BONE CHANGES IN LEPROSY:

pathogenesis, palaeopathological diagnostic criteria, and clinical interpretation.

1. PATHOGENESIS

1.1 Direct effect of Mycobacterium leprae invasion of bone

1.1.1. Leprous osteomyelitis:
      due to haematogenous spread of *M. leprae* to medullary cavities, principally of the
      bones of the hands and feet. This lesion is only present in lepromatous leprosy.
1.1.2. Rhinomaxillary syndrome:
      secondary to oronasal soft tissue infection by *M. leprae*. This change is only present in
      lepromatous leprosy.

1.2. Indirect effect of peripheral neuropathy due to *Mycobacterium leprae.*

General considerations:
Because M.leprae has a predilection for cool environments, there is no involvement of
pathological significance, of the central nervous system of brain and spinal cord. Neuropathic
changes are mainly in peripheral subcutaneous nerves of the bodily extremities of limbs and head
and neck.

1.2.1. Sensory neuropathy:
    a. cutaneous anaesthesia: predisposes to painless superficial trauma leading to
       ulceration, secondary pyogenic bacterial invasion from external sources, and to deep
       tissue spread to bone and joint cavities, giving rise to osteomyelitis and septic
       arthritis. The changes are exacerbated by ischaemia due to *M. leprae* arteritis in
       lepromatous leprosy.
    b. deep pain anaesthesia: facilitates spreading deep tissue sepsis, exacerbated by
       ischaemia due to *M. leprae* arteritis in lepromatous leprosy.
    c. proprioceptive loss: dysfunction, or loss, of joint spatial sensation, leading to
       subluxation, dislocation, and the disintegration of hand and foot architecture.
1.2.2. Motor neuropathy:
    paralysis of muscle groups with loss of synergistic action, leading to:
    a. hyperextension of metacarpophalangeal joints and hyperflexion of interphalangeal
    joints producing claw hand deformity due to ulnar nerve dysfunction.
    b. paralysis of the muscles of dorsiflexion of the ankle joint producing drop foot due to
    dysfunction of the lateral popliteal nerve.
    c. longitudinal arch collapse of foot
    d. transverse arch collapse of foot
    e. hyperextension of the metatarsophalangeal joints and hyperflexion of the
    interphalangeal joints producing hammer toe deformity, due to dysfunction of the
    posterior tibial nerve.
    f. subluxation of the proximal phalanges at the metatarsophalangeal joints and
    metacarpophalangeal joints produces a cup deformity at the proximal articular surface

of the proximal phalanges. The articular surface remains intact, but there develops a collar of bone from the juxta-articular area in response to traction upon the joint capsule. It is usually associated with concentric diaphyseal remodelling of the metatarsal or metacarpal, forming a peg-shaped distal end.

g. paralysis of the lower eyelids, and consequent inability to close the eyes, producing lagophthalmos. Due to dysfunction of the facial nerve. The potential sequel is facilitation of superficial eye infection, and secondary pyogenic infection of the orbits.

1.2.3. Autonomic neuropathy:

the disfunction of sympathetic control of arteriolar muscle tension leads to arteriolar dilatation and a change in arteriolar blood flow dynamics. There may be, coincidentally in lepromatous leprosy, damage by M.leprae invading the endothelial cells of capillaries and small arteries, leading to blood flow restriction and ischaemia. A consequent change in the blood oxygen tension, by stimulating regional osteoclast or osteoblast activity, may be the cause of:

a. concentric diaphyseal remodelling in which there is outer cortical surface bone absorption and simultaneous endocortical bone deposition with consequent reduction of the dimensions of the medullary cavity in phalanges, metatarsals, and metacarpals.

b. Knife edge remodelling of metatarsals and metacarpals in which there is maintenance of the superoinferior diameter if the bones, but outer cortical surface absorption and simultaneous endocortical bone deposition at the medial and lateral surfaces.

1.3. Indirect effects of *Mycobacterium leprae* infection.

1.3.1. Achro-osteolysis:

the loss of peripheral bone substance through diffuse absorption. This may affect one or more bones, usually metacarpals, metatarsals, phalanges of the hands and feet. The individual bone may undergo complete loss, and be radiologically absent. The cause of achro-osteolysis is not known.

1.3.2. Osteoporosis:

Osteoporosis may be localised and associated with disuse of a limb or part thereof. It may be generalised in males due to testosterone deficiency caused by testicular infection by M. leprae in lepromatous leprosy.

2. DIAGNOSTIC CRITERIA: palaeopathological features.

General consideration. Only leprous osteomyelitis, concentric diaphyseal remodelling, and the rhinomaxillary syndrome, are, per se, pathognomonic of leprosy. Other bone changes in the upper and lower limbs, in isolation, are not positively diagnostic but are indicative of the clinical sequelae in the disease process. Only the composite pattern of peripheral bone changes can be positively diagnostic of leprosy.

2.1. Rhinomaxillary syndrome:
This syndrome is only present in lepromatous leprosy.

2.1.1. Anterior nasal spine (ANS): absorption and ultimate loss with exposure of medullary bone followed, possibly, by cortical remodelling.
Quantification: 1. Well-defined reduction of the spine.
2. Advanced absorption but spine remnant remains.
3. Complete absence of spine.
2.1.2. Alveolar processes of maxilla (APM): absorption and recession of APM, usually with little or no inflammatory cortical pitting, commencing centrally at the prosthion and extending to the alveolae of the central and lateral incisors and canines, with loss of these teeth. This zone corresponds to the embryonic premaxilla. The process is bilaterally symmetrical about the prosthion.
Quantification: 1. Recession of prosthion and early exposure of central incisor roots.
2. Marked recession of bone with exposure of central and lateral incisor roots and loosening of one or more incisor teeth.
3. Severe recession of bone with antemortem loss of one or more incisor teeth, initially central but extending with progression to the lateral incisors and the canines.
2.1.3. Palatine process of maxilla (PPM): inflammatory change of the nasal surface of the palatine process of maxilla (PPMN) leading to localised bone destruction and ultimate perforation of the palate, usually in the median or paramedian position. The change may or may not be associated with inflammatory change of the PPMO.
Quantification: 1. Slight inflammatory pitting of the cortical surface.
2. Extensive pitting possibly associated with irregular subperiosteal new bone formation.
3. Irregular perforation of the palate.
2.1.4. Palatine process of maxilla (PPM): inflammatory change of the oral surface of the palatine process of maxilla (PPMO) leading to localised bone destruction and ultimate perforation. This change may or may not be associated with inflammatory change of the PPMN. The change is usually in the median or paramedian position towards the middle or posterior zone of the palatine process.
Quantification: 1. Slight inflammatory pitting of the cortical surface.
2. Extensive inflammatory pitting with irregular subperiosteal new bone formation..
3. Advanced destructive change with extensive perforation.
2.1.5. Conchae (turbinate bones) and nasal septum: inflammatory pitting with or without slight irregular subperiosteal new bone formation. There may be destruction and ultimate loss of the bony nasal septum, and loss of one or more conchae.
2.1.6. Nasal aperture: progressive smooth absorption with recession of the normally sharp basal and lateral margins of the nasal aperture, inferiorly. The change may or may not be associated with inflammatory pitting.
2.1.7. Posterior alveolar margins of the maxilla: A later development in the rhinomaxillary syndrome is alveolar absorption in the region of the molar teeth, commencing at the 3rd molars. This may have a similar pathogenesis to the change in the alveolar process of the maxilla anteriorly.
Clinically, the oronasal infective changes are associated with nasal stuffiness, and bloody purulent nasal discharge containing multiple M.leprae in addition to pyogenic bacteria. There is offensive halitosis. The nasal discharge from lepromatous individuals, in sneezing and coughing, is the source and mode of transmission of M.leprae in leprosy infection.

2.2.   Leprogenic odontodysplasia:

Concentric constriction around the tooth root followed by arrested tooth growth, usually of the incisor, principally maxillary, teeth. Radiologically the affected teeth show constriction and irregular pulp cavity.

2.3. Upper limb:
2.3.1. Distal phalanx:
   a. Destruction and smoothing of the palmar surface of the distal end, sometimes with palmar and dorsal inflammatory pitting, leading to irregular and progressive erosive destruction of the distal end. This may be associated with absorption of the shaft of the distal phalanx leading to the creation of a flat plate of bone at the proximal articular surface, and, ultimately, to the total loss of the distal phalanx. The process is probably due to a combination of terminal pulp space infection associated with cutaneous anaesthesia and trauma, to achro-osteolysis, and to the mechanism of concentric diaphyseal remodelling. The absorptive process may occur in the absence of pulp space infection.

2.3.2. Middle phalanx:
   a. Concentric diaphyseal remodelling: true concentric remodelling commences and is maximal at mid-diaphysis. Midshaft bone loss may lead to pathological fracture and, through achro-osteolysis, the distal fragment may absorb, with a conical proximal fragment remaining. The process may continue, creating a flat "cap-like" proximal end of the bone, and, ultimately, to the total loss of the middle phalanx.
   b. Basal bevelling: in association with proximal phalangeal palmar grooving there may be smooth absorptive remodelled bevelling of the palmar edge of the proximal articular surface.

2.3.3. Proximal phalanx:
   a. Concentric diaphyseal remodelling: change as with middle phalanx, but the change of the proximal phalanx usually precedes and is more marked than the middle phalanx. The early stages of concentric remodelling in phalanges of hands and feet give rise to an hour-glass appearance of the bone.
   b. Palmar (volar) phalangeal groove: there may be a shallow groove, hemispherical in shape of the palmar surface of the proximal phalanx at the distal end in the juxta-articular zone. The flat base of the hemispherical shape is at the distal end. The absorptive outer cortical surface change is associated with coincident compensatory endocortical new bone formation at the site, producing a greater overall thickness of cortical bone at the site of grooving. This is a sequel to, and only occurs in association with, claw-hand deformity, in which there is metacarpophalangeal joint hyperextension and interphalangeal joint hyperflexion. The lesion arises because of constant unremitting pressure of the palmar juxta-articular margin of the proximal articular surface of the middle phalanx into the palmar margin of the juxta-articular zone of the distal end of the proximal phalanx. It is only present in fixed flexion deformity of the finger (claw hand) in which both passive and active finger movement is not possible. In earlier stages of the claw-hand development, there is still passive mobility of the fingers.
      Clinically, the fingers may be ulcerated, particularly on the palmar surface due to trauma to anaesthetic fingers in hand usage. The claw-hand deformity severely

limits grasping ability and normal hand usage, and individuals tend to push objects with the back of the hand. The progressive absorption of the distal, middle, and proximal phalanges results in soft tissue contraction of the fingers, but with preservation of nail remnants. Ultimately, the hand may consist only of the carpal and metacarpal bones, with remnant stumps of fingers.

2.3.4. Phalangeal osteomyelitis due to M. leprae. This is not a pyogenic process, and is, essentially, medullary. It may cause some enlargement of the bone associated with a cystic appearance of X ray. The lesion is only present in lepromatous leprosy.

2.3.5. Metacarphophalangeal and interphalangeal joints:
   a. Juxta-articular dorsal inflammatory change: because of hand-clawing and hyperflexion of joints, normal hand usage in grasping may not be possible. There may be superficial pitting of the dorsal surface around the interphalangeal joints, secondary to soft tissue damage caused by changed hand usage and trauma to the dorsal surface.
   b. Septic arthritis: destructive disorganisation of joint surfaces due to pyogenic sepsis secondary to dorsal ulceration in claw-hand deformity and to spreading infection from terminal pulp spaces. This is a sequel to cutaneous and deep anaesthesia and to motor paralysis.
   c. Subluxation and dislocation: may occur at interphalangeal joints resulting from hyperflexion secondary to motor paralysis and loss of proprioception. May be associated with palmar phalangeal grooving.
   d. Ankylosis: osseous ankylosis may occur, usually at interphalangeal joints resulting from pyogenic septic arthritis.
   e. Cupping, with or without peg deformity: the proximal ends of the phalanges may become cupped secondary to subluxation and circumferential osteophyte formation in joint capsular tissues. The proximal joint surface may be delineated and remain visible and intact. Coincidental achro-osteolysis and concentric diaphyseal remodelling may produce a peg deformity of the distal end of the proximal bone in the affected joint.

2.3.6. Metacarpals and carpals: concentric remodelling, septic arthritis and bone absorptive processes occur uncommonly in metacarpals. Septic arthritic destructive changes are uncommon in the carpus. Inflammatory changes in the bones of the distal forearm are uncommon.

Clinically, the infective changes in the hand will be associated with painless swelling and redness of the hand, particularly in the palmar space.

2.4. Lower limbs:

2.4.1. Distal phalanx:
   a. inflammatory changes are the same as those in the distal phalanx of the hand, but occur less commonly in the feet, and are usually associated with hammer-toe deformity secondary to motor paralysis. In the absence of interphalangeal hyperflexion there may be no terminal inflammatory changes seen.

2.4.2. Middle phalanx:
   a. Concentric remodelling and achro-osteolytic changes are the same as those in the middle phalanx of the hand.

2.4.3. Proximal phalanx:
   a. Concentric remodelling and achro-osteolysis: the changes are the same as those in the proximal phalanx of the hand. Proximal phalangeal concentric remodelling

precedes and is greater than the change in other bones of the foot. With progressive achro-osteolysis and loss of distal bones, overlying soft tissue infection may lead to inflammatory change and destructive nicking in the distal ends of the remaining bones.

2.4.4. Metatarsus:
    a. Surface inflammatory pitting: indicative of overlying soft tissue infection, and maybe an early stage in the deep tissue spread of pyogenic infection.
    b. Concentric diaphyseal remodelling: the change commences at and is maximal at the distal third of the diaphysis. Progressive development and achro-osteolysis leads to peg deformity. The 5th metatarsal is frequently the most severely affected. Concentric remodelling of the metatarsals is of two types:
    i. 'true' pancircumferential concentric remodelling is often associated with metatarsophalangeal joint sepsis.
    ii. knife-edge remodelling. Concentric remodelling maximal at the medial and lateral sides of the metatarsals produces a knife shaped bone with pronounced inferior borders. Knife-edge remodelling occurs most commonly in the absence of metatarsophalangeal joint sepsis.
    c. Achro-osteolysis: as with the phalanges, achro-osteolysis is progressive proximally. Achro-osteolysis leading to complete bone absorption may occur in the absence of conincident or pre-existing concentric remodelling. Rapid and complete absorption of bone can occur in as short a time as six weeks, but the process is usually much slower.

2.4.5. Tarsus:
    a. Surface inflammatory pitting: may be of both plantar and dorsal surfaces, as a sequel to overlying soft tissue infection. Advancing infection leads to pyogenic osteomyelitis, destruction and disorganisation of tarsus.
    b. Dorsal bar formation: transverse bars of bone may develop on the dorsal surface of the neck of the talus, navicular, cuneiforms and cuboid in response to dorsal ligament stress consequent upon intertarsal joint subluxation with longitudinal arch collapse. This is a result of motor paralysis and loss of proprioception. The bars appear more radiolucent than the parent bone.
    c. Navicular 'squeezing': as a result of navicular dislocation in the development of loss of the transverse arch, the navicular may be compressed as a thin plate.
    d. Tarsal disintegration: the tarsus may be so changed by infection by pyogenic bacteria, be altered morphologically by dislocation, and the joints ankylosed through sepsis, that the total tarsal architecture and anatomy may be destroyed.
    e. Calcaneal erosion: there may be localised cortical destructive erosion of the postero-inferior zone of the calcaneum, resulting from the spread of pyogenic infection from an overlying soft tissue infection of the plantar surface of the heel. This results from cutaneous anaesthesia and associated trauma to the heel. The superficial infective invasion may progress to the development of a calcaneal osteomyelitic abscess.

2.4.6. Joints:
    a. Interphalangeal: changes of pyogenic arthritis, subluxation, dislocation and cupping may occur as with the upper limb.
    b. Metatarsophalangeal: pyogenic septic arthritic change occurs mainly in the first and fifth metatarsophalangeal joints in the presence of integrity of the transverse arch. In the presence of transverse arch collapse due to motor paralysis and loss of proprioception, ulceration of the plantar surface of the mid metatarsophalangeal joints with subsequent septic arthritis of the second, third and fourth

metatarsophalangeal joints occurs. There may sometimes be a transient phase of calcification concentrically around the distal end of the metatarsal, proximal to metatarsophalangeal joint sepsis.

    c. Cupping and peg deformity: peg deformity in association with cupping is more common in metatarsophalangeal joints, because of the more distal zone concentric remodelling in metatarsals. The development is associated with dorsal subluxation of the proximal phalanx, and circumferential enthesopathy in the joint capsule of the metatarsophalangeal joint, commencing at the base of the proximal phalanx.

    d. Intertarsal joints: Infective destructive change of joint surfaces, with dislocation, ankylosis and disorganisation. Midtarsal infective change without infective change in the forefoot may occur in the presence of longitudinal arch collapse, midfoot plantar ulceration and spreading deep sepsis.

Clinically, the phalangeal absorptive changes result in the progressive shortening of the toes, but with maintenance of nail remnant.

The traumatic and subsequent infective changes result in the development of painless ulceration, and gross deformation of the foot. The transverse and longitudinal arch collapse and drop foot result in deformity and disability in walking.

General points in relation to change in the hands and feet:

a. The changes in the limbs due to, and secondary to, peripheral nerve damage are always bilateral and qualitatively symmetrical in distribution in lepromatous leprosy. In tuberculoid leprosy the changes may be regional and unilateral.

    b. Concentric diaphyseal remodelling: the process is one of smooth absorption of the outer cortical surface with coincident deposition of new bone on the endocortical surface. In consequence there is a progressive loss of medullary bone at the site, leading ultimately to a site of diaphysis which consists only of compact bone. After obliteration of the medullary cavity by endocortical new bone, progressive absorption of outer cortical surface leads to thinning and ultimate pathological fracture at the site.

    c. Bone absorption: achro-osteolysis, with or without osteomyelitis, particularly of metatarsals, may lead to absorption of cortical bone with exposure of medullary bone beneath. Such a defect at the distal end of the bone may be confused with post-mortem taphonomic bone loss. Later in the process the end defect may be covered by new compact bone in a thin plate. Osteoarchaeologically therefore, the absence of phalanges or metatarsals or the loss of the distal ends thereof, may not indicate post-mortem loss, but may be indicative of the ante mortem achro-osteolytic and osteomyelitic process resulting in loss of digits.

    d. Plantar trauma and ulceration occurs predominantly at the 1st and 5th metatarsophalangeal joints, and the base of the calcaneum in the foot of normal architecture. In the present of transverse arch collapse, the change is predominently beneath the 2nd, 3rd, and 4th metatarsophalangeal joints and the base of the calcaneum. In the presence of longitudinal arch collapse, particularly with the development of a "boat-shaped" foot deformity, the change is predominantly in the midfoot.

2.4.7. Tibia and fibula:

    a. Inflammatory change: bilateral symmetrical inflammatory change of pitting with marked subperiosteal new bone formation. The new bone is initially of woven type, but subsequently becomes compact bone and appears as a smooth undulating layer which is completely applied to the cortical surface. In the initial stages of

development, the woven subperiosteal bone appears as a distinct entity external to and separate from the cortical surface. The changes are most marked on the adjacent surfaces of the tibia and fibula, and, predominantly, are of the lower two thirds of these bones. This may be a toxic 'abacterial' process. Tibiofibular change is only associated with infection in the foot, but the infection may, in the early stages of pathogenesis, be of soft tissue only, and may not have involved bone. The tibiofibular change seems to be more common in the presence of longitudinal arch collapse and midfoot plantar ulceration.

Clinically the tibiofibular change is associated with marked swelling of the lower legs, initially during the day and resolving at night, but later becoming permanent. There is associated coarse thickening of the skin, and ulceration of the distal end of the lower leg may develop.

2.5. <u>Miscellaneous lesions:</u>

2.5.1. Erosive joint lesions: 'osteochondritis dissecans' type lesions, principally of the base of the first proximal phalanx in the foot, are probably not directly associated with leprosy. The lesions may be a manifestation of chronic subluxation, due to motor paralysis and loss of proprioception.

2.5.2. Bone cysts: lepromatous cysts are uncommon, but are frequently juxta-articular, regular and smooth-walled, with surrounding osteosclerosis.

Conclusion.

It is only by an examination of the total skeleton, and by recognition of individual pathological skeletal elements that a diagnosis of leprosy can be established, and an inference made with regard to the specific clinical type and the symptoms and physical signs in the once living person.

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