. KLINGMÜLLER, V. Die Lepra. In: *Jadassohn's Handbuch der Haut- und Geschlechtskrankheiten.* Vol. X/2. Berlin: Springer, 1930, pp. 542–546. Cited by Fite in n. 3.
9. LEITNER, A. J. Les osteo-arthropathies lèpreuses du pied. Int. J. Lepr. **6** (1938) 471–476.
10. MITSUDA, K. Leprous changes in the blood vessels, especially of venae. *Collected Works on Leprosy.* Nagashima, Japan: Chotoka, 1935, vol. 1, pp. 22–23.
11. MUKHERJEE, A., GIRDHAR, B. K. and DESIKAN, K. V. Leprous phlebitis. Int. J. Lepr. **48** (1980) 48–50.
12. MUKHERJEE, A., GIRDHAR, B. K., MALVIYA, G. N., RAMU, G. and DESIKAN, K. V. Involvement of subcutaneous veins in lepromatous leprosy. Int. J. Lepr. **51** (1983) 1–6.
13. PATERSON, D. E. Radiological bone changes and angiographic findings in leprosy with special reference to pathogenesis of "atrophic" conditions of digits. J. Fac. Radiologists **7** (1955) 35–36.
14. PHILLIPPSON, L. Intorno agli erithema lebbrosi a'alla flebite lebbrosa. G. Ital. Mal. Ven. **34** (1899) 279–289. Cited by Fite in n. 3.
15. POPOV, K. P. [Changes in blood vessels of skin in leprosy.] J. Dermatol. Monatsschr. **152** (1966) 945–950. Abstract in Int. J. Lepr. **35** (1967) 540.
16. RIDLEY, D. S. and JOPLING, W. H. Classification of leprosy according to immunity; a five-group system. Int. J. Lepr. **34** (1966) 255–273.
17. RIECKE, H. G. Ueber einen Fall von Lepra Tuberosa mit besonderer Bertücksichtigung der Histopathologie. Arch. Derm. Syph. **148** (1925) 448–453. Cited by Fite in n. 3.
18. SAKURANE, K. Ueber die histologischen Veränderungen der Leprösen Haut. Beitr. Path. Anat. **32** (1902) 563–572. Cited by Fite in n. 3.
19. SEHGAL, V. N., GHOSH, S. K., MANERKER, A. N. and DUKLE, P. D. Angiogram—a means to assess trophic changes in leprosy. Lepr. India **45** (1973) 17–19.
20. SILVEIRO-FILHO, B., OPROMOLLA, D. V. A., FLEURY, R. N. and TONELLO, C. Vascular involvement in lepromatous leprosy. Int. J. Lepr. **41** (1973) 583.
21. UHLENHUTH. Ueber die Verbreitung der Leprabacillen in menschlichen Körper. Deutsche Med. Wochnschr. **26** (1900) 127–128. Cited by Fite in n. 3.
22. WAHI, P. L., KAUR, S., VADWA, M., SODHI, J. S. and CHAKRAVARTI, R. N. Peripheral arteriographic studies in leprosy. Clin. Radiol. **27** (1976) 365–370.
23. YADAV, S. S. Arteriographic evaluation of vascular changes in leprosy. Angiology **29** (1978) 17–21.