II. REVIEW OF LITERATURE
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AEETIOLOGY

Leprosy is an infectious disease caused by *M. leprae*, characterised by prolonged latent period and a chronic course with dermal and neural manifestations. The disease was regarded contagious long before, but from the seventeenth to the later part of the nineteenth century it was considered to be hereditary, although convincing proof for this was lacking. However, the hereditary theory of origin of leprosy received most influential support from the report of the Royal College of Physicians of London, prepared in 1862. Later in 1875, the British Guina Leprosy Commission favoured its contagious origin. Many others had favoured the theory of communicability of the disease. Another theory which attracted some attention was the fish theory of Sir Jonathan Hutchinson in 1880. It was believed that consumption of fish caused leprosy. It is now accepted that leprosy is an infective disease caused by *M. leprae*, more popularly known as Hansen's bacillus or lepra bacillus. It was discovered by C. Armauer Hansen in 1874. Few leprologists appreciated the significance of Hansen's remarkable discovery but Danielssen and Boeck (1848) the foremost leprologists of that era, who attributed leprosy to
multiple causes, firmly opposed Hansen's view that the rods which had been observed by him, were the cause of the disease. Jeanselme (1934) remarked that the discovery of specific bacillus of leprosy by Hansen ruined many cherished hypothesis and redeemed to the status of secondary causes of many aetiological factors to which previously a preponderant role had been attributed. A considerable long period had elapsed since the discovery of the causative organism and a good amount of research work had been done all over the world without having yet fully elucidating the manner in which the organism passes from the diseased to the healthy and until now the organism does not fulfil the Koch's postulate. That *M. leprae* is the causative agent of leprosy should be supported by the following factors: (1) The constant presence of the bacillus in leprous lesions, (2) The organism should be cultivable outside the body of the host in vitro, (3) The organism when inoculated should be capable to produce the particular disease in the susceptible case. Perhaps, the first condition has been fulfilled, although in practice, by routine examination, leprosy bacilli are found only in serious types of cases. The second and the third conditions still remain unfulfilled.

*M. leprae* is the organism of a Schizomycete of the order *Actinomycetales* and of the family *Mycobacteriaceae* and
of the genus Mycobacterium. The organisms of this genus are called acid fast bacilli because of their property of resisting decolourisation by dilute acids, once they have been stained with strong basic dyes such as carbol fuchsin. The bacilli vary in size and shape but are usually straight or slightly curved. The leprosy bacilli are usually found in agglomeration termed globi which have the appearance of tightly packed bundles of cigars. Denny (1934) suggested that the globi are colonies growing within an unidentified membrane. The clumps of bacilli appear to be bound together by a lipid-like substance called glia. \textit{M. leprae} appear in both intracellular and extracellular glial masses, by this it suggests that they are enclosed in a capsular membrane. Babes (1901) also described a surrounding slime or capsule which has been recently confirmed by Hanks (1961). They are non-motile and non-sporing. The organism in size, morphology and acid fast staining reaction, closely resembles \textit{M. tuberculosis}, but the form is more deeply stained with carbol fuchs in and with Gram stain. It resists decolourisation with weak mineral acids to a lesser degree than \textit{M. tuberculosis}. \textit{M. leprae} are less granular, have larger and more clearly defined granules and are more frequently observed intra-cellularly. The morphology of \textit{M. leprae} was reviewed in detail by Lohnis (1922). It has been shown by Ghosh et al
(1961) that X-ray radiation does not change the morphology of *M. leprae*. It has got no effect on the cell membrane, nor is there any change in the acid fastness of the bacilli.


Attempts of cultivation of *M. leprae* on artificial media or its transmission to lower animals has been difficult and produced conflicting results. Many workers reported the cultivation of one or more bacilli from the tissue of leprosy patients. Diphtheroid like non acid fast organisms have been isolated by Kedrowski (1901), Williams (1911), Bayon (1912), Duval and Wellman (1912) and Sarkar (1962). Chromogenic acid fast organisms have been reported by Clegg (1909), Rost (1911), Williams (1911), Duval and Wellman (1912), Currie *et al* (1912) Mc.Coy (1914). The non-chromogenic forms were observed by Duval (1910), Duval and Wellman (1912), Soule and Mc.Kinley (1932 b). With a view to explaining the difficulty encountered in cultivating *M. leprae* interesting hypothesis had been put forward by Hanks (1945). Shepard (1957), Fjelde (1957) and others
studied the behaviour of different mycobacteria using different types of tissue culture.

Experimental leprosy:

It is still a debated question whether or not infection can be induced by inoculation into skin. Klingmuller (1930) reviewed elaborately the evidence for and against experimental inoculation in man. de Langen (1933) reported an accidental inoculation of a physician using hypodermic syringe which had been used on a person suffering from leprosy. Marchoux (1934), however, demonstrated the development of leprosy by inoculation. Lagoudaky (1936, 1937) reported that repeated injections of blood of leprosy patients to healthy subjects developed cutaneous lesions. Porritt and Olsen (1948) described the development of leprosy over the site of a tattoo mark in two men from the same community who were tattooed by the same person on the same day in Melbourne.

The successful inoculation of the disease in monkeys was done by Nicolle (1905) and Soule and Mc. Kinley (1932 a), Collier (1940) and Lai (1955). But Cochrane and Ramanujan (1945) did not find general dissemination of infection. Adler (1937), Dharmendra and Lowe (1940), Burnet and Jadford (1940), Chatterjee (1958 b) and Binford (1958 a, b) all reported their
success in producing leprosy infection in hamsters. There is no unanimity of opinion about the success of inoculation of mice with human leprosy organism. While de Souza Arujo (1928, 1929), Shiga (1936), Nojima (1939) and Yamamoto (1939) claimed success in producing human leprosy organism in mice but others such as Sellards and Pinkerton (1936), Suzuki (1939), Burnet (1940), Nakagawa and Nakamura (1954) were of opinion that there was no definite sign of multiplications of the bacilli with general dissemination. Fite (1941 b), de Souza Arujo (1941), Barman (1945), Fielding (1946), and Bergel (1958) succeeded in producing human leprosy in rat. They all adopted different methods. Feldman (1956), Kelkar and Ranadive (1958) reported success in producing lesion in animals while Binford (1958 a,b) Ghosh et al (1961) failed to produce lesion in irradiated animals. Sato (1949) employed various methods of inoculation in gold fish, frogs, toads and birds. The results were mostly negative. Tanimura and Nishimura (1953) inoculated fowls, white rats, guineapigs, rabbits and golden hamsters producing only local reaction. Successful inoculation of the testicular substance of small pigs had been reported by Mitsuda (1941), in breast muscles of the hen, by Ota (1941) and of the local and visceral tissues in fowl by Sato (1949). Wade (1948) had summarized several cases of accidental transmission from man to man.
It is true a great many attempts have been made by various workers to cultivate this organism, the majority have been unsuccessful, and though successful results have been claimed and cultures of acid fast bacilli have apparently been isolated from leprosy lesions, it is doubtful whether these strains represent the true leprosy bacillus.

CLASSIFICATION

The clinical manifestations of leprosy are varied. These are further influenced by immunological and epidemiological factors.

There is considerable controversy over the classification of leprosy even to-day. The W.H.O. Expert Committee on Leprosy (1952) classified leprosy into:

I Lepromatous
II Tuberculoid
III Borderline
IV Indeterminate.

However, this classification does not include maculo-anaesthetic and polyneuritic types, recognised by some of the Indian leprologists (1955). The term 'dimorphous' was

CLINICAL FEATURES

The tuberculoid type: This is a non-infectious form with lesions localised to skin, nerves, and regional lymph nodes. Routine 'slit' smears are usually negative, but sometimes a small number of leprosy bacilli may be found. The skin lesions consist of slightly to markedly thickened, anaesthetic patches, varying in size, number and location. The hypopigmentated patches may be found anywhere, but more commonly on face, lateral or dorsal aspects of extremities and buttocks. The patches have a well defined outline. The surface is usually dry due to impairment of sweat secretion. With the onset of reaction, the lesion suddenly becomes more red and raised, soft and oedematous. There is definite loss of cutaneous sensibility, but all the sensations are not equally affected, pain sensation is lost earlier and the sensation of light touch later. There is thickening of the
cutaneous and peripheral nerves. There may be localised abscess in the affected nerve.

The lepromatous type: This is an infectious type, lesions are wide spread throughout the body with the affection of the mouth, nose, throat, eyes and other systemic organs. The nerves are infected but the thickening of nerves is lesser compared to that in tuberculoid type. The routine 'slit' smears from the affected skin and usual mucosa are moderate to strongly positive for acid fast bacilli. The skin lesions are wide spread and generalised. They are specially marked on face and ears, back, buttocks, knees, elbows and dorsal aspect of the hands. The affected skin shows loss of hair. It produces diffuse thickening with some erythema, with the affected parts appearing smooth and shiny. There is considerable thickening and corrugation of skin. Definite infiltration and thickening may be found in the ear lobes. The skin lesions may be numerous, flat and hypopigmented, the margins are ill defined. The nodule is a definitely thickened, rounded, circumscribed mass of leproma. There is slight or no sensory change.

In borderline group: This group includes cases with thick skin lesions, which resemble both the tuberculoid and lepromatous patches, while others are in between the two polar varieties. They are in an unstable state clinically,
bacteriologically, histologically and immunologically. Bacteriologically, these are moderately positive. Lepromin reaction is variable. The skin lesions are usually multiple, red, thick and uniformly raised or there may be depression at the centre. The patches are well defined, soft in consistency. Anaesthesia may be present in lesions on the extremities. Both cutaneous and peripheral trunks may be thickened, but less frequently than in tuberculoid cases.

The indeterminate group: This group includes the flat macular lesions of leprosy. They may evolve towards the lepromatous form or tuberculoid form or may remain unchanged indefinitely. They are very slightly positive or negative bacteriologically. Lepromin test is usually negative. There is less sensory change, less involvement of cutaneous or peripheral nerve. The skin lesions are multiple or may be single with ill defined margins.

PATHOLOGY

General:
The leprosy bacilli spread along the lymphatics to drain into the regional lymph glands. The other way of attack is via the perineural lymphatics to the nerve trunk. By way of lymphatics and blood vessels, or directly the eyes are
affected by lepra bacilli causing episcleritis, conjunctivitis, iritis, iridocyclitis and panophthalmitis. The liver, spleen, kidney and even bone may be affected, and lepra bacilli may be found in these organs. In advanced cases secondary amyloidosis may occur in the liver, spleen and the kidney, and there may be osteomyelitic changes in the bone.

Studies on the contacts of leprosy patients by Figueredo and Desai (1949) showed that unlike other Mycobacterium infection, the reaction of the primary focus of infection by M. leprae can hardly be detected by any histopathologist nor the clinical feature by any dermatologist. Acid fast bacilli may be present in the dermis and immunologically a patient with negative lepromin reaction may gradually turn positive. It is a common belief that leprosy bacilli enter the body through a breach in the skin or mucous membrane but Khanolkar (1951, 1955) asserts that the bacilli can make its way through healthy skin. He is of opinion that the bacilli move about in the lymphatic fluid of the dermis in any part of the skin more so in the exposed areas. The onset of the disease depends on the susceptibility of the individual which is again dependent on the immunological status of the patient. When the defence mechanism of the host is on the low side, the invading organisms multiply and organise themselves in the cutis. Of the invading bacilli, some become a prey to
wandering histocytes but considerable time will elapse before the micro-organisms are completely digested.

Nishiura et al (1957) demonstrated by electron microscope that the bacilli are taken up by the phagocytic activity of the axons of the nerves. By tissue culture studies Nakai (1955, 1956) showed an engulfing action of the growth cones of axons and probably these are lodged in the axoplasm. In this process, the vacuoles move in the direction of the spinal ganglion along with the bacilli moving streams. Nishiura et al (1957) observed that the cytoplasm of the Schwann cells which surround the normal fibre lack in the presence of leprosy bacilli but they may be found in the degenerative stage of Schwann cells, e.g., in Bungner's bands. This is an example of phagocytosis of the bacteria. Being phagocytosed the bacilli continue to multiply in the axoplasm of the nerve fibres and may remain inert for a considerable period. Subsequently during some altered circumstances, the bacilli proliferate in the nerve fibres and burst in the endo and perineural tissues.

In lepromatous type in the very early stage there is usually only perivascular and perineural infiltration with granuloma consisting of collection of massed macrophages and bacilli laden with epitheloid cells; well formed foam cell may also be present. The granulation tissue is held together in
a very fine network of reticulin fibres. In well developed cases, the epidermis becomes thinned out and flattened and clear sub-epidermal zone is free from infiltration. There is distortion, and destruction of hair follicles, the sweat and sebaceous glands. The nerves stand out prominently in the midst of granulomatous foci, as nerves are free or comparatively free from infiltration although there may be perineural infiltration. Their morphological description was made by Virchow (1860, 1861) and even today it is known as 'Virchow's cells or lepra cells. These large cells vary much in size and shape. The protoplasm is homogenous. Yamamoto et al (1958) and Nishiura (1960) described the morphology of lepra cells under the electron microscope as cells which contain leprosy bacilli in the cytoplasm. Single bacillus and small group of bacilli are tightly surrounded with a limiting membrane which seems to be the cell membrane of the same lepra cells indented deeply during the phagocytic process along with various normal cytoplasmic components such as microsomes, mitochondria, lipid granules and endoplasmic reticulum. Bacilli are often embedded in opaque droplet and the dense granular material of the opaque droplet in which the foamy structure develops form another inner limiting membrane. Each unit of foamy structure has a single layer of markedly electron dense membrane. The nucleus of the lepra cells is found by the side of foamy structure of the cytoplasm. The cell membrane is a continuous
single structure but in a fully developed leproma it is often very hard to find the boundary of each lepra cells. As the disease gradually advances the lepra cells become foamy, multivacuolated and multinucleated and pushed to the periphery. This type of histology is characteristic of lepromatous type and is found in the skin, nerve, mucous membrane, lymphatic nodes, bone marrow and internal glands. When the disease regresses, there is often an absence or loss of tissue or deep scarring which is characteristic of other productive inflammatory conditions. The healed lepromatous lesions in the skin show a peculiar wrinkled crushed tissue paper appearance. Histologically it is found that the granulation tissue gradually disappears, there is a collapse of the reticular frame work and there is regeneration of the elastic tissue and collagen fibre network. But still lepra cells may be found. These observations have also been made by other workers, such as Henderson (1929), Mitsuda (1936), Bertellotti (1939), Fite (1943), Tilden (1945) and Noel and Suzanee (1949).

Cases of tuberculoid leprosy were described by Arning (1884) and Jadassohn (1898) but its existence was not confirmed by other workers. Initially there is appearance of groups of epitheloid cells inside the fine nerve twig and the formation of sharply circumscribed foci of such cells surrounded by lymphocytes and histiocytes. The epitheloid
cells show a tendency to coalesce and form under certain circumstances typical Langhans' giant cells. The epitheloid cell has a fairly outlined cell body which is irregular in form. The protoplasm is non-granular and takes faintly acidic stain. Sometimes the epitheloid cells are somewhat small in size with darkly staining nucleus and cytoplasm. They may be bi-nucleated. The lymphocytes are mostly about the size of a red blood cell. Generally it has a thin rim of clear, non-granular, slightly basophilic cytoplasm with a large nucleus which is round or oval in shape with chromatin network. Plasma cells are almost like lymphocytes but without granules. They are larger and have more definite basophilic cytoplasm. These cells are round, oval or pear-shaped and they contain spherical nucleus which is situated eccentrically and chromatin masses are arranged like the cart wheel.

The reticulum network in which the granuloma develops is recognizably different from that of leproma. The fibres vary in thickness, but usually are coarse. This localised and compact granuloma spreads in the sub-epidermal zone in the dermis in a cord-like manner, usually along the neuro-vascular bundle. The epidermis at places is thinned out due to extension of the granuloma. The granuloma is composed of a central core of large cells with faintly acidophilic, finely granular cytoplasm and indistinct cell margin and rarely
necrosed tissue. In between these cells there are few Langhans' giant cells. The central zone is surrounded by layers of lymphocytes of variable thickness, epitheloid cells, histiocytes and cells with acidophilic granules in the cytoplasm. The most peculiar and probably the most consistent feature of tuberculoid leprosy lies in changes in the nerves. The nerve shows endo, peri and epineural infiltration. As a result of these cellular infiltration amongst the nerve fibres which causes pressure, there may be slight to complete destruction of nerve fibres. The degree of the tuberculoid change varies with the clinical activity and, therefore, with the thickness of lesions the greater the thickening, the more marked the tuberculoid change. Bacilli are usually found in the axon, Schwann cells and there is extreme paucity of acid fast bacilli in the cells of the inflammatory exudate.

The mixed or dimorphous type shows all kinds of gradation and combination of both tuberculoid and lepromatous histology, but none of them is well defined to be classified into two polar groups, as one or the other type of histology may be prominent but some features of other types may also be present.

Many workers have tried to find out the definite histology in simple or uncharacteristic type, but most of
them have failed to observe any special histology as this type of histology may be found in any chronic disease. There may be non-specific granuloma with round cell and epitheloid cell infiltration in the skin and nerves. But in this type of leprosy endoneural infiltration with the presence of acid fast bacilli are found. (Kedrowski, 1914; Tebbut, 1926; Henderson, 1929; Muir and Chatterjee, 1933; Wade, 1934, 1937; Lowe, 1936; Wade and Rodriguez, 1937; Hughes, 1938; Grieco, 1936; Oberdoerffer and Collier, 1939; Saenz and Palomino, 1939; Bosq, 1940; Fite, 1943; Dharmendra, 1949; Saikawa, 1951).

Wade and Rodriguez (1940) stated that the 'borderline lesions' histologically, showed indeterminate, picture in most cases, neither tuberculoid nor frank lepromatous. Wade (1941) in borderline histology observed the greater tendency for the granuloma to be separated from the epidermis by a narrow zone which is usually found in leproma. Cochrane (1940a) also observed the same with numerous dilated capillaries in the clear zone between the epidermis and granulomatous masses. The nerves are grossly invaded, although sometimes the invasion is less marked than that seen in massive tuberculoid leprosy. de Souza Lima and his associates (1947) observed a multitude of epitheloid cells, scarcely forming tuberculoid arrangement
with a few lymphocytes accompanied by vascular dilatation.
The anatomical substrate by de Souza Lima (1952) is that bacilli are found in greater number in the tuberculoid granuloma, than what is usually the case in the rectional leprides although much fewer than in lepromatous lesions.

Wade (1961) and Wade and Perrin (1961), Currie (1961) and others noted histopathological changes in borderline lesions with wide variations. Almost all of the bacilli were in good condition without the degeneration so commonly seen in the bacilli of the leproma. Leiker (1963), observed globi in sections of borderline cases on the lepromatous side and absence of them in sections more inclined to the tuberculoid side. In the description he also demonstrated globi in section of lesions with an interrupted sub-epidermal zone, marked cellular nerve infiltration and dense masses of epitheloid histiocytes some of which do show globi. Gay Prieto (1961) accepted the histological diagnosis with presence of both lepromatous and tuberculoid appearance in the same lesion or in different lesions.
Nature of changes:

Barrington James (1931) observed pyogenic osteomyelitis histologically in neural leprosy. Barneston (1950) tried to correlate histological and radiological findings. Histologically he observed fraying of distal margins of bones, associated with breakdown in continuity of cortex. The gaps were filled up by connective tissue extending from the periosteum to the marrow. In cases of gross deformity, when no diffuse osteoporosis was visible radiologically, cortical bone remained dense and of normal width up to the distal bone margins. When diffuse osteoporosis existed, the cortex was narrowed and active osteoclastic activity would usually be found. In concentric atrophy there was absorption of the marrow cavity which was greatly reduced in width. There was increased osteoclastic activity in comparison to osteoblastic one. There were myxomatous change and fibrosis of bone marrow with abundant lymphocytes and plasma cells. Hashimoto and Kozuma (1960) observed considerable amount of atrophy of the bone specially where lepra bacilli, could be detected.

Basu (1962) observed granuloma in the bone marrow of lepromatous cases and pyogenic osteomyelitis in neural cases.
Observation of Job (1960) indicated that the bone looked yellowish brown in colour. Microscopically, invasion of inflammatory granulation tissue in the bone trabeculae was observed. There were also scattered collections of lymphocytes and occasional plasma cells and plenty of acid fast bacilli. Fragmentation and necrosis of the bone trabeculae were also found. In some cases, proliferation of osteoid tissue was seen with no evidence of calcification. The invading macrophages destroyed the osteoid tissue.

In many parts of the sections there were proliferating fibrous tissue which showed areas of hyalinisation.

Attempts have been made to find out the aetiological basis of the bone changes. In neural leprosy, chronic non-specific infection is assumed to be the main cause of the ulcer in addition to the mechanical factors. (Khan, 1939; Silveria, 1944; Milroy Paul, 1947; Brand, 1950; Fisher, 1955; Paterson, 1955; Price, 1959, 1960a; Anderson, 1961 and Hassan, 1965). Hirschberg and Biechler (1909) observed lepra bacilli in large numbers in the bone in lepromatous cases. Gass and Rishi (1934) studied bone marrow of 69 leprosy patients living or dead. The bone marrow in 17 out of 21 mixed cases was positive for M. leprae, and in neural cases none showed acid fast bacilli. Lowe and Dharmendra (1937) searched sternal puncture aspirate of 50 patients for the acid fast
bacilli; in 32 patients with lepromatous leprosy 16 were positive. Among 18 neural cases, only 1 had acid fast bacilli. Faget and Mayoral (1944) have demonstrated the presence of lepra bacilli in bone cysts and thought that the bone changes were due to \textit{M. leprae} de Dulanty (1948) observed lepra bacilli in 44% of lepromatous cases revealed by aspiration of bone marrow. Two of them showed typical Virchow cells with abundant globii. The acid fast bacilli in the bone marrow of patients with negative skin smear, was observed in 1 out of 8 dimorphous cases and in 2 out of 52 indeterminate cases by Karat (1966) while studying 382 leprosy patients.

**Pathogenesis of bone change:**

Neurological factor: Both the cutaneous and the nerve trunks are involved, thickening being a salient feature. Thickening may involve the entire nerve or section of it. In long standing cases the nerves may be thickened due to fibrous tissue formation. The sensory changes are more marked than the motor changes. The nerves may be involved by the lepra bacilli.

Neural or neuro-vascular factors as the main cause of the bone changes were thought by many workers. (Chamberlin \textit{et al.} 1931; Murdock and Hutter, 1932; de Josselin de Jongh, 1934;
Karaseff, 1936; Cooney and Crossby, 1944; Faget and Mayoral, 1944; Cuervo et al 1948; Casacci, 1950; Barneston, 1950; Cherlinzonal and Pirastu, 1954; Paterson, 1955; Silva, 1959; Anderson, 1961; Karat et al 1968).

Miller (1913), Colombier (1914) found bone changes in the feet before the patients could be diagnosed clinically as leprosy, suggesting that the peripheral nerves were involved earlier than the skin. Lowe (1936) found lepra bacilli in the nerve fibres in about 60 per cent of patients without skin lesions on routine examination.

Muir (1944) mentioned that the destruction or blockage of the sensory nerves, by cellular pressure and later by fibrous constriction of the axis cylinders depress the sensation of the foot and hand and also involve the vascular supply. The motor paralysis of the muscles also helps in the formation of ulcers. Faget and Mayoral (1944) have attributed that long standing leprous neuritis, resulting in disturbance of the nutritional functions of the affected nerves was the main cause of bone absorption. They further observed that this did not occur in pure cutaneous and lepromatous type. Erickson (1948), Barneston (1950) observed that the leprous neuritis must be sufficiently of long duration and of an advanced stage with degeneration and fibrosis of nerve fibres before bone absorption takes place.
Paterson (1955) while studying the bone changes in leprosy observed that nearly all the patients had some nerve involvement either sensory or motor. Of these 90 per cent showed non-specific bone changes. Primary changes were due to nerve involvement and the secondary changes were due to soft tissue infection.

Silva (1959) studied 400 leprosy patients in Peru. He found that sensory disorder was the commonest. Lesion of the terminal branches of the nerve fibres was the most important cause of the sensory disturbance in Leprosy. Motor affection occurs in 76 per cent and were exclusively in hands and feet. He found perforating ulcers in the feet in 47.5% and in the hand in 0.5%. He considered that the perforating ulcers were due to multiple factors, but the neural factor causing loss of sensation and destruction of autonomic fibres was the prime cause. Da Varies (1959), Price (1959, 1960b), Karat et al (1968) all had suggested that similar ulcers were seen in other neuropathic conditions, such as peripheral nerve injury, neurosyphilic, diabetic neuropathy and spina bifida.

Price (1959, 1960a), Languillon et al (1960) found no correlation between the presence of ulceration and sensory loss. They stressed that not more than half of the cases clinically showed any anaesthesia. On the contrary others thought that the anaesthesia was the prime cause for
the formation of ulcer. Oberdoeffer and Collier (1940), Srinivasan (1953), Ross (1959), Anderson (1961), Hassan (1965), Susman (1967) and Karat et al. (1968) have found bone changes most marked in those bones where muscles were paralysed. This paralysis was due to lepra affection of the supplying nerves. Muscular paralysis secondary to the nerve lesion is given the principal role in the pathogenesis of trophic ulcers of the foot by Muir (1943), Cooney and Crossby (1944), Karat et al. (1968) with consequent progressive shortening and deformity of the phalanges. Susman (1967) was of opinion that the plantar ulcers occurred due to multiple factors such as sensory loss, motor loss and vaso-motor loss. Nerve tissue are, however, most susceptible to damage when these are invaded by the lepra bacilli as had been known undisputed since many years. (Lie, 1904; Grecio, 1936; Torrssujew, 1940; Reddy and Krishnamurthy, 1963; Hargrave and Mother Marion, 1964).

Vascular factor: It has been recognised for many years (Joelsobuni, 1893, quoted by Fite, 1941a; Phillipson, 1899; Uhlanhutt, 1900; Sakurane, 1902; Herheimer, 1923; Riecke, 1928; Klingmuller, 1930; Cowdry, 1940; Fite, 1943; Castello et al., 1949) that the blood vessels related to leprous nodules and skin may be involved in the pathological process.
Barringto (1931), Barneston (1950), while describing the pathogenesis of neural leprosy observed that in lepromatous neuritis there was destruction of vaso-motor fibres but Barneston (1950) observed no organic occlusion of the arteries. He showed that the cause of failure of the vaso-motor reflex lies in the nerves and it was considered that this failure was the essential factor in the bone atrophy. On this ground, to relieve the peripheral vaso-constriction, lumbar sympathectomy was tried by Goheen (1933), Marty (1938), Kirkaldy-Willes (1945), Guadagnine (1945), Kobayashi (1953) and Silva (1957); perifemoral sympathectomy by Py and Riveros (1929), Black (1933), Virichhli (1941) and Kiraldy-Willes (1945) and epineurectomy by Vishnevsky (1938) and Ranade et al (1957). However, de Josselin de Jongh (1934) found that the blood vessels were unaffected and Oberdoerffer and Collier (1940) believed that the sympathetic nerves which regulate the blood supply show little or no affection by lepra bacilli, which was contrary to the views held by many workers. Oberdoerffer and Collier (1940) held that nutritional change caused by inefficient circulation is the cause of ulcers. Carlos (1940), Languillon (1946), de Veiga (1947) suggested that the ulcer was due to vascular stasis and tried parenteral acetyl choline as a vaso-dilator but Languillon (1946) did not find satisfactory results. On the idea of vaso-constriction Gokhale (1957) and Maney et al (1958)
treated the leprosy patients with hydrazine as a vaso-dilator agent. Job (1960) pointed out that the defective circulation due to irreversible changes in blood vessels play some part in plantar ulceration, whereas Anderson (1961) could not find any influence of circulation in the formation of trophic ulcer. da Veiga (1947) expressed that the joint changes are 'neurotrophic'.

Barneston (1950) carried out oscillometric studies of the arteries of the wrist and ankle in 37 leprosy patients but failed to detect any abnormality. In skin temperature tests of smaller digital vessels he showed that there was a failure of reflex dilatation of vessels in the affected hands, when the opposite healthy limb was immersed in hot water. Local warming and cooling produced normal vascular response. These findings, corroborate the assumption that sympathetic nerve fibres are damaged in leprosy. He showed that local blood vessels had not lost dilatability but vaso-motor control was disturbed. Chatterjee (1959) while studying the cause of blister formation with the help of thermo-couple studies, demonstrated defect in the absorption and radiation mechanism of heat of the affected parts.

Llano (1943), Casacci (1950) and Gokhale et al (1959), while studying the cause of trophic ulcer observed deficiency of blood supply in the foot of leprosy patients with ulcers;
Gokhale et al (1959) further believed that some inherent inadequacies of the circulating system could predispose to ulceration of foot under condition of stress and strain. Llano (1943) also emphasized that the neurotrophic factor may be another cause of plantar ulceration.

Fite (1941a) found vascular lesions due to specific action of *M. leprae* in 32 out of 77 cases. In most of the cases organisms were found in the endothelial cells of the terminal vascular loops including arterioles, capillary and efferent venules. In only one case a leprous mass was found, projecting into the lumen of an artery. The arteries and the veins appeared to be involved with equal frequency.

Cooney and Crossby (1944) noticed very strong pulsation of the large arteries of the wrists and ankles indicating good circulation. Negree and Fontan (1956) observed that the bone lesions of leprosy occur due to fatigue or repeated trauma of the structures which are poorly vascularized because of nerve damage and the vascular changes are entirely secondary to neuritis.

Price (1960b) was of opinion that the lepra bacilli might involve the venous system. He described that phlebothrombosis of the foot and the lower leg starts in the vicinity of the ulcer and spreads along the deep channels
into the calf. The valves are incorporated in the clot, so that when the vein recanalises the venous channels lack vulvular support, chronic venous stasis ensures and the post-phlebitic syndrome is established. He further emphasised that the acute attack of phlebitis may pass unnoticed but usually there is pain and swelling of the calf and sole. The oedema of the feet may completely subside but becomes more permanent with each fresh attack until it hardens into a firm non-pitting swelling of the lower leg. The venous stasis hinder normal healing process and predisposes to subsequent inflammatory phlebitis.

**Traumatic factor:** Bechelli and Rotberg (1951) described that the distribution of plantar ulcers corresponded to 'walking pressures' and concluded that the cause was primarily 'neural' and secondarily 'mechanical stress'. Khan (1939) observed healing of plantar ulcers with rest. This was confirmed by Haythornthwaite (1943), Silveira (1944), Milroy Paul (1947), Fisher (1955), Newman and Anderson (1955), Bose (1956), Languillon (1946) and Price (1960a). Faget and Mayoral (1944) while elucidating the causes of trophic ulcers were of opinion that trauma is an important contributory factor. Cochrane (1964) states "we believe all trophic ulcers commence from injury, this may be slight so
hardly to be noticed". Muir (1944) and Brand (1960) expressed the same opinion.

Brand (1950) supported the trauma theory for the formation of ulcer. He thought that it was due to the spreading of the weight over a wide area of the sole. He further concluded that the 2 factors which produce ulceration are sustained pressure and active injury. In general people who were known to suffer from anaesthesia of the sole of the foot have sustained pressure and people who walk bare foot get direct injury. He believed that prolonged standing is very harmful. Barneston (1950) writes that the destruction of proximal bones was occasionally due to secondary infection. Such destruction took place in bones adjacent to metatarso-phalangeal joints and was largely due to trauma on insensitive bones and joints as an effect of weight bearing. Paterson (1955) has described that undoubtedly mechanical factors play an important part in the bone changes in neuro-leprosy but when fingers are contracted and protected from trauma and thus from soft-tissue infection, no bone erosions take place. Where the metatarsal heads take excessive body weight as in foot drop, callositis develop under these metatarsal heads, cracks appear, and soft-tissue infection and ulceration take place. If a patient is confined to bed or if weight is taken off the metatarsal heads ulcers heal up and bone changes also heal up.
Ross (1959) observed combination of a few factors for the causation of ulcers, such as the scarring which reduces loss of friction mechanism; the necrotic blister - which favors secondary infection; fixed deformity i.e., the insensible hand and foot are always under over pressure, causing damage to the tissue over the heel or forefoot; the inter-metatarsal abscess due to pathogenic organism found in the anaesthetic foot. With the insensible feet the patients walk with high stepping gait and foot descends on the ground on the lateral border. Predominance of forefoot ulceration was found by Ross in 76% and he claimed that these ulcers were actually lying in front of the metatarsal heads and not directly under them.

Price (1959, 1960a) in Nigeria observed in 2000 cases that the ulcers occur in the anaesthetic foot over the point of maximum trauma on the bony prominences. Thus 71% of the ulcers were under the forefoot, i.e. sites which closely follow the dynamic pressures on the walking foot. On the other hand, the heel area is affected in only 16.5%. Similar observation was made by Anderson (1961), Srinivasan (1963) and Tio et al (1966). It may be that heel bears most of the standing pressure, hence the least common area that is affected. It may be said that cushion or pad is more in the heel than in any other portion of the foot. Price (1959) has
also confirmed Ross's view (1959) that the insensible hand and foot work under more pressure than what they need. The lack of plantar sensation automatically involves increased pressure on the sole during walking. It has further been observed that in the anaesthetic foot, the extent of the infection is commonly more widespread than what appears clinically. Srinivasan (1953) observed that proximal phalanx of the great toe is the most common site of trophic ulceration. He further observed that ordinary walking foot-prints of normal feet showed that much of this region does not come into forcible contact with the ground. Thus the part which is not normally subject to much compression especially during walking was found to be the most frequent site of ulceration. Hassan (1965) in VI Conference of Indian Association of Leprologists (1965) has pointed out four factors for the formation of plantar ulcers. The primary factor is the anaesthetic foot, the other three secondary factors are the walking foot, pressure bearing area, and bony prominences.

Metabolic factors: Nishi (1932) observed disturbance of the ossification of the costal cartilage in cases of nodular leprosy and this seemed to him to be due to disturbed calcium metabolism. Banley and Legar (1922) and Villela (1938) observed increased alkaline phosphatase activity of serum of advanced leprosy patients and attributed this to the changes
in the bones. Possibly the power to hydrolyze phosphate esters by plasma was disturbed. Venkatasubramanium (1941), Dhople and Mager (1962) noted a definite increase in values of phosphatase activity of serum accompanied by bone changes.

Lancepleine (1949) studied 37 leprosy patients with ulcers for calcium metabolism of which 15 were lepromatous, 10 mixed, and 12 neural. He observed low serum calcium but he didn't attach much importance to this and could not find any correlation between the hypocalcaemia and the occurrence of ulcers.

**LUNG PATHOLOGY**

Conflicting opinion still exists on the etiology of lung lesions in leprosy. Some workers hold that the lesions are due to *M. leprae* while others attribute them to associated to *M. tuberculosis*. According to Hansen and Looft (1895), and Lowe (1929) there exists a sharp distinction between leprosy and tuberculosis. They further suggested that the acid fast bacilli found in the sputum were due to the bursting of a nodule in the larynx. They recommended that in order to establish a differential diagnosis in doubtful cases, a thorough examination of the
bronchial glands should be made. In fact, they never failed to find tuberculosis of the glands and to the contrary they had never seen anything resembling leprous glands in autopsy.

Scagliosi (1896), Bruster (1898) expressed grave doubts regarding the existence of leprosy of the lungs. Wade (1927) on the autopsy evidence of a large number of cases, stated that he never saw a gross leprotic lesion of the lungs. Fambri (1914), Saga-Masaki (1914), Kobayashi (1929), Ranade and Gokhale (1954) all have stated that lung lesions in leprosy are always associated with tuberculosis. The observations of Kobayashi (1929) were based on the autopsies of the lungs of leprous patients. In 32 out of 60 cases he found tubercle bacilli with pathological changes of a tubercular nature. In 8 out of 32 tubercular lungs and 11 out of 28 non-tubercular lungs he observed lepra bacilli.

Ranade and Gokhale (1954) studied 8 cases of leprosy with lung lesions and considered that these were due to leprosy in 7 and due to tuberculosis in 1.

Sticker (1905) was of opinion that leprosy may affect the lung in any form, from that of chronic-peri-bronchitis to caseous pneumonia, in which case it may resemble tuberculosis. On the contrary, there may also be no pathological change although bacilli may be numerous. Babes (1906) observed varying degree of lung lesions in leprosy. His evidence was
in favour of these lesions being due to leprosy and their differentiation from tuberculous lesions depended on the arrangement and the morphological characteristics of the two organisms. Wise (1912) confirmed occurrence of pulmonary leprosy and to eliminate conflicting opinions about the tissue, searched for acid fast bacilli in all cases and planted a portion of lung tissue in the thigh of a guineapig. Out of 11 cases he found acid fast bacilli in all excepting two. The lungs of the experimental animals showed petichial haemorrhages, and slight anthracosis and but no gross pathological lesion was found. On microscopic sections there was a diffuse round cell infiltration with occasional giant cell, slight catarrhal cellular exfoliation in the surrounding area with no fibrosis. Blood vessels and capillaries were greatly congested, no increase of leucocytes or inflammatory exudate could be seen; there were numerous lepra bacilli. Wise (1912) considered that the lesions in the lungs comparatively recent even in advanced cases resembled more a final general dissemination, rather than the natural sequence of leprosy.

Muir (1933) drew his conclusion from his experiments on guineapigs who were intubated with acid fast bacilli positive sputum. He was of opinion that all the 9 cases suffered from lung leprosy. He stated that the condition was
due to leprosy of the lungs in most if not in all. But he further mentioned that before making a final diagnosis of pulmonary leprosy, septic lung abscess, without leprosy of the lungs but accompanied by the bursting of a suppurating leprous nodule of the laryngeal and pharyngeal mucosa, must be excluded. Isamu (1935) observed that hardly any change in the lung be detected macroscopically. But one or two leprosy bacilli could be detected microscopically in the alveolar septa, in the foamy and endothelial cells together with lymphocytes and plasma cells.

Rabello, Jr. et al (1938) also observed involvement of the lungs in leprosy. Ermakova (1940) microscopically observed bacillary emboli in the pulmonary capillaries of the leprosy patients during reaction. Fite et al (1947) also noted lepromatous infiltrations in the lung. Junnakar (1957) in Poona made autopsies on 20 bodies, and the sputum of 100 cases were studied by him. In 10 cases the sputum concentrate was injected into guineapigs, which were sacrificed after 10 weeks and examined histologically and bacteriologically. From all these observations he concluded that lung lesions occur in leprosy.
RADIOLOGICAL STUDIES

Bones and joints:

Honeij (1916) observed that the earliest changes were either thinning of the epiphyses, specially the distal ends or a decrease in circumference of the distal phalanges of the little finger. He further observed that the changes may range from early atrophy to total absorption, distortion or fracture. He was of opinion that the atrophic changes were expected in the neural type and the inflammatory or hypertrophic changes in lepromatous type. But he further added that both types of changes might be seen in any of the polar variety of leprosy.

Chamberlin et al. (1931) studied radiologically the bone changes in leprosy and found in 15 percent of 150 selected patients in Honolulu. Baringto James (1931), Paget and Mayoral (1944), Cuervo et al. (1948), Casacci (1950), Kung et al. (1959), Paterson (1961), Basu (1962), observed that the bone changes are mainly 'neurotrophic' where atrophy of the bones begins in the distal margin of the terminal phalanx of both hands and feet and proceeds proximally. The basic bone lesion is 'neurotrophic' type that varies in accordance with the degree and duration of peripheral nerve damage due to leprous neuritis which leads to destruction of the vasomotor
fibres. The other change is the secondary one, which is due to repeated trauma to insensitive bones and joints. The pyogenic infection of the soft tissue as well as of the bones, is the contributory factor. They further observed the specific involvement of bone by leproma causing 'cystic changes'. In addition to this neurotrophic and cystic changes, Paterson (1959), observed in 10% cases osteoporotic change due to disuse out of 894 patients.

Murdock and Hutter (1932) found bone changes in the hands and feet in 50% out of 140 patients at Kalihi Hospital, Honolulu. They mentioned that the infection is carried to the bones through vascular channels. By curreting the cysts in the phalanges in lepromatous cases they found acid fast bacilli. Karaseff (1936), found deformity of the hands and feet of the leprosy patients in 95% out of 77 patients in an institution near Irkastik. Hayashi (1940), in the meeting of 10th Japanese Leprosy Association gave evidence of bone involvement of patella, and the medial and lateral malleoli of the ankle, olecranon process, styloid processes of wrist joints. He further observed by X-ray and pathological section, that the articular cavity is free from any change. Very little information is available about the nature of disease process in these areas. Marino and Silva (1938), found osteolysis and osteoporosis. Similar changes were observed by da Veiga (1947),
in India. Marino and Silva (1938), further observed osteo-
arthritic change among 100 leprosy patients with ankylosis 
and pathological fracture of the phalanges and metatarsals 
which were dependent on perforating ulcers either directly or 
indirectly. The areas most commonly affected were in the 
following order, 1st, 2nd, 3rd metatarsals and lastly heel. 
Oberdoerffer and Collier (1939), were of opinion that the 
bone changes were earliest and most extensive in lepromatous 
cases which was not supported by Karat (1966); and the change 
was essentially an atrophy of the ivory and cancellous tissues. 
According to them there may be formation of sequestrum from 
chronic osteomyelitis due to secondary infection of the bone 
and the soft tissue.

Faget and Mayoral (1944), found bone changes in 29% 
of 505 patients in United States Public Health Service Hospital. 
Furthermore, they observed that the bone absorption is often 
marked where atrophy and contracture are minimal. Among 160 
lepromatous cases, 9 sustained bone involvement, in 4 enlarged 
nutrient foramen and in 5 cyst formation were found in 
phalanges. Aspiration of the cysts revealed acid fast bacilli. 
There were also osteomyelitic changes. They particularly 
mentioned that the bone changes in 'neural' leprosy are due to 
'neuro trophic' change and most lepromatous cases are free 
from bone changes even in advanced stage. Cooney and
Crossby (1944) have seen cases with marked destruction of the metatarsal and tarsal bones with preservation of phalanges. A close study of fifteen cases by them showed that the bone absorption was due to multiple factors, e.g., circulatory disturbance, anaesthesia, and mechanical pressure.

Erickson and Johansen (1948) studied the bone changes of 82 patients who were under treatment and found that 'cystic' bone changes improved with sulphone therapy but 'atrophic' changes did not. It may be 'cystic' changes are due to M. leprae and disappearance of the cystic changes was due to specific therapy. They tried to correlate between the nerve involvement and the bone changes. They suggested that the nerve involvement is slow in its evolution and the bone involvement is even slower. They further contradicted the observation of Oberdoerffer and Collier (1940) and suggested that lepromatous leprosy is relatively free from neural involvement and also from bone lesions excepting those due to direct involvement by M. leprae. Such lesions in the bones are 'cyst' formation and chronic osteomyelitic change.

Esquerra Gomez and Acosta (1948) studied radiograms of 483 leprosy patients in Agua de Dios Leprosarium, Columbia. They found decalcification and rarefaction in the early stage. There were prominent trabeculations and many ruptures of trabeculae leaving clear zones. Hypertrophy and hyperostosis
were typified by widening of the proximal ends of one or more phalanges. The bone changes may occur with or without mutilations. They further observed that resorption and atrophy for all bones of the hands follows the ulnar nerve distribution. In that case the diaphysis of the distal phalanx resembles a sharpened pencil. Similar changes were observed by Cuervo et al. (1948) of Brazil.

Barneston (1950) studied bones of hands and feet of 107 neural leprosy patients in Pretoria. He classified the bone changes as 'early' when the external deformity was slight or absent. Duration of symptoms in this group ranged from one to 20 years and the anaesthesia was of varying degree being almost nil to complete. At this stage there were 'nicks' sliced at the terminal phalanx and loss of the phalanx and 'drawn out' appearance of the shaft. Similar change was observed by Gokhale (1959). He observed that the changes were always bilateral but rarely symmetrical. Like previous workers he observed that the bones of the feet were usually more affected than those of hands; whereas Languillion and Boissan (1955) while studying 302 unselected cases observed that the majority of bone lesions were in the hand. There were prominent trabeculations indicating osteoporosis. In advanced stage moderate or marked external deformities of hands and feet were present. Duration of symptoms varied
from 2 to 33 years and in all cases anaesthesia was complete. The principal lesions were periosteal reaction and osteosclerosis. Sequestrum formation was rare in absence of osteomyelitis. Diffuse osteoporosis was seen in 5 of 63 advanced cases. He observed that the phalanges were more affected than the metatarsals. Involvement of tarsus was uncommon and he found no evidence of involvement of carpal bones; concentric atrophy occurred frequently. Involvement of joint was almost always present adjacent to the affected bones. The concentric atrophy was either associated with changes in the cancellous bone and medulla or with sub-periosteal new bone formation. Erickson and Mayoral (1950) found moth-eaten appearance of the hand and neck of the talus. He studied 441 patients and out of them 8 showed unusual bone changes in the talus. This occurred only in lepromatous type and 85% of 441 cases were of this type. Charidome and Lechat (1955) found involvement of the bones of the hands and feet in all except 10 out of 128 patients at the Younda Leprosinum in Congo. Languillon and Boissan (1955) studied 302 unselected leprosy patients at the Institute of Marchona at Bamako. Of them 57% were lepromatous, 36% tuberculoid and 7% intermediate. He observed osteoarthritic change in more than 50% in the interphalangeal joints of the hands. The most frequent lesions in the upper and lower extremities were osteolysis at the end of the digits.
Paterson (1955) in Vellore (South-India) observed bone changes in 95% of 116 selected cases. He described the bone changes as bone destruction, joint changes, contraction, osteoporosis and absorption. These were either in the form of specific bone destruction due to lepra reaction or due to leproma formation or due to secondary infection. Destructive, absorptive or erosive changes occur due to secondary infection in hands and feet when there is sensory loss resulting in disturbed physiology of skin repair. He further observed that in lepromatous cases the patients may show formation of granuloma in the bone marrow comparable to 'Tuberculous multiplex cystica'. Similar leprous caseous dactylitis was observed by Gokhale (1959). Paterson (1955) further observed compensatory new bone formation at the medullary side of the cortex and also eccentric absorption, and irregular bone erosion in the terminal phalanges or concentric type of bone absorption in metatarsals due to non-specific infection.

Negree and Fontan (1956) found bone changes in 8 out of 10 cases and they followed the cases for years and observed that the bone changes were in progress even when the patient was under treatment and was bacteriologically negative. Kung et al (1959) studied 55 patients in Sanghal Munial Hospital. Among them 32 were lepromatous and 23
tuberculoid. In specific lesion they found *M. leprae* in the medullary canal of 17 patients. In 5 of them there appeared small areas of decreased density with hazy border and distortion or disappearance of the trabeculae usually located in the metaphyses of the phalanges and metacarpals. In other 2 there were expansion of the tubular bone, thinning of the cortex and rarefaction of the trabeculae. In non-specific changes there were enlarged nutrient foramina in 6 patients of whom 5 were lepromatous. They observed diffuse osteoporosis in various degrees in all patients except 3. They also found concentric absorption in 26 patients with small tubular bones gradually narrowing evenly. There were small loose bony fragments with subluxation of the joint similar to 'Charcot's joint'. Hashimoto and Kozuma (1960) in X-ray examination of femur and humerus found bone atrophy in considerable number of cases and particularly in the cases in which bone marrow examination was positive for lepra bacilli and atrophy was marked in those cases. Caryon et al (1962) studied extensively the bone changes in leprosy. In 35 without plantar ulcers, periostitis was found in 5 and in 25 with plantar ulcers periostitis was observed in 14 cases in small bones of the feet. There were two types of lesions, the osteolytic and the osteogenetic. The lytic lesions consist of diffuse decalcification with osteoporosis. The osteogenetic type consisted of 4 sub-types: (a) periostitis
mantle, (b) periostitis proliferation such as spicule, (c) periostitis blisters and (d) periostitis proliferative leading to worm eaten appearance.

Basu (1962) in Calcutta observed incidence of bone changes in 85% of 100 cases of unselected leprosy patients. Biopsy of bone marrow showed specific infection. In the lepromatous cases the patients showed formation of granuloma in the bone marrow known as the bone cyst. There were subarticular bone destruction in the same.

Karat et al (1968) studied the bone changes in leprosy and suggested that the generalised osteoporosis was more in lepromatous cases than in other whose bacilli index was more. They further emphasised that there was no definite correlation between the clinical appearance and the osteoporosis. With the control of the disease the osteoporosis also improved. Generalised osteoporosis was considered as transient phenomenon during reaction in both lepromatous and non-lepromatous patients. Osteoporosis could be due to prolonged immobilisation and/or long continued steroid therapy. Generalised as well as well defined localised osteoporosis might be seen in lepromatous or in borderline, nearing to lepromatous variety. Periostitis is often found during reaction. The authors particularly mentioned that there was no definite radiological character of bone change due to plantar ulcer, and the pattern was variable.
Blood vessels:

Leitner (1938) did arteriography and showed the presence of an ample blood supply even in cases with advanced bone changes. Bang and Tiep (1958), as reported by Price (1961), found normal arteriograms in 26 out of 34 ulcerated foot. Similar normal arteriograms were found by Faget and Mayoral (1944) in neural leprosy. But in advanced lepromatous cases localised arterial defects and decrease in size of the arterial branches were observed, suggesting leprous endarteritis; secondary bacterial infection played a part in the process. The enlargement of the nutrient foramen was believed to be the result of leprous endarteritis.

Paterson (1955) in order to investigate the blood supply of the affected bones studied angiograms and compared with the angiograms of the normal persons. He found narrowing of the digital arteries where there had been soft tissue absorption but in presence of inflammation dilatation of digital arteries and some venous engorgement were noticed. There was poor filling of vascular end loops in areas where there has been soft tissue absorption. He did not find any deficiency in vascular end loops in cases with punched out bone destruction. He observed in some patients arterial occlusion where there was soft tissue infection.
Lechat et al. (1959) as quoted by Price (1961), could establish no correlation between arteriographic findings and the results of cutaneous thermometry and plethysmography.

Basu et al. (1960a, b) carried out angiographic studies with a view to elucidate the cause of blister formation in tuberculoid leprosy. The changes noticed were thinning and corkscrew appearance of the digital vessels in areas of bone absorption. Venous stasis was also noticed in the tufts of the phalanges at 30 seconds after infection. It was suggested that the cause of blister formation in leprosy is circulatory stasis producing delayed dissipation of heat. Carayon et al. (1962), observed evidence of the arterial block and lack of venous return in their arteriography. They concluded that the early surgical procedure might relieve the arterial block.

Lymphatics:

No information on the radiological appearances of the lymphatics in leprosy could be obtained from the available literature.
Lungs:

Lowe (1929) was of opinion that radiological signs in the lungs were usually caused by tuberculosis rarely by leprosy. Tanimura and Yamamoto (1938), studying 100 cases of different age groups and finding numerous dissemination, small spotty shadows in both the lungs. These were usually sharply outlined, mostly acinous and seldom peribronchial. They considered that these were leprotic changes. Rodriguez (1952) mentioned after reviewing several patients radiologically and examining the nasal smears that the leprosy patients suffer from lung leprosy. And he noticed that such patients improved under treatment with oral administration of Chaulmoogra oil. Negree and Fontan (1956) studied the skiagrams of the chest of 110 leprosy patients. The examinations were repeated within a year. They observed radiological signs which were not suggestive of tuberculosis. In patients with lepra reaction shadows cleared up spontaneously. They were of opinion that these shadows were due to local allergic reaction in the lungs in leprosy.