V. DISCUSSION
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Leprosy is a disease that results in crippling deformities. Prevention of these require better understanding of their causation. With this object in view, the radiological investigations on the bone and joint changes were undertaken in leprosy patients. Only patients with lepromatous and tuberculoid types of the disease have been included as the other types usually do not develop these lesions. Attempts have been made to study radiologically the bone and joint changes in leprosy by previous workers like Chamberlin et al (1931), Barringto James (1931), Faget and Mayoral (1944), Cuervo et al (1948), Casacci (1950) and Kung et al (1959). More detailed studies were done by Paterson (1955, 1959, 1961), Basu (1962) and Paterson and Job (1964).

Incidence of bone and joint changes:

The incidence of various forms of bone and joint changes in case of lepromatous leprosy observed in the present study compared favourably with that in Paterson's (1955) series except that expanded cortex was observed in 5.5% of his series compared to 18.5% in the present series. In the study of Faget and Mayoral (1944) the presence of bone changes was noted in 9 out of 160 lepromatous cases, in 59 out of 92 neural cases, in 79 out of 241 mixed cases.
and in none out of 12 tuberculoid cases. (This classification had been based on old nomenclature). These figures show that the overall incidence of bone changes was 29.1% in his study. Paterson (1955) observed these in 32.1% and Basu (1962) in 35%. The figures of Faget and Mayoral (1944) appeared to be very low probably because in his group was included unselected cases whereas Paterson (1955) and Basu (1962) studied selected patients. The present work, undertaken also in a group of selected patients, shows an overall incidence of bone and joint changes as 61%.

The incidence (49%) of various types of bone and joint changes in 107 cases of tuberculoid leprosy patients observed in the present study is largely in agreement with that observed by Paterson (1955). However, the findings differed so far as tuft erosion and concentric absorption were concerned. The joint changes with contractions showed an incidence 37.3% (40 out of 107 cases).

Nature of bone and joint changes:

Paterson (1961) and Basu (1962) divided the bone changes into 2 main groups, e.g., (a) bone destruction and (b) bone absorption according to whether it was due to specific infection by M. leprae, or due to neurotrophic change. Workers like Faget and Mayoral (1944),
Paterson (1961) and Basu (1962) had attempted to study the nature of bone changes in leprosy.

In the present work, the bone lesions and their evolution were studied in detail in relation to the 2 clinical polar varieties of leprosy, viz., the lepromatous and the tuberculoid types. In the lepromatous type, the changes such as bone cyst formation (7.4%) and honeycombing (14.8%) have appeared to be due to specific infection. Subarticular bone erosion (29.6%) observed very commonly also appeared to be specific and caused by lodgement of M. leprae in the subarticular area producing lepra eruption, 'explosion' as it is called. A breach of skin favouring secondary infection was followed by a soft tissue swelling. Another type of specific change observed was the expanded cortex (18.5%). Paterson (1955) has attributed this change to the presence of a destructive lesion in the medulla. Osteoporosis has been seen in a small proportion (18.4%) of cases. This was probably due to lodgement of the lepra bacilli in the medulla of the shafts of small bones. This abnormality represented some irregularity on the medullary side of the cortex. In others, the shaft showed some expansion also. Enlarged nutrient foramina was found in 4 (14.8%) in the lepromatous series.
Tuft erosion comprised 32.3% of tuberculoid leprosy in the form of nicks, slices and disappearance of the terminal phalanx in longitudinal axis. The cause of such changes was not apparent. However, it is also seen in scleroderma, psoriasis etc., where there is evidence of osteitis. This may be either due to trophic change or vascular change or both. Concentric absorption of phalanges and metatarsals with cupping of joint surface and apparent increase in density constitute other changes. The incidence in this series was 30.8%. The several events that occurred in the production of this type of lesion were hazy reaction with the subperiosteal bone involvement accompanied by soft tissue swelling and ulceration. The articular ends were eroded. Subperiosteal bone formation was depressed when there was compensatory activity of the medullary side of the cortex with obliteration of the medulla. There was apparent increase in density, the cause of loss of contrast by deposit of bone in the medulla. The shaft assumed the shape of a 'sharpened pencil' or 'dagger'. The joints, assumed a peculiar shape of 'pin and cup' instead of 'ball and socket'. This type of deformity was not only seen in leprosy but also in non leprosy patients with an infective process. Disuse osteoporosis was present in 18.6%. There was diminution of transverse trabeculae in the subarticular layer followed by disappearance of the longitudinal layers.
in the cortex. There was also associated increase in the longitudinal trabeculae of the medulla. Another phenomenon which was often seen with an incidence of 11.2% was 'saucer joints'. This occurred in the small joints of the hands and feet. The sockets which received the ball were 'saucer' shaped. The joint space was not lost and there was no evidence of any bone erosion. Subperiosteal new bone formation or calcification with an incidence 14.0% appeared to be a manifestation of chronic osteomyelitis. There was also evidence of sequestration in some cases. The calcification which was often seen, was probably the end result of organised blood clot as a result of mild trauma. This could be compared with myositis ossificans.

**Biochemical investigation:**

Banley Leger (1922), Villela (1938) observed increased serum alkaline phosphatase and thought that this was due to the changes in the bone. Lancepleine (1949) observed low serum calcium but did not consider that this was due to bony change in leprosy. Thirteen samples of blood serum were examined for serum calcium and serum alkaline phosphate belonging to equal number of lepromatous and non-lepromatous with and without bone changes and 3 human volunteers. The values of serum calcium, inorganic phosphorus, and alkaline phosphatase were within normal
limits and did not indicate the presence of any metabolic bone disorder.

Bone biopsy:

Relation of bone affection to the presence of M. leprae in bone biopsy has also been studied. Faget and Mayoral (1944) did biopsy of bone cyst and were able to isolate M. leprae from the biopsy material. With this idea in view 50 cases of leprosy, (15 lepromatous and 35 tuberculoid) were selected for bone marrow biopsy for the detection of M. leprae. Cases with and without bone affection were chosen for the work. Areas without bone affections proved by X-ray, were punctured, to find out whether M. leprae might be present in the osseous tissue in such conditions. It was interesting to note that lepromatous cases who had bone involvement showed the presence of acid fast bacilli in all and also in 2 others who had no bone involvement. Furthermore, biopsy from 2 of the tuberculoid cases with bone involvement showed the presence of M. leprae in biopsy specimen. Of the 4 areas (the sternum, ilium, upper end of tibia and calcaneum) selected for bone puncture but the areas excepting calcaneum were seldom affected by M. leprae. It is well known that M. leprae have a predilection for bones of the hands and feet.
Barneston (1950), Job (1960), Basu (1962) tried to correlate the histological and the radiological findings. In the present study 13 cases (4 lepromatous and 9 tuberculoid) were chosen for histopathological study, of these 13 bone specimens, 4 were sequestra embedded in the soft tissue (Fig.66,67). The sequestra were clearly demonstrated by X-rays and confirmed by surgery. Of the rest 9 cases X-ray densities were seen as small bony fragments lying in the soft tissue (Fig.68), with loss of definition of the articular ends and borders showing process of absorption and destruction.

Bone histology showed complete disorganisation of bone resembling a piece of small stone (Fig.35). Continuity of the cortex was lost and in some cases osteoclastic activity with chronic inflammatory cells were observed (Fig.29,30,31,32). In addition to the above changes myxomatous changes were observed in lepromatous cases (Fig.34).

The neural factor:

Previous workers like Hirschberg and Bichler (1909) and Harbitx (1910) described the nature of bone change as neurotrophic in neural and tuberculoid types. Workers like Chamberlin et al (1931), Murdock and Hutter (1932), Taget and Kayoral (1944) and Barneston (1950), all described the changes under bone absorption and bone destruction and also
Fig. 66

Scanogram showing a sequestrum removed from the 1st metatarsal area - a case of lepromatous leprosy. (Please note dense compact layer and loss of medullary structure). Histology in Fig. 35.

Fig. 67

Scanogram of a piece of bone removed for biopsy. There is beginning of sequestration of the proximal phalanx of the great toe with disintegration of metatarsophalangeal joint. The proximal phalanx is seen telescoped on the head of the first metatarsal. (Please see histology in Fig. 32).
Fig. 68  X-ray of the hand showing a sequestrum embedded in the soft tissue of the terminal phalanx of the 4th digit, which was removed for biopsy. (Please see histology in Fig. 52).
brought in another factor, viz., the neurovascular, in addition to the neurotrophic.

In the present study the nerves of the superior extremity showed involvement on 130 occasions whereas those of the inferior extremity were involved in 202 occasions. It may be noted that ulcers developed in the inferior extremity in 76 cases (34.8%) and 22 cases of superior extremity (10%). Thus the incidence of ulceration was more in the inferior extremity that in the superior extremity.

The incidence of ulnar nerve involvement was as high as 75.4% and the next was the musculocutaneous nerve (52.4%). The figures given by Chatterjee (1943) as quoted by Murdock (1949) were 56.9% in case of ulnar and 53.5% in case of musculocutaneous nerve. Murdock and Hutter (1932) observed nerve involvement in 70.1% in case of ulnar and 45.8% in musculocutaneous nerve.

The figures as given by Faget and Mayoral (1944) are lower in respect of lepromatous and higher in neural and mixed (according to old classification) types. Paterson (1955) gave a much higher figure in case of lepromatous and lower figures in case of tuberculoid leprosy. The present work showed the presence of nerve involvement in 16 lepromatous cases out of 54 and in 106 tuberculoid cases out of 164.
Reddy and Krishnamurthy (1963) studied 6 cases of leprosy patients of whom 3 were lepromatous and 3 tuberculoid. They found marked thickening of the perineurium and endoneurium with diffuse round cell infiltration and epitheloid cells reaction, but in lepromatous leprosy, the perineural and endoneural thickening was less intense and round cells were present but no epitheloid cells. In tuberculoid variety degenerative changes of the myelin sheath and axons were frequently seen in the bigger nerves. In some cases there is complete disappearance of myelin sheath. Hargrave and Mother Marion (1964) studied histologically on a section of terminal branch of the radial nerve and described that there were collection of inflammatory cells within the nerve. Possibly these inflammatory cells press the finer nerve terminals. Five cases were selected for histopathological study of ulnar nerve, of whom 2 were lepromatous and 3 tuberculoid. In all of the 3 tuberculoid and 1 lepromatous cases there were marked thickening of the perineurium and endoneurium. There were areas of caseation in case of the tuberculoid leprosy (Fig. 27, 28).

Sprensky (1935) and Murray (1936) did some experiments to produce trophic ulcer of the foot by doing nerve section. Wyburn Mason (1950) believes that plantar ulcers were neurotrophic. He described that a local nerve plexus grew with local tissues independently of the central nervous system. This local plexus of nerves can stimulate...
the osteoblastic and osteoclastic cells for the repair and
destruction of the tissue. Experiments were undertaken in
the present work to produce trophic ulcers in the foot or
any bone change after crushing the sciatic nerves in
rabbits. However, the results were inconclusive.

Secondary infection and ulceration:

The present study included 54 lepromatous cases and
104 tuberculoid cases. Of the lepromatous patients 16 had
nerve involvement and 6 had ulceration and 6 had both nerve
affection and ulceration. Bone changes were seen in 27.
Those with bone changes showed nerve affection alone in
12 ulceration in 4 and both in 3. In the tuberculoid series
106 had nerve involvements, 92 had ulceration and 73 had
nerve affection and ulcerations. Those with bone changes
showed nerve affection alone in 82, ulceration in 71, and
both these features in 63. According to Paterson (1953),
ulceration in feet was present in 23 lepromatous and
6 tuberculoid cases out of a total 42 and 12 cases respec-
tively. The highest incidence was in the unclassified
variety of patients, not included in the present study.

A study of the relation of bone changes to the presence of
ulceration and nerve involvements showed that in a group of
54 lepromatous leprosy, 16 had nerve involvement, 6 had
ulceration and 87 had bone involvement. In the tuberculoid
group of 164 patients, 107 had bone involvement in the presence of 106 with nerve involvement and 92 with ulceration. In the lepromatous patients studied by Paterson (1955), a high association of bone and nerve involvement and ulceration was noted. Also in the tuberculoid variety, the observations were similar (although the number of cases studied was small). The present study also showed higher incidence of bone changes in patients showing nerve involvement and ulceration.

Radiologically sequestration and other changes as seen in other diseases such as tabes dorsalis, syringomyelia, and diabetic neuritis, were also seen in these patients. Diseases, other than those of the nervous system can also produce similar changes, e.g., psoriasis, mycetoma, and Aïnhum. Absorption of the tufts can occur in thromboangitis obliterans, Raynaud's disease and Scleroderma. In diseases like diabetes and mycetoma an infective process plays some part whereas in psoriasis, Aïnhum, Burger's disease, Raynaud's disease and scleroderma a vascular factor is probably the main cause. In diabetes, a neural factor and an infective process in the presence of high glucose content of tissue may combine together to produce the lesion. Antidiabetic treatment can cure ulceration, neuritis but probably not the bone lesion. Erickson and Johansen (1948) observed the efficacy of sulphone therapy in curing the bone changes in lepromatous
leprosy. Similarly, chemotherapy can also minimise the bone destruction. In mycetoma a combination of factors, e.g., fungi like Nocardiosis or Madura mycoses and secondary organisms from soft tissue ulceration take part in producing the bone changes. So it appears that nerve lesion, soft tissue infection (ulceration) and diminished blood supply singly or in combination can produce absorptive bone changes. However, certain changes in the medulla, e.g., cyst formation honey combing subarticular erosion and expanded cortex are due to specific bacilli.

Role of trauma:

Bone changes in leprosy are usually regarded to be associated with deep ulcers. However, in some instances no bone changes could be found in presence of ulcers. In the present series in such cases the ulcers were superficial and of recent origin. The trophic ulcerations of the foot is not peculiar to leprosy but occur in other neuropathy, e.g., tabes dorsalis, syringomyelia and diabetes mellitus (Oatley et al 1956). Ulcers on the sole in lepromatous leprosy were rare and were about 11.1% of the total lepromatous cases (ulcers in 6 out of 54 lepromatous cases). Hemerijkh (1959) found 9.2% plantar ulcers out of 2,479 out-patients at Polambekkan in South India. Ross (1962) found a similar percentage in East Nigeria. The relationship between the
69 a. A diagram of the right foot. The shaded area reflects the area of weight bearing during walking in anaesthetised foot.
Fig. 69b A diagram showing areas marked (x) as common sites of plantar ulceration in anaesthetic walking foot.
ulcers and force acting on the foot during walking was given by Brand (1950), Barnett (1956), Fritschi and Brand (1959) and Price (1959).

Plantar ulcers only occur on walking feet which are essentially anaesthetic. Casual trauma such as, cracks, blisters probably play an important part in the formation of plantar ulcers. But with this casual unnoticed repeated minor trauma the patient continues to walk. The wound becomes infected and infection spreads through plantar fascia or tendon sheath and affects bone. Ulcers can also occur as a sequence of infected cracks common in people walking bare footed. In others, the ulcers is due to pressure leading to ischaemia and localised gangrene of tissue due to weight bearing on an anaesthetic foot. The distribution of ulcer correspond to the distribution of weight bearing during walking (Fig.69 a,b). Hence the ulcers occur not over the metatarsal heads but in front of them because the weight of the body fall not on the metatarsal heads but in front during the process of walking when the foot is anaesthetised. The friction forces set up within the foot during walking lead to mechanical damage to the tissues. Many workers (Cochrane 1940a,b, Dharmendra et al 1953) thought that the ulcers were due to lepra bacilli and advocated anti leprosy drugs locally. However, the beneficial effect observed could be due to bed rest alone in such cases.
Drop foot occurs due to lateral popliteal nerve paralysis particularly anterior tibial. The patient walks with high stepping gait and the foot slaps on to the ground with the whole lateral border, because the peroneus longus and brevis are also paralysed due to lateral popliteal and musculocutaneous involvement. This causes ulcer at the head and the base of the fifth metatarsal. Due to intrinsic paralysis, the toes are clawed, and the tissues under the metatarsal heads are put on stretch and the toes no longer can take part in walking and all take off thrust is borne by the head and base of the fifth metatarsal.

During walking the arch is raised and the metatarsal heads are lowered. If the process goes anatomically the tissue maintains normal health, but if one toe is a little more clawed than another, then the associated metatarsal head is pushed down below the adjacent heads and bears all increased proportion of the take off thrust and thus ulcer may be formed. Recurrent ulcer is an important problem. In addition to anaesthesia, there is formation of scar. This results in loss of the protective mechanism to reduce friction and deformity. The net effect is the formation of recurrent ulcerations. Small abscesses in the intermetacarpal spaces may give rise to acute inflammation with formation of chronic ulcer and ultimately invade the bone. In such cases metatarsals and/or calcaneum may be involved.
These observations as also the evidences in the literature strongly suggest that nerve affection and ulcer formation favouring secondary infection are the two very important factors for the production of bone changes. However, mechanical trauma plays an important role in the causation of ulcers.

**Angiography:**

Angiography has been tried by many workers (Faget and Mayoral 1944, Paterson 1955, Basu et al 196Ca) to ascertain the role of blood vessels in the formation of trophic ulcers. But the results were not consistent. The changes in the haemodynamics were not consistent.

Reflex vasodilatation occurred in affected limbs where the healthy ones were immersed in hot water (Barneston 1950). Chatterjee (1955), after reviewing the nature of blister formation in the affected digits of hand, came to the conclusion that the dissipation of heat was deficient in the extremities of tuberculoid patients and that, probably leads to the blister formation when they come in contact with hot objects. Other investigations such as difference of temperature between the affected and unaffected limbs was noticed by Chatterjee (1955) by thermo-couple studies. Previous workers, like Fite (1941a),
Paterson (1955), Basu et al. (1960 a) and others have suggested involvement of arteries also. All these suggest that the vascular stasis may play some role in the formation of trophic ulcer. In the present study arteriography was done in 14 cases (6 tuberculoid, 5 lepromatous including 3 healthy control) and have found stasis in 4 (3 tuberculoid and 1 lepromatous) and endarteritis obliterans with corkscrew appearance in 1 lepromatous patient in presence of absorption of terminal phalanx. This findings are similar to those observed by Basu et al. (1960 a). Narrowing of the digital arteries as seen by Paterson (1955), was also noticed but stasis appeared to be a more potent factor and the venous return was also necessarily delayed. This vascular stasis perhaps play an important role in the production of blister in anaesthetised digits due to delayed dissipation of heat (Basu et al. 1960 a). De Camp et al. (1952) as quoted by Price (1960a) observed chronic venous stasis as a result of post-phlebitic syndrome. Twenty-two tuberculoid cases were studied by venography with 3 human volunteers as control by modified Moore's technique (1955). All were in the age group of 20-40 years and the duration of the disease varied from 2-10 years. No sign of thrombo-phlebitis or venous obstruction could be observed.
Lymphangiography:

According to Forbes (1937-38) the dermis is divided into three layers - the outermost layer, middle layer and the innermost layer. The outermost and middle layers are filled up with polygonal lymph spaces and are intercommunicating because of absence of valves. The innermost layer possesses valves. These receive lymph from the outer two spaces. The innermost layer again drains into the lymphatic spaces of the subcutaneous tissue (Fig. 70). The innermost layer because of the presence of valves direct the lymph flow into the corresponding lymph nodes. Thus it appears that any inert substance, once it finds entry into the outermost layer of the dermis can move freely in the lymphatic spaces and travel from one layer to another via the lymph capillaries on to the body surface. From the above it may be presumed, that *M. leprae* coming in contact with the skin may travel via the lymphatics to the endoneurium and perineurium of the lymph trunks producing neuritis. Otherwise, the bacilli may produce skin infiltration with the formation of nodules. Thus it is seen that lymphatics may play a vital role in the production of neuritis and infiltration of the skin and may contribute indirectly in the production of bone changes. It is presumed that *M. leprae* make an entrance into the
Fig. 70 Diagram showing the arrangement of lymph space in the sole of the foot.

(SECTION OF SOLE FOOT
SHOWING LYMPHATIC DRAINAGE OF SOLE OF FOOT

(After Forbes)
body tissue through lymphatics (Khanolkar 1951). Price (1960a) observed chronic lymphoedema or chronic lymphatic blockade. He had the privilege of observing visible lymphatic channels. Basu (1969) in a personal communication mentioned that a case of lymphoedema was in advertently referred for lymphangiography but this patient was actually suffering from lepromatous leprosy and the patient responded to antileprosy treatment. No other radiological work on lymphatic channels or glands in the form of lymphangiography or lymphadinography in leprosy patient is available.

In view of these facts lymphangiography was done in 6 lepromatous and 5 tuberculoid leprosy patients to investigate the status of the lymphatic channels. No obstruction or collateral circulation or dilatation was, however, observed; the channels practically looked normal in the radiograph.

Histopathology of blood vessels:

It has been observed by many workers (Phillipson, 1890; Sakurane, 1902; Klingmuller, 1930, Fite, 1941a) that the blood vessels are affected with lepra bacilli. Goosen (1933), Kirkaldy Willes (1945), Silva (1959) tried lumbar
sympathectomy to relieve vasoconstriction. Similarly perifemoral sympathectomy were tried by Py and Riveros (1929), Virinichhi (1941), Barneston (1950), Job (1960) observed organic occlusion of the arteries.

In the present study histopathology of blood vessels were carried out in 21 cases of which 5 were lepromatous and 16 tuberculoid. M. leprae were observed in 11 cases of which 4 were lepromatous and 7 were tuberculoid patients.

The evolution of bone changes:

From the foregoing discussion, an account of the chronological events leading to the bone changes in leprosy will appear to be as follows. With nerve involvement there is anaesthesia and trophic changes in the muscles in old standing cases. Vascular stasis and impaired circulation results from affection of blood vessels. Whether the lymphatics play any role is not quite clear. Subsequently, the traumatic factor including friction operates leading to cracks, blisters, and haematomata. Ulcers develop at the pressure points on the sole of the foot commonly under first digit during walking. Similar ulcers develop in the fingers which are exposed to trauma in the claw hand. The ulcers then get secondarily infected and infection burrows
into the soft tissue and produce abscesses. Because of the presence of anaesthesia, patients do not feel the effect of trauma. Later, the bones and joints are involved toes and digits fall off leading to claw hand and club foot. The bone involvement is commonly observed in tuberculoid cases where the above factors work often in combination. In lepromatous cases, the bone changes are less frequent but may be more due to the infection with the specific bacilli rather than due to the other factors. The bacilli lodge either in the medulla of the small bones of the hands and feet or their articular ends. There is acute inflammation with soft tissue swelling or 'explosion' as we call it. There is formation of bone cyst in the medulla simulating 'Tuberculous multiplex cystica' and we may call it as 'Leprosy multiplex cystica'. In case of joints, the articular margins are lost with disintegration of joint space and there is often subluxation of joint to the extent of one bone being telescoped on the other.

Lung affection in Leprosy:

There were 2 divergent views regarding the affection of lung parenchyma by *M. leprae*. Early workers like Hansen and Looft (1895) as quoted by Muir (1933), Wise (1912), Wade (1927) and Lowe (1929) held that the lung affection
which the patients develop were due to associated infection of tuberculosis, a view not corroborated by other eminent workers like Muir (1933), Fite (1943) and Ranade et al (1957). Muir (1943), later confirmed that the lung is exempt from leprosy infection. X-ray examination of lungs of 128 leprosy patients (46 lepromatous and 82 tuberculoid) done in the present study simulated tubercular lesions in 13% of lepromatous and 3.6% of tuberculoid cases. Allergic manifestation in the form of pneumonitis was recorded in 6.5% of lepromatous and 0.8% in tuberculoid patients. Patients showing signs of pneumonitis were re-examined 15 days after and skiagrams showed a clearing of the process.

It is often confusing to differentiate between leprosy and tuberculous infection of lungs by routine examination of sputum when the acid fast bacilli are present. In course of this investigation sputum from 18 leprosy cases (6 lepromatous and 12 tuberculoid) were examined for acid fast bacilli, of whom 5 cases (2 lepromatous and 3 tuberculoid), radiologically showed abnormal signs in the lung fields. Two of these cases, 1 of which variety showed acid fast bacilli in sputum. The bacilli could be identified as \textit{M. tuberculoid} by a special staining process which seemed very helpful (Petropfffer's method).
The experimental study undertaken to induce leprosy and tuberculoid by instillation of sputum from lepromatous leprosy and pulmonary tuberculosis patients, where acid fast bacilli were positive into the bronchi of guineapigs succeeded in producing tuberculosis in lungs. But experiments failed to produce any leprosy of lungs. Macroscopical examination supported the view. Microscopical examination of lung tissue also confirmed tuberculosis of lungs. Pulmonary leprosy as an entity could not be established.