Indian Journal of
Radiology. Nov 1947.

The Indian Journal of Radiology

A quarterly Journal devoted to clinical radiology and allied Sciences

Owned and published as its Official organ by the Indian Radiological Association

VOLUME 1 NOVEMBER 1947 No 4.

THE

INDIAN JOURNAL OF RADIOLOGY

Vol. I November, 1947 No. 4

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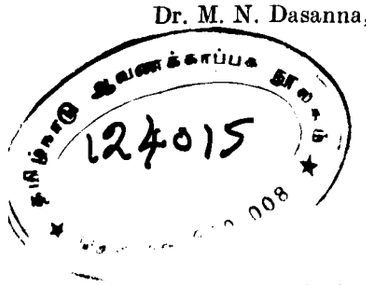
Programme for the Second Indian Congress of Radiology, to be held at Bombay during the X'mas week this year is given on page 188 of this issue. Members are requested to so arrange their X'mas holidays as to make it convenient for them to attend the Congress and make it a success.

P. RAMA RAU,
General Secretary.

THE INDIAN JOURNAL OF RADIOLOGY

(Owned and Published as its Official Organ by
The Indian Radiological Association)



QUARTERLY

Subscription : Rs. 12 per annum. Single Copy Rs. 3

Free to members of the Indian Radiological Association

Annual Subscription for membership — Rs. 12-0-0.

The
Indian Journal of Radiology

Vol. I. NOVEMBER, 1947 No. 4.

Paget's Disease of Bones—A Complete Survey

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INTRODUCTION

THE subject of my presentation is an interesting syndrome that was recognised for the first time as a distinct disease in the late seventies of the last century by Sir JAMES PAGET, and subsequently named after that distinguished clinician, I mean Paget's Disease of Bones, also known as osteitis deformans.

This however is not a new disease but dates back to antiquity. Bones recovered in excavation work, and from old Egyptian tomb have been known to show Pagetic changes.[45, 75] Findings in the skeleton of Neanderthal man have been cited by Butlin[17] as proofs of the occurrence of this disease in the very remote past.

No originality is claimed in the following comprehensive and critical survey that I have made of the accumulated knowledge of this osteopathy, except in the matter of viewing its pathogenesis from a new standpoint, in other words, of suggesting a fresh hypothesis on the causation of this disease.

There is report of a case of osteitis deformans that I diagnosed radiologically a few years ago. A complete bibliography of the publications which have been referred to in compiling this article is also appended.

In this connection one cannot help noticing the disproportionate volume of the literature both European and American, (in contrast with the absolute barrenness from India) that has grown up around a supposedly rare clinical entity, and that in this legion of contributions there is hardly any which has surpassed Paget's original communication[73, 74] in clarity and comprehensiveness, or, which has materially affected our conception of the etiology and pathology of

this disease. Except for some minor alterations in matters relating to age incidence, distribution and nature of the lesions, strength of the affected bones, and recording of some bio-chemical changes not possible in the past, no substantial advance has been made, since.

On perusing the literature one is amazed at the divergence of views and observations expressed or reported about the etiology, pathology, and identity of osteitis deformans with those of certain other diseases of bone showing more or less similar histological changes. Claims in respect of therapeutic results are not less conflicting.

The credit for recognition of this disease has been given to Paget: his masterly papers will for ever remain as classics in medical literature, and testify to his clinical and scientific acumen, but eight years before his first publication two other authors, WRANY and WILKS[104] had described a case each of this disease. Wilk's' case published under the title of "Osteoporosis, or Spongy Hypertrophy of the Bones" is in fact the first brilliant account of this osteopathy in the English language, and at par with that of Paget's. Sir JAMES was within an ace of loosing his credit to a Continental worker, CZERNY[27] who had described four years previously some cases showing some of the clinical features of this condition, and even used the nomenclature-osteitis deformans. PAGET had referred to Wilks' case, but not to those of CZERNY, since at the time of his first contribution PAGET did not know of Czerny's cases.

Signs, symptoms & clinical course. *Classical picture of the disease.*— It may be summarised thus:— An elderly individual in apparent good health, complaining of aching pains in the bones, supporting himself on a stick, walking stiffly with a stoop, on bowed legs, the feet set apart, and the toes turned outwards: the head big and mis-shapen; the chin drooping on to the chest, in extreme cases reaching as much as one inch below the upper border of the breast bone, and so requiring to be lifted up and thrust forwards by the hand to see ahead during progression; the abdomen protuberant and pendulous; shoulders rounded, arms apparently too long, and hanging by the sides of the thighs with the hands in front of them: the whole appearance calls vividly to the mind of the observer the picture of an anthropoid ape.

But, all cases do not present these features of a fully developed Paget's disease. Usually, the disease is of very insidious onset, without any urgent or definite symptom, and is accidentally discovered during X-ray examination for some other complaint, *e. g.* fracture, bone tumour, indefinite aches and pains, or urinary

calculus. Fully two thirds in a series of 104 cases reviewed by GUTMAN and KASABACH in 1936[40], did not present sufficient clinical evidence to justify a diagnosis. Radiological examination was necessary to come to a decision.

Signs and symptoms.— *Pain in the bones* is a more or less constant feature in the earlier stages of the disease, though occasionally it may be absent. It is felt in the long bones of the lower extremity, and only rarely in the head and arms. The pains are either periodic or continuous, and range in severity from a dull ache to an agonising throb. Nocturnal exacerbation may or may not be present. The pain is usually put down to "rheumatics" or "neuralgia" by the patient and so neglected.

The pains have been attributed to periosteal overgrowth, or have been described as "directly connected with bone changes"[57]. The pains may appear and often do, months before gross lesion can be detected in the bones. WINDHOLZ in 1932[105], reports that there is no periosteal bone formation till late in the disease though bone ache is an early feature.

KAY *et al* in 1934[54] appear to be the first to offer a convincing explanation for this association when they state that the pains are due to periosteal distension in the early stages.

Rate of bony changes in this disease has been noted to be proportional to the severity of the pains.

Deformities.—These are almost constant features. Increasing size of the *head* requiring purchase of hats of increasing size is another common accompaniment to his aching bones, noted by the patient. It is due to thickening of the skull bones, chiefly of the frontals. Total increase during a number of years may be pronounced, but the rate of increase is slow. The circumference has been known to increase from 22½ to 27½ inches, in 32 years, that is about sixth of an inch per year. As a result of this increase in the size of the skull, without a corresponding increment of size of the facial bones the head becomes big and mis-shapen. Sometimes, though rarely, the facial bones are also affected in the overgrowth, giving a leonine appearance to the face. The condition is then known as "leontiasis ossea."

Bending, bowing and elongation of the *long bones of the extremities* though frequent, are not invariable. The bones of the thighs and legs are most often affected, the former are bent outwards and the latter forwards. Bones of the arm are less frequently involved, when the curvature is backwards. Apart from these, generalised or localised, regular or irregular swellings are met with.

Exaggeration of the normal *spinal curvatures* is a frequent incidence,

Kyphosis in the cervico-dorsal, or dorsal segment of the spine is one of the causes of shortening of the stature, (the other being bending of the long bones of the lower extremity), which sometimes has been as much as one foot. LORDOSIS in the lumbar portion contributes to the protuberance of the abdomen.

Chest is flattened laterally, and the *pelvis* is widened.

WHITE[101] in 1922 noted that alkali hunger may be present in this disease, starting before the onset of the deformities and disappearing with their establishment.

Arterio-sclerosis and cardiac diseases are very common in Paget's disease. It has been noted[54] that in the same age group arterio-sclerosis is more frequent in persons affected with osteitis deformans than amongst those who are not. Arteriosclerosis is more or less generalised and severe, but is said to be, not often associated with hypertension. Atheroma is almost a constant feature.

Nerve symptoms.—usually absent, may be met with at times, and are due to extensive involvement of the bony housing of the nervous system. These will be considered in detail hereafter in this paper. Intelligence and mental activity do not suffer even up to the end. Homicidal tendencies and loss of memory have been noted[54], but such are not more frequent than what may be in persons unaffected with Paget's disease.

The course of the disease.—This is very chronic and variable. Twenty to thirty years may elapse without any impairment of the general health, death taking place in the natural course of events. But, the exit in a majority of cases is from pulmonary complications because of rigidity of the chest wall, or from supervention of malignant disease - a frequent incidence in *this* osteopathy.

The prognosis.—It is always uncertain and unfavourable, as chances of sarcoma formation in the bones are great, and there is no specific therapy to cure or to abort this disease.

Etiology.—*Age.*—Osteitis deformans is usually discovered in advanced middle age,—after 40, and over. The peak of incidence is in the sixth decade of life; a few authentic cases in the third decade are also reported.[8, 14] It is not possible to say with any measure of exactitude when the disease actually started before its discovery, because of the insidious onset, asymptomatic course, and variability of the rate of progress.

HUMMEL[44] reported in 1934 two cases of this disease in children, 9 and 11 years old. The diagnosis in the former was by the X-ray alone, in the latter by microscopical examination in addition to the X-rays. Experienced observers like BRAILSFORD and KNAGGS look upon such

cases with a measure of suspicion as to their being true cases of osteitis deformans. BRAILSFORD however recommends that particular care should be exercised in reporting the juvenile cases, since bone-dystrophies in the young bear a superficial resemblance to osteitis deformans.

Points that help in differentiation are symmetrical distribution and equal age of the lesions in dystrophies, as against the asymmetry or imperfect symmetry of the lesions, their wide-spread distribution and unequal age in Paget's Disease of Bones. 131

Class.—All classes are equally affected.

Sex.—According to some[14, 54] both males and females are about equally affected; whilst in the experience of others[72, 80] incidence in the males shows a greater preponderance.

Heredity.—Sometimes a distinct heredo-familial character has been noted, the disease occurring in either of the parents, and their sons and daughters, or amongst brothers and sisters.

Up to 1926 in the 300 cases recorded in the literature, only 13 showed familial or hereditary incidence[80]. Eight years later KAY and others refer to this[54], and mention having seen the disease in two sisters whose mother also was probably affected.

Occurrence in other members of the animal kingdom.—Osteitis deformans has been reported in other animals apart from civilised man. STEGMAN[93] found several cases in the *savage* and *semi-savage tribes* amongst the American Indians (? cave dwellers).

Several authors have reported the incidence of this disease in the *lower* animals, *e.g.*, BARTHELEMY[6] in horses in 1901; GODMAN[34] in fowls in 1902; JOST[50] in goats, monkeys, and horses in 1910; and WHITE[101] in monkeys in 1922. All these articles are interesting, especially that of White. These animals were *invariably* domesticated, and kept in captivity.

Some doubt has been expressed about the identity of this disease as reported in goats and horses, but with respect to that in the monkeys the evidence is conclusive.

Frequency of occurrence—Osteitis deformans is described as "rare" or "infrequent". There are *apparently good* reasons for such an appellation, Statistics compiled from the annual admissions in big general hospitals show on an average 1 case of osteitis deformans per 21,000 admissions. (Table I, in the Appendix.)

Up to 1926, that is in about 50 years after the attention of the medical profession had been drawn to the existence of the disease, only about 300cases were recorded in the world's medical literature, giving an average of only 6 records per year. This annual average improved to only 9 per year during the next seven years,

by which time the total record mounted to about 500.[48]

At the same time, one cannot neglect the import of the publications of case reports and reviews in quick succession and in increasing numbers in recent years. In hospital practice also, one meets with a considerably larger number of cases in the hospitals for chronic diseases, than in big general hospitals. For instance, in the case of the Clifton Spring Sanatorium the ratio of Paget's disease cases to the annual admissions is 1/2,639, or roughly, the case incidence is eight times greater in such places than in general hospitals. Record of 200 cases in seven years (between 1926 and 1933) as against 300 in forty nine, shows an amazing increase in detection by 500%. In this connection, Schmorl's figures of detection of this disease through successive years (Tables II & III in the Appendix) might be examined. Inside of a completely short course of investigations, he has conclusively shown that about 3% of people over 40 are affected with Paget's disease of bones.

The above facts show that with a closer watch, many more cases can be detected of this supposedly rare malady, than if we stick to our former ideas about its frequency, and are not on the alert.

When we consider the insidious nature of the onset, and particularly of an asymptomatic course of the disease the reason for the *apparent* dearth of incidence at once becomes manifest.

We are justified to conclude from the above discussion, that although the classical picture of Paget's disease may not be very frequently seen, the disease by no means is rare in Europe and America. JAFFE[48] in 1933 refers to its occurrence amongst the Japanese, but does not mention if they were emigrants in America.

In my opinion, the disease is very rare in the East, at least in India: to the best of my knowledge, the case that I am going to report is the first to be published from India after 70 years that have passed since Paget's discovery. In my own experience of over 20,000 cases of bone diseases of all sorts, over a period of 25 years of radiological practice in India, and also in the experience of some of my colleagues in Calcutta who have handled a larger number of cases than I have done during the same period, this case happens to be the first, reported. Since the detection of this case about eight years ago, I have come across only one more in which the disease is limited only to one tibia.

The fact that there is no reference to this disease in Indian medical literature of the past, and that we have not met with any case of this nature amongst the Indians or the

European-residents, warrant the conclusion that the disease must be either non-existent, or at the most, *exceedingly* rare in our part of the Globe. like some other diseases of bones albeit to a lesser degree.

Later in this contribution an attempt has been made to explain the rarity of this disease in India on the basis of a new theory of causation advanced by the present writer. If after the publication of my case, many more are reported from India, my present observations and hypothesis will need revision.

Pathology.—*Pathogenesis.*— The subject is shrouded in mystery. As is usual under such circumstances, numerous theories have been advanced to account for the causation. Incontrovertible proof of our ignorance and indecision lies in the very multiplicity of the hypotheses. Moore rightly expressed in 1936 at the annual meeting of the American Roentgen Ray Society, that Paget's disease of the bone was probably a general disorder in which at the present time we knew only of the bone changes. None of the prevalent theories can stand close scrutiny, or, is able to explain the diversities of manifestations that are met with. Observations of one author are positively contradicted by those of another equally competent.

Reasons for such discrepancy and also of dearth of essential knowledge, lie in the nature of the disease, which offers insuperable, obstacles to a continuous study of the evolution, career, and the finish of the process. The serial picture has to be built up by piecing together of the views from different cases, Many important links thereby being liable to be missed, the result is that the composition of one worker is not in harmony with that of another.

Theories of causation.— These might be classified as (1) Inflammatory; (2) Toxic; (3) Syphilitic; (4) Neurotrophic; (5) Endocrino-metabolic; (6) Dietetic; and (7) Vascular.

Discussion of the theories — (1) *Inflammatory.*— PAGET[73] himself and others after him considered the disease to be inflammatory in nature. Even up to the present day some of the standard books in Surgery[82, 84] describe it as such. There is however no feature common to osteomyelitis, osteitis (if a sharply demarcated inflammation of the cortex is at all possible, without involvement of the medulla) and osteitis deformans, in their manner of onset, mode of progress, clinical course, radiographic appearances, haematological changes, and bacteriological findings. ARCANGELI[2] an Italian worker claimed to have isolated a diplococcus from the Pagetic bones; and improvement in the patient's condition from the use of a vaccine, has been reported[28]. But in the experience of other workers the bones have been always sterile.

In the discussion relating to his cases, PAGET stated that although the changes in the earlier stages of the disease had not been observed, there could be nothing against their being of an inflammatory nature, for the softening of the bone was associated with enlargement, and formation of imperfectly developed structures with increased blood supply.

The genesis of the inflammatory theory lies in the sameness of the histological changes that take place in the osseous tissue as response to various stimuli, microbic,—metabolic, toxic, traumatic, and neoplastic. The essential pathology in all, is a destruction followed by repair, that is initial porosis, and subsequent sclerosis, if and as circumstances permit. It is not possible therefore, to make out from the histological appearance alone, the underlying cause. Other authors[26, 60] have made identical observations.

A comparison of two histological reports (extracts from Brailsford's paper[14] by Professor HASWELL WILSON on two specimens,—one, the curetted contents of a cystic formation in tibia, and the other, an aberrant ossicle,—from two undoubted cases of Paget's disease will clarify my above stated contention.

"The sections show trabeculae of rather degenerative-looking cancellous bone, the interstices of which are filled with fibrous tissue. The appearances *suggest* a very chronic *inflammatory* lesion. There is nothing to suggest tumour." This is in the case of the cyst contents.

"This consists of cancellous bone with very dense coarse trabeculae. Most of the space contains fat, but in some there is calcareous debris, in relation to which the bone has apparently developed. There is *nothing to suggest why* bone formation has occurred." This is about the ossicle.

The italics in the above two reports are mine.

(2) *Toxic.*—The disease is said to result from chronic irritation of the bones by 'toxins' which may be either metabolic, intestinal, chemical, "products of inflammatory action of bone elsewhere", and bacterial products of focal sepsis.

HUTCHINSON[46] advanced in 1889 a rather attractive theory that osteitis deformans was the result of a 'poison' produced by inflammation of bone elsewhere, and this 'poison' circulating in the blood affected the osseous system generally.

Focal infection[58] as a cause of osteitis deformans was also advanced, but removal of the suspected foci did not bring about any improvement in the disease.

Intestinal toxaemia from dietetic errors causing osteitis deformans found some supporters. TUBBY[99] in 1912 cited the case of a patient suffering from Paget's disease who invariably remained well on a rich protein and spare carbohydrate diet; as soon as potatoes were added to his diet the pains increased tremendously.

OETLINGER and LAFONT quoted by KNAGGS[57] ascribe the disease to ingestion of mineral acids which have a decalcifying action upon bones. Cases of osteitis deformans were met with by these authors amongst workers and others who were exposed to fumes of Chlorine and Hydrochloric acid, because of their occupation.

According to KNAGGS[57] some metabolic or intestinal toxin injures the bone *via* the circulation. In his opinion the power to resist toxic influence is inherent in the bone, and the incidence of the disease is determined by individual idiosyncrasy.

On this theory, osteitis deformans, osteitis fibrosa (von Recklinghausen's disease), and osteomalacia are all due to the same causative toxin. The difference lies only in the severity of bone reaction which is greatest in osteitis deformans, and least in osteomalacia. The same toxin is held to be responsible for the arterial changes that are most frequently found in Paget's disease.

But, dissimilarity in age incidence, distribution of the lesions and the special predilection of the toxins for the arteries in osteitis deformans are not explicable on this theory. Further, at the pre-senile stage of life, when the reactive or the reparative power of the system in general, might reasonably be expected to be on the ebb, to get more active repair than in the younger ages (of malacic and fibrocystic diseases), is almost a paradox.

And again, there can hardly be any good ground to discard the well established and satisfactory theories of parathyroid causation in osteitis fibrosa (von Recklinghausen's disease), or of vitamin D deficiency in osteomalacia, in favour of a problematic toxin.

(3) *Syphilis* congenital or acquired, has been accredited with causing Paget's disease, probably from early identical bone changes in both. This theory finds great favour amongst the French workers[12] but it has not been generally accepted[29, 97]. THIBIERGE[97] in 1924 emphatically denied syphilitic origin of osteitis deformans; bones injured by syphilis might show a predisposition, just as injury from any other cause may make the bone more vulnerable to a Pagetic attack. The two diseases may however coexist in the same case.

(4) *Neuro-trophic* causation of this osteopathy has not received much support in view of the absence of any pathological changes in the spinal tract.

(5) *Endocrino - metabolic*:—The largest number of hypotheses are included in this class.

Derangement of calcium metabolism as a cause of the disease claims a good number of supporters. Opinion is divided on the question of mechanism of the derangement.

From the well known influence of the parathyroids on calcium metabolism, these glands have been incriminated the most. Some authorities are emphatic in their assertion that hyperplasia and hyperfunction [8, 62] of these glands bring about the decalcification and porosis met with in the initial stage of Paget's disease. From identical decalcified appearance of the bones in osteitis fibrosa cystica (generalised) others go further [31, 60] and say that these two diseases are the same, the only difference is that Paget's is one of old age, and von Recklinghausen's is that of youth. Two cases one of Paget, and the other of von Recklinghausen, were treated successfully by the same remedial agents. This has been claimed as evidence for the unitarian nature of the two diseases [30].

Opponents to these views [3, 7, 19, 23, 52, 54, 65, 71] take their stand on the facts that in Paget's disease there is no hypercalcaemia, and no adenoma, or hyperplasia of the parathyroids, and the bone changes are essentially dissimilar in the two diseases that have been sought to be unified. Bone deposition predominates over bone destruction in Paget's disease, while the opposite is the rule in von Recklinghausen's.

Increase of blood and urine calcium has been noted by some observers in the osteoporotic stage of Paget's disease, which they put down to hyperactivity of the parathyroids. The normal blood and urine calcium in the later osteo-plastic stage of the disease is not regarded by them as evidence of underactivity of these glands. From the large amounts of osteoid tissues that have appeared in the skeletal system, according to these observers over-activity may be said to persist in the later stage also, with derangement as an added factor.

Absence of parathyroid adenoma [18] at the usual site is not a proof that the theory of hyperplasia and hyperactivity of those glands as causes of osteitis deformans, is fallacious, for according to the supporters of this hypothesis the glands may be present in the superior mediastinum.

The above two answers to the objections are not convincing though ingenious.

The *pituitary* has not escaped from being held as responsible for the causation of this osteopathy, because of its established role in bone growth and carbohydrate metabolism, and also because of associated derangement of sugar tolerance [19, 65] in some osteo-lytic diseases of bones, Experimental and clinical investigations to ascertain if the pituitary has any etiological bearing on the genesis of Paget's disease, have yielded results which though not conclusive are significant. For instance, a large percentage of Paget's disease cases give history of familial diabetes, show a low sugar tolerance, and present a constitutional background of familial obesity and tallness. Further, these cases improve clinically on diabetic diet and Insulin [64]: the bone-pains disappear, the patients feel brighter and stronger, and the usual high blood phosphatase drops to normal.

Phosphorus compounds take part in the storage and utilisation of the carbohydrates [65]. Phosphorus is also needed for deposition of new bone. The controlling link between phosphorus and carbohydrate utilisation lies in the pituitary. Conceivably therefore, pituitary dysfunction may produce not only a defective carbohydrate metabolism but also a defective phosphorus metabolism with abnormal bone changes.

Results of animal experiments [64] injecting dogs with anterior pituitary and parathyroid extracts have shown that massive replacement of the bone marrow by calcium took place when the animal received both the extracts, but there was no such change on parathormone injection alone.

Basophil tumour of the anterior pituitary produces osseous decalcification and other symptoms constituting the well known Cushing's syndrome.

RUMMERT [85] reported in 1934 that a case of Paget's disease complicated with diabetes insipidus responded very favourably to spraying of the nasal mucosa with hypophyseal extract. This is certainly significant, though not conclusive of a causal relationship between the pituitary and Paget's disease.

Other endocrine glands have also been under suspicion, but the evidence against them is not so strong. They have been inculpated because of the osteoporosis that is sometimes found, when they are the seats of hyperplasia, or of tumour; I mean the *thyroid* and the *supra-renals*. With respect to the latter it is to be said that KAY and others [54] in 1934 claimed a favourable therapeutic response in Paget's disease when patients are placed on adrenal extract along with calcium diet. It is not known whether they did any control treatments by cutting out the high calcium diet. That would have been illuminating.

(6) *Dietetic.*—Urinary calculus and Pagetic bone changes have been observed by GOLDSTEIN and ABEHOUSE in 1935 [36], in animals placed on low

vitamin A diet. WHITE [101] said in 1932 that the disease developed in animals kept on diets that are deficient in inorganic salts, vitamins, but contain an excess of calcium. What these vitamins were, are not stated.

All the suggestions discussed above lend support to the view that the cause of Paget's disease is either some metabolic disorder under the influence of one or the other of the ductless glands or, deficiency of vitamin A. But all these theories are open to some serious objection. It is rather unusual that a systemic disturbance or metabolic disorder can cause localised changes in some of the bones as is usually the case in Paget's disease. The entire skeleton and all parts of the individual bones are expected to show the Pagetic changes, if the disease were caused by a systemic or metabolic disorder. In the mono-osseous type of Paget's disease the metabolic theories entirely fail. SOSMAN has expressed similar views against systemic disorder being responsible for the origin of Paget's disease and production of localised bony lesions, during discussion of KASABACH and Gutman's paper on osteoporosis circumscripta of the skull [52].

Changes in the ductless glands have been reported in osteitis deformans, but the findings and the lesions are neither constant nor distinctive [29]. Changes have been found in the thyroid, the pituitary, and the parathyroids. Obviously all these glands cannot be causes at random for the disease on the ground of certain changes being found in them, in some case or other of this osteopathy. Besides, no significant changes in the ductless glands have been consistently observed by other careful workers.

Presence of a disorder of the calcium metabolism cannot be denied in a disease with such active and extensive bone changes, but such derangement should be regarded as a secondary phenomenon and not the primary pathogenic factor.

(7) *Vascular*:—Because of the inherent deficiencies of the theories discussed so far, a hypothesis has been put forward that Paget's disease is a localised disease of bone caused primarily by some vascular pathology affecting the nutrition of the bone or the bones involved. The vascular condition may be endarteritis, arterio-sclerosis, or haemorrhagic infarction.

According to this theory, the initial porosis and subsequent sclerosis are only secondary phenomena, that is, evidences of injury and of repair. The same view has been still better expressed by saying that Paget's disease is primarily a disease of the arteries; the osseous changes are only part of the general changes that supervene on the whole system

including the endocrinic, as sequal to the arterial disease. The bone changes initiated by arterial cause may secondarily be influenced by the action of the altered or affected organs of internal secretion.

Support is lent to this theory of vascular causation by the fact that in a series [24] of 112 cases of cardio-vascular diseases (including arterio-sclerosis, valvular and myo-cardial affections) all showed severe bone changes, and in some of the long standing cases, the changes could not be distinguished from the Pagetic. Most of the cases described by PAGET [73, 74], had cardio-vascular disease. The very great frequency of atheroma and arterio-sclerosis has already been noted earlier in this paper. Pathological examinations of the osteoporotic areas in the skull bones of Paget's disease cases, reveal findings identical with those seen in "haemorrhagic infarction of the calvarium" [52].

Analogous bone changes are seen in syphilis [71] from endarteritis obliterans, or, the sclerosis in the later stages of osteomyelitis when ischaemia has followed on the initial hyperaemia.

Presentation of a new theory.—Common with all the other hypotheses, the last one (vascular) also does not explain the paucity verging on the absence of Paget's disease in India, a fact which I have already pointed out in an earlier section of this paper. This peculiarity is not restricted to the children of the soil, but is exhibited equally by the people of the Western hemisphere resident in this country. It appeared to me therefore that there must be some other causative factor in addition to the vascular.

Speaking generally, no disease is the result of an exciting cause. It is always the resultant of two opposite or opposing causes—one, exciting, and the other restraining. How and to what extent these operate in any particular case, is necessarily in the realm of speculation and conjecture, but it is certainly not beyond the range of possibility that the restraining factor may be the healing agent in some cases, that is, the tissue changes or the functional alterations brought about by the excitor may be simultaneously repaired or rehabilitated by the influence of the "restrainer", and so the occurrence of morbidity is prevented.

I suggest that in Paget's disease the initial stage of injury from arterial cause is manifested as a halisteresis or porosis of bone, only because a simultaneous repair is in abeyance from want of enough vitamin D in the system to make available to the depleted bone extra calcium and phosphorus for the repair. If however the level of vitamin D is maintained high,

regenerative process can be expected to run *pari passu* with the destructive, and thus prevent the onset of the disease.

My contention is that in India we get the benefit of such an abundance of sunlight that the vitamin D production from the Ergosterol of the skin is always at a maximum, which by influencing the calcium and phosphorus mobilisation, helps to bring to the afflicted bone the materials needed for repair, and thus prevents, or reduces to a minimum the incidence of porotic bone diseases in India. Paget's disease is no exception, for as we shall see later, in the initial phase of this disease decalcification and cancellar loss dominate the picture.

In support of my statement, I refer to the negligible incidence of rickets, of osteomalacia, and even of bone tuberculosis in India (although pulmonary tuberculosis is rapidly increasing), as compared to their incidence in the less sunny countries, or under circumstances when sunlight is habitually kept out from exerting its beneficial action through the skin.

Additional support is lent to my hypothesis from the therapeutic measure that have been adopted with success, and all of which have one object in common, namely an adequate supply of calcium and vitamin D to the sufferers.

Further presumptive evidence in support of this hypothesis, possibly lies in the reported incidence of the disease in the lower animals *in captivity*, when exposure to the sun's rays is very much less, than in their natural wild state of existence.

In this connection I would further mention that KNAGGS attributed a common etiologic factor to both osteo-malacia and osteitis deformans, and explained the difference between the two on their respective response to reparative process. Osteo-malacia is admittedly a vitamin D deficiency disease. I do not think I contravene the rules of deductive logic if I ascribe to vitamin D, or to the actinic rays of the sun an important, or even a determining auxillary role in the manifestation of this disease.

This is my, for want of a better name, the *vitamino-vascular* hypothesis about that causation of Paget's disease of bone.

I am conscious of the necessity of further proofs in support, beyond what I have advanced, such as comparative statistics of incidence of this osteopathy amongst people of the Western hemisphere who habitually keep out the sun from their skin by garments, and those who not because of the present hygienic craze for sun bath, and the experimental results of causing osseous injury through the circulation in animals if such is possible, and observing the effects of

plus and *minus* vitamin D supply at the same time.

Morbid anatomy—Macroscopic and Microscopic. — *Macroscopic* :— The bones from a fully developed case of Paget's disease are bigger and thicker, usually with, or sometimes without deformity of contour; the surface is furrowed and pitted; hard and stone like in general, with an ivory sheen at places when recently preserved, but very soon taking on a chalky look from shedding off of a fine white dust from the surface, which collects in the specimen jars.

The bones give an appearance of being heavy, and are often confused with syphilitic bones from superficial inspection. In reality, the bones are lighter than normal, and when struck on any hard surface, contrary to expectation emit a dull thud, instead of a sharp clang, and are liable to break.

In the earlier stages the bones are very vascular and soft, and can be cut through with a knife, and also plastic enough to be bent by superincumbent weight, and muscular pull.

Microscopic:—No description of morbid histology has excelled in clarity and brevity the report that Mr. BUTLIN submitted to PAGET which ran thus:—"The whole microscopical architecture of the bone has been altered: the structure appears to have been almost entirely removed and laid down afresh on a different plan and in a larger mould."

The *essential features* of the bone changes are:—destruction or bone resorption by the multi-nucleated osteoclasts, and replacement by a highly proliferative vascular connective tissue in which later on, new bone is laid down.

The affection may start either as a *subperiosteal* or as an *endosteal* involvement, or both.

In the *subperiosteal* type the membrane is raised and the cortical bone undergoes "halisteresis" that is decalcification and porosis, with possibly a few irregular streaks of the old osseous tissue surviving here and there. By the lifting of the periosteum a sharp zone of demarcation between the affected and the normal segments of the bone, becomes apparent.

In the *endosteal* type, there are cortical porosis, and loss of cancellous structure. The changes are slower, and the lesion is rather diffuse in outline.

The affection may remain in this porotic stage for a considerable period (sometime years), before the next phase that is, repair supervenes. Hence some authors not getting a chance to follow up the progress of the disease, wrongly concluded that there is a "monophasic" type of Paget's disease, showing only porosis.

At some subsequent date, usually about a year after the onset, osteoid tissue is deposited in the vascular connective tissue matrix; the soft osteoid tissues harden up later from deposit of lime.

Opinion is divided on the mechanism of new bone formation. Some hold that it is due to the activity of the *osteoblasts* of the original bone; others[57] deny osteoblastic activity, and are inclined towards the latest theory of LERICHE and POLICARD and so regard the new bone as a result of *metaplasia* or metamorphosis of the primitive mesenchymal tissues that replaced the original bone.

Be the mechanism what it may, the fact remains that new bone is formed, and it is this reparative phase, or *bone apposition* as it is called, which presents certain characters peculiar to Paget's disease.

First, there may be no lamellar arrangement in the new bone deposit: the whole affected area is filled up with dense osseous tissue without any trabecular outlines. In this state the appearances resemble those of plastic carcinoma, or fluorosis or Albers-Schonberg's disease.

Secondly, there may be a lamellar arrangement in the new bone but the arrangement is erratic; the lamellae are laid down without regard to functional stress. The trabeculae are coarser than normal. The result is that affected portion of the bone is less dense, and is composed of network, or grill of irregular, or bizarre mesh.

Thirdly, there may be a combination of the above two types; some portions of the bone showing homogeneous chunks of the new osseous tissue of irregular shape and disposition, and connected with each other by coarse trabecular strands.

These three alternative types of repair have been very aptly described by BRAILSFORD[14] as *osteolithic, osteoporotic or fibrous* and *litho-cystic* respectively.

Some authors have described "cyst formation" in Pagetic bones. These are not true cysts, but areas in the bone filled up with soft osteoid or fibrous tissue and surrounded by osseous tissue causing only a cystic appearance. In course of time they fill up with bone, which is never the case with true cysts[79].

For the sake of convenience, phases and types of bone changes are described as occurring separately, but it is worthwhile to remember that in actual practice a combination of types, and a co-existence of phases are met with. KNAGGS[57] has referred to it still more forcibly by stating that absorption and ossification go on simultaneously.

Special features of Pagetic lesions.—Pagetic changes affect all new bones that appear in the system as the result of injury, disease, senility,

e.g., callus, myositis ossificans, osteophytes, calcified costal and laryngeal cartilages.

The changes start at either end of the shaft of a long bone, and extend usually about half way up or down the shaft. Affection of the middle part of the shaft without involvement of one of the ends, is not known.

The affection does not involve the articular surfaces of bones at least not till very late in the disease. But if the articular surfaces are already damaged by a previous arthritic process, they are involved in the Pagetic affection without delay.

Osteo-arthritic changes are apt to develop on the neighbouring joint from derangement of joint mechanics[4] as a result of deformities of the bones. ROBERTS and COHEN[80] noticed it in 7 out of their 16 cases.

Production of curvatures and deformities.—The mechanism varies according to the special functional peculiarities, and situation of the bones; the essential predisposing cause is however the same in all cases, namely, a plastic state of the bones in the earlier, or rather the pre-sclerotic stage of the affection.

In the case of the long bones of the lower extremity and the bones of the spinal column the superincumbent *weight* is the main determining factor.

Elongation of the tibia fixed as it is by its two ends to the fibula is an accessory factor in the production of bowing deformity in this bone. In the case of either of the two bones of the forearm a similar elongation results in dislocation at a radio-ulnar joint.

Muscular pull contributes also, as when the femora apart from the bowing outwards are also twisted, which can result only through the pulls of the various muscles in different directions, or when the bones of the arm (not required to support weight) are found bent at times. But weight factor also acts in the case of the bones of the arm and the forearm, when the patient subjects these bones to intermittent stress and strain by throwing the weight of his body on to them, at the time of rising from the bed or the chair.

Frequency and magnitude of the curvatures and deformities are governed by the acuteness and the extent of the bone changes, functional activity of the affected parts, and the duration of the plastic stage of the bone.

Radiographic Appearance.—This varies according to the morbid anatomy present in the bone at the time of the examination. In the initial stage, one sees on the film in the affected segment of the bone,

some expansion in girth, rarefaction, and "combed-out" appearance of the trabeculae. "Combing-out" is due to decalcification and loss of some of the trabeculae. With progress of the change, radio-lucency increases, and except for a few straggling survivors, there is loss of cancelli and cortical bone. It is in this changed state, that most of the confusion in the identity of osteitis deformans with osteitis fibrosa cystica (genaralised or localised), has occurred, as it will be observed that there is nothing characteristic about the radiological change in this porotic phase of Paget's disease.

To quote an eminent authority, SHERWOOD MOORE, "it is the repair process in the bone of Paget's disease which is Roentgenographically, characteristic of the disease." In this phase, one sees on the film[98] according to the type of repair, either a homogeneous opacity without a trabecular outline—a "ground glass" effect; or, a network of intermingling and interlacing coarse, dense, and irregular trabeculae—"a tangled skein of wool"; or, a mottled opacity with opaque fibrils coursing through the lighter areas—"flakes of cotton wool" irregularly strewn over the part. These radiographic types have been described alternatively as *felt-like, grill-like* and *pseudo-cystic*, and correspond with the three types of bone changes described by BRAILSFORD (*vide supra*).

Bio-chemical Findings.—From all accounts Calcium and Phosphorus of the blood are within normal limits in osteitis deformans. Occasionally there might be a slight lowering. BELDEN and BERNHEIM [8] claimed in 1932, to have noted an increase of Calcium in the early stages of the disease, falling to normal in the later stages.

In 1922 WHITE [101] stated that lowering of the Alkaline reserve, and of carbon dioxide-carrying power of the blood, have been noted.

ORTON[71] quoting DONALD HUNTER, says that urine calcium increases to four or five times of the normal in a great majority of the cases, even with normal blood calcium.

KAY[53] was the first to report in 1929, increased blood phosphatase activity in osteitis deformans. GUTMAN and others[39] corroborated his findings in 1936. The height of phosphatase activity is proportional to the amount of bone involved and is a measure of *osteo blastic* activity. This is not a special feature of Paget's disease, and hence is devoid of diagnostic importance. In the osteoplastic type of carcinoma phosphatase activity is also increased, and may be as high as that in the generalised form of Paget's disease. On the other hand, in the localised, mono-osteitic types there may be only a slight phosphatase increase, if at all.

Calcium and Magnesium percentage in bone are diminished as also other inorganic constituents; the ash percentage is lowered. But the total Calcium and Magnesium show an increase due to increased size of the bones.

Bio-chemical changes in the bones have been summarised as increase of organic and decrease of inorganic materials.

DISTRIBUTION OF LESIONS: SPECIAL PATHOLOGY

All the bones are liable to be involved, but some more than others. Long bones of the lower extremity (particularly the tibiae), the spine, the skull and the pelvis might be arranged in a decreasing order of frequency. Bones of the upper extremity, the thorax, and the small bones of the hands and feet are usually not involved, except in a very generalised form of Paget's disease. Sometimes this routine is reversed, majority of the changes taking place in the bones of the upper extremity whilst those of the lower escape. CLUTTON[22] described, in 1888 such an instance in a woman.

Previous statements about frequency of affection of the different bones are not to be taken too rigidly. Pathological investigation of the disease by SCHMORL has revolutionised our ideas not only about its frequency of occurrence, but also about its distribution in the different bones of the skeleton. As a result of his researches, SCHMORL emphatically states that it is not correct to say any longer that the skull, tibiae, and femora are most often affected. It is the lumbar spine and the sacrum that are most subject to this disease. A table showing the percentage of affection of the different bones will be found in the appendix. Sites of earliest localisation of this disease correspond to the sites that are most subject to strain,—an observation supported by autopsy results. Anybody interested in Schmorl's original papers will find a complete index under the tables in the appendix.

There is always a difference in the percentage of frequency, of involvement of a particular bone in the series of different observers, especially if their mode of investigation also differs; for instance, in the autopsy group it is the spine, and in the radiological group it is the tibia which shows the highest incidence, the reason being that more examinations are done of the lower extremities for fractures and bone-aches, than of any other part of the body.

Usually the disease is multi-osseous, and extensive, but sometimes may be limited to a small portion of a single bone. These types of the disease are extremely

difficult to recognise. In the mono-osteitic type, incidence of a previous trauma to the affected bone may sometimes be elicited by close enquiry.

The Skull.—It may not be involved at all, or gross changes may be absent for years [54]. When affected, practically always the lesion is in the vault; the basal portion usually escapes. KNAGGS [57] holds otherwise; according to him the base is involved, in a fair proportion of cases. The apparent immunity of the base is due to the lesser number of examinations, and less satisfactory radiological visualisation of the structural alterations in this region.

With involvement of the base, the skull is pushed down on to the spine, by its weight and plastic softening [25], producing, the "convexo-basie" deformity of French workers. The petrous bones, semicircular canals, and the ossicles of the middle ear have been found to be sclerosed, causing deafness and giddiness. Some authors have denied a Pagetic origin for these changes, but have not indicated an alternative cause.

Early changes are seen most frequently in the frontal and fronto-parietal regions, but may be in the temporal and occipital regions also.

As usual the changes are of both types, porotic and sclerotic.

The porosis may be either (1) *generalised;* except about the sutures where there is some opacity, the bones present a dissolved appearance; or, (2) *localised*; an ill-defined diffuse type of rarefaction between the tables, difficult to detect except on slanting examination of the film; or, discrete circumbscribed areas of translucency with distinct but thinned out tables.

In the stage of sclerosis, one sees multiple, small, dense areas with woolly margins, in the decalcified bone the inner table remaining distinct, the outer apparently destroyed and replaced by an irregular and woolly margin—the "*Negro-hair*" appearance, characteristic of Paget's disease of the skull. The loss of the outer table is not real; with a strong light behind the film the table is seen to persist with an intervening translucent zone between it and the woolly border (BRAILSFORD)[14]. Translucency is due to the osteoid and vascular fibrous tissues. With progress in calcification of the osteoid tissues the mottled woolly appearance disappears; the cranium becomes *uniformly dense*, vascular markings and suture lines are lost, as also definition of the inner table.

Instead of a general and uniform sclerosis, coarse and *dense trabeculation* has also been described as occurring at times.

Localised *bosses* particularly over the frontal area, with or without general thickening of the calvarium have also been seen. Very rarely, as in the experience of BRAILSFORD the only change present is an *area of increased density* over a large portion of the cranium. Sometimes, there might be just a slight *thickening* of the calvarium, which it is hard to assign to any distinct pathology.

Osteoporosis circumscripta of the skull.—At one time was regarded as distinct clinical entity of unknown etiology.

SHERWOOD MOORE [67] in 1923, and SCHULLER [88] in 1926, described one and two cases respectively of circumscribed osteoporosis of the skull, but were ignorant of their etiological relationship with osteitis deformans. Moore's case was particularly remarkable, as even in the presence of Pagetic changes elsewhere in the skeleton, the possibility of a causal relationship between the two was missed.

SOSMAN [92] after examining the second case of SCHULLER (a man of 45), reported in 1927 a histo-pathological picture similar to that in Paget's disease of bone, and suggested for the first time, that localised osteoporosis of the skull was an atypical manifestation of osteitis deformans.

The outstanding contributions of KASABACH, DYKE and others [51, 52] in 1932 and 1937, have now established beyond doubt or cavil the identity of osteoporosis circumscripta of the skull with Paget's disease of bone. This condition is a type of the porotic phase in osteitis deformans of the skull not an obligatory phase, but a precursor when it appears at all.

The condition begins as small, round *sharply demarcated* areas of rarefaction at the base of the frontals, that is above the orbits; the areas increase and coalesce producing either a band of translucency extending sometimes from the frontal to the occipital region, or, a well delimited zone of translucency, remaining localised to a section of the cranium.

On the decalcified area at a later date, usually a year after, sometimes twenty, the *condensing phase* supervenes, with the production of one of the types of the sclerotic change described above as characteristic of Paget's disease. It is this very delayed sclerosis that sometimes happen, which was responsible for the introduction of the term "mono-phasic" Paget's, to denote as was erroneously believed, that in some cases of osteitis deformans only the bone resorptive phase was present. KASABACH and GUTMAN [52] noted in 1937, *regression* in the osteoporotic areas in 2 of the 22 cases published by them. Unfortunately, the authors have not expressed themselves clearly

as to what they wanted to convey. Is it restitution to normal architecture?

The condition is asymptomatic, and thus only 47 cases were recorded up to 1937, as accidentally discovered during a complete radiological investigation of the skeleton in known cases of Paget's disease, or of the skull in fractures, intracranial affections, and sinus pathologies.

Circumscribed porosis of the skull may be the only sign of Paget's disease in a patient for years, before characteristic changes appear in other parts of the skeleton, or, it may be associated with Pagetic changes already present in other bones, or, in other areas of the skull itself.

Bones of the face.—Bony tumours and thickenings of the upper jaw are very frequent—about 15%—in osteoporosis circumscripta of the skull [52]. The association is too frequent to be devoid of significance. In such cases, the adjacent portion of the frontal bone is practically always the seat of circumscribed porosis.

In this connection reference is to be made to another clinical condition not yet recognised as a distinct disease, which starts in the first two decades of life [21], and shows as a diffuse thickening of the facial bones—maxilla, mandible, malar and nasal—and gradually spreads to the adjacent skull bones (frontal). The face assumes a leonine expression; hence the condition has been fittingly described as *leontiasis ossea*, also as cranio-sclerosis, or hyperostosis cranii. Its etiology is unknown, and the histo-pathology is sometimes like that of osteitis deformans [24, 32, 37, 56], and sometimes like that of osteitis fibrosa cystica (generalised)[32], and hence considered a type of either of the two diseases. Pagetic changes have sometimes been described in some of the long bones in this condition.

Nasal sinuses.—These are enlarged when the skull involvement is very pronounced, when the *teeth* also drop out.

Vertebral column.—According to the pathological studies it is most frequently involved; the lumbar segment is affected twice as often as the thoracic, and thrice as often as the cervical (SCHMORL). The lesion may start in one or more of the bodies, or in their transverse processes. The earliest detectable change is either a zone of porosis, or of sclerosis, or, of course trabeculation suggestive of angioma of the bone. During autopsy, one may have to search for the minute lesions in the sectioned vertebral bodies with a magnifying glass. The bodies are bigger antero-posteriorly, and laterally, but compressed from above downwards; at times the flattening may be extreme; destruction of the bodies has also been reported. Thickening of the spinal

arch from periosteal deposit, exostosis, spurs, and ridges, ossification of the anterior common ligament,—all can be met with. The new bony formations are sometimes so big, or the narrowing of the vertebral canal is so marked that the cord and the nerve roots are pressed upon. Normal curvatures of the spine as previously noted, are accentuated. If the spine is already the seat of bone changes as from tubercular spondylitis, those adventitious bones are also involved in the Pagetic change.

Pelvis.—This is another of the frequently affected members of the skeleton. Typical Pagetic changes in all their varieties are met with. Because of plasticity and fragility during one or the other of the stages, pelvic deformities of all sorts, protrusion of the acetabulum, and fractures through the rami are not uncommon.

POLGAR [78] in 1933 described in a case complaining of sacro-iliac pains, condensing osteitis of the iliac bones just near the sacro-iliac joint, and of the superior ramus of the pubis as an initial stage or fore runner of Paget's disease of the pelvis. According to this author, the periosteal bone apposition may show not only an increased sclerosis with the passage of time, but also regressive changes, namely decalcification and cystic formations. No histo-pathological report is available yet.

The first observation—sclerosis as an initial stage—if correct, challenges the foundation of the pathology of Paget's disease. Considering the asymptomatic nature of the disease, it is probable that the initial porotic stage was not observed by this reporter from want of any examination earlier, which was necessitated only when the pains were complained of, by which time transition from the porosis to the sclerosis had taken place. Further no fixity of interval between the two stages of this osteopathy has ever been observed.

The second observation—regression of changes—is open to serious objection in the absence of histological finding, and of the subsequent history of the case. The regressive osteolysis might have been due to supervention of malignancy. Even if that is excluded, the phenomenon though interesting and in my experience the first reported, admits of a simple explanation, namely, recurrence of Pagetic changes on the adventitious bones laid down in a past attack of the same disease. There is no objection to such a possibility.

A full discussion of the various pathological changes and deformities having already been entered into, such will not be repeated *Seriatim*, in the further consideration of the bones now following.

Femur.—Coxa vara deformity is frequent. Of the fractures that take

place through this bone in Paget's disease large majority are transverse and subtrochanteric. Oblique cleavage is very rare. Next in frequency is fracture of the neck; the least frequent are those through the middle of the shaft (probably because of the strengthening struts that form on the concave aspect of the bowed shafts.)

Tibia.—This bone shows best the pathological changes, and admits of easy clinical detection in the earlier stages of the disease by the enlargement and irregularity. Thickening may be very marked in this bone.

Humerus—According to some [14] it is the most frequently involved bone of the upper extremity, and shows in common with the long bones of the lower extremity, liability to spontaneous fracture.

Clavicle.—By the autopsy method of investigation, it is found to show a large percentage of incidence (13 per cent) of Paget's disease; it is thus most often affected amongst the bones of the upper extremity—humerus being only 4 per cent in the pathological series of SCHMORL. The bone is thickened, deformed, and the curves are accentuated.

Ribs and Sternum.—These are affected with a generalised form of Paget's disease; only a few ribs or the whole thoracic cage including the sternum may be the seat of the disease.

Scapula.—This is the least affected bone in the skeleton.

Small bones of the hand and foot—Complete obliteration of the medullary canals and sclerosis are recorded in the metacarpals, metatarsals, and phalanges. HARVIER and others [43] reported in 1938, dense parallel lines as of a grill in the epiphyseal portions of the phalanges. Os Calcis is the most frequently affected bone in this group; it usually shows coarse trabeculation and expansion.

Calcification in the soft tissues.—In Paget's disease of the skull and of the long bones, calcification of the pineal body, of the choroid plexus [52] and also of the walls of the vessels of the extremities are met with. Although atheroma is almost a constant feature in this disease, the reason for a local association is not apparent.

SOME OBSERVATIONS ON THE REPORTED PATHOLOGY

The *role of the periosteum* in bone regeneration in this disease is a subject of controversy. It has been said that the periosteum does not lay down new bone [102] but only stimulates and nourishes the osteogenic proliferating connective tissue that replaces the bone destroyed by the osteoclasts in the initial stage. It is this osteogenic connective tissue alone which forms, without the help of the osteoblasts all the new bones that are laid down in the process of repair [57], According to ILLINGWORTH and DICK [47], the periosteum does not take part in the disease, and is not thickened. It is significant, that a pathologist of Schmorl's experience cites barely two cases in which the periosteum was thickened, and that also in patients who were long confined to bed with fracture. The periosteal bone formation was found in the broken bone alone.

On the other hand, experienced pathologist and radiologist, like BOYD and BRAILSFORD have expressed differently. BOYD [12] says, "the new bone is chiefly deposited from the periosteum, but a slight deposit may take place from the medulla."

According to JAFFE [48], gross evidence of periosteal activity was invariably present; periosteal new bone is sometimes 4 to 5 mm. thick. Histological evidence of periosteal proliferation is not at all unusual. The difficulty of recognition of periosteal activity in the earlier stages is due to the slight degree of activity then present. Periosteal bone formation about the tubular bones, has been recorded by JAFFE and others, and in their opinion it is an evidence that the thickening of the tubular bones is due to periosteal bone deposit. The failure to demonstrate a distinct layer of periosteal bone in strata, is due to the fact that the new bone deposited is soon afflicted with the disease, and blends with the rest of the new bone of the cortex underneath, whereas in periostitis from trauma, it is only the periosteum that is affected, and thus when the new bone develops as a matter of reactive response, it remains separate from the underlying original cortex.

STENHOLM [94] even doubted the existence of a separate endosteal type of Paget's disease; according to him such changes are non-Pagetic.

BRAILSFORD[14] clearly states that the disease may start "either as an endosteal, or sub-periosteal affection" and that the "disease may spread *via* the periosteum and/or the endosteum;" furthermore, that the tibia "exhibits the periosteal progression of the disease in an almost diagramatic clearness." Unfortunately, nowhere in his paper he has made any explicit statement that periosteal bone formation occurs in osteitis deformans. It appears to the present author that he referred to the same event "periosteal bone formation" of JAFFE by a different nomenclature when he mentioned "sub-periosteal affection and Periosteal progression." It is very difficult to reconcile these two groups of essentially opposite statements, even though the periosteum has been shorn of its pristine glory as an osteogenic membrane as the result of Macewen's, and Leriche and Policard's works on bone growth.

Bone Expansion in Paget's disease is caused by two different mechanisms in the two types of diseases.

In the *periosteal* type, where the periosteum is lifted, the space thus formed is filled with vascular fibrous tissue, which ultimately forms new bone, and thus adds to the girth of the old. In the *endosteal* type, where the periosteum is *not* lifted, the same connective tissue fills up the osteal space from the medullary canal to the periosteal membrane of the bone. The young connective tissue proliferates, and distends the space limited by the periosteal membrane externally, thus bringing about expansion of the bone in both the stages of this disease, *i.e.* porotic and sclerotic.

COMPLICATIONS

Fractures.—These constitute the commonest complications of osteitis deformans, and are either *complete* cleavage or *incomplete* fissure.

Complete fractures are nearly always transverse and occur readily from such trivial injuries as would not affect a normal bone. The bone simply snaps like a piece of chalk, without any comminution. ROGER and ULIN [81] when reporting their 8 cases in 1936 stated that the cause for increased liability to fracture in osteitis deformans (if such liability ever existed) was ill understood in view of the density and thickness of the bones. They appear to have overlooked that increased fragility results from impairment of both elasticity and rigidity of the bones due to the pathological process, namely, replacement of the closely woven normal cancelli by irregularly disposed coarse trabeculae laid down without regard to functional stress, and relative loss of the inorganic constitutents. Fragility is so marked at times that fractures have occurred through ordinary movement[14], not to speak of trauma!

Pain is said to be less in fractures of Pagetic bones [81]. Healing takes place firmly and readily with minimum of callus.

When callus becomes involved in the underlying pathology the broken ends of the fragments may appear dissolved out, and simulate malignancy. Differential diagnosis is rendered all the more difficult by the fact that a callus in Paget's disease is a favourite site for sarcoma. Serial radiographic examination helps in this predicament.

Delay in union of fracture in this disease, is sometimes due to onset of malignancy [100], a fact worth remembering by the surgeon.

Spontaneous complete fracture can also occur through a sarcoma already existing in the bone.

Incomplete fissures which occur on the convex aspect of the long bones vary from slight indentations to clefts in the cortex. Tibia is the site of election; numerous fissures are sometimes present on one bone. On the film the fissures appear as translucent chinks in the cortex bordered by two dense lines, one on either side of the chink.

The mechanism of causation of these fissures has been aptly likened to the bending of an over-ripe banana [1]. They heal rapidly by callus which soon becomes involved in the underlying pathology, and all trace of a previous disruption is thus lost.

SCHMORL has ascribed the elongation of Pagetic bones to numerous fissures repeatedly appearing on the convex surface and getting healed by new bone deposit.

The nature of these "fissures" is a matter of dispute. Some authorities[13] do not admit them as solution of continuity in the bone, but as evidences of stress on the convex cortex producing focal decalcification, and thus akin to similar appearances in late rickets, osteomalacia, and osteogenesis imperfecta. They further admit the possibility of a complete fracture occurring through these "fissures" if the stress goes beyond a certain limit. They call them "pseudo-fractures" and point out that these are never bridged peripherally by new bone on the surface of the cortex as is always the case in true fractures. Schmorl's histological works do not lend any support to such theory, since he found in these fissures newly formed bony tissue showing Pagetic changes.

But both the school are unanimous in recognizing the surgical importance of these appearances. When discovered, the patient should have proper braces and splints to prevent a complete fracture being precipitated on the slightest trauma.

Sarcoma:—In osteitis deformans, there is a special liability to the development of bone sarcomas. This was observed by PAGET in 5 out of his 8 cases. Other old writers have also referred to this by stating that Paget's disease predisposes to gout and "osseous cancer"[41].

Statistics show that, (1) 14% of all cases of Paget's disease succumb to osteogenic sarcoma; (2) 5% of all sarcomas occur in Paget's disease; (3) 40% of all sarcomas between the age of 55 and 70 are in Paget's disease; and (4) osteogenic sarcoma is not found over 50 except in Paget's disease ([41] and SOSMAN in [52]). Males are more often affected than females; the cases are rapidly fatal.

After a careful investigation of the records of the amazing number—1,200,000 (one million two hundred thousands)—of patients, and of subsequent follow-ups BIRD[9] practically corroborated in 1927, the finding

noted under (1) above. He says that 11% of Paget's disease cases die of osteogenic sarcoma.

The statistics noted are from the American Registry of Bone Sarcoma as quoted by different authors [14, 70].

This tremendous incidence cannot be merely fortuitous, but is due according to KOLODNY, to a "local loss of growth restraint" in Paget's osteopathy. Pre-sarcomatous stage is not necessary[77] for the development of sarcomas are subperiosteal, or endosteal and may be giant-celled, spindle-celled, or fibro-sarcoma.

Sarcomas are usually detected very soon after the diagnosis of Paget's disease has been made, but sometimes, this catastrophe occurs very late, as late as 20 or 30 years after the diagnosis. It is questionable to connect these late cases with those that appear early in the disease, on the fallacious logic of *post hoc. ergo propter hoc.*

Foci in other distant bones appear in quick succession after the first tumour forms in one of the bones, but pulmonary or other visceral metastasis being rare or absent [14] in such cases the spread does not appear to be haematogenous. These multiple sarcomas are of the myeloid type.

Mature fibrous bone marrow, and callus are favourite sites for the sarcomas to start. Normal callus is dense and homogeneous; if it be rarefied or mottled, one may be sure that sarcoma has developed in it.

Neurological complications :— These are caused from pressure of the proliferating bone upon the central nervous system, or on the peripheral nerves as they lie in their bony housings, or when a fracture-dislocation of the spinal column occurs.

In this disease the vertebrae are frequently affected, but symptoms of cord compression are infrequent. Manifestations of the nerve symptoms are many and varied, and depend on the differences in nature, extent, and rate of evolution of the causes. These might be rapid or slowly progressive, diffuse or localised bone proliferation, compression of a vertebral body causing gradual collapse of the spine, or fracture-dislocation resulting in sudden collapse. Slower the onset of the causes, the more gradual or delayed are the symptoms, which may not even appear because of the well known adaptability of the spinal cord to abnormal positions and pressure if such are of slow growth as in Paget's disease, or cord tumours.

Disturbance of function of the spinal cord is produced either directly by pressure on the tracts, or, on the blood supply, or, on both. Arteriosclerosis being a common accompaniment of Paget's disease may indirecty affect the blood supply of the cord, and thus produce the nerve symptoms that are caused by direct pressure. Hence, this question of indirect vascular causation of the symptoms should be thoroughly excluded before any intended surgical relief, by investigating, the pressure in the sub-arachnoid space by the manometer, complete chemical and cytological examinations of the C. S. fluid, and radiological examination of the vertebral column, and of the sub-arachnoid space.

Brain symptoms are very rare, as the bony changes do not encroach on the cranial cavity. When the basilar part is affected, the base is softened and pushed up, but, inspite of compensatory changes in the shape and size of the cranial cavity by the elongation of its antero-posterior and lateral diameters an increase of the intra-cranial pressure is produced with the resultant symptoms of a brain tumour.

The altered shape of the base of the skull by stretching, and the bone proliferations in the foramina and canals by pressing on, the cranial nerves produce characteristic symptoms, *e.g.*, headache, giddiness, tinnitus, deafness, blindness, facial palsy etc. But all these symptoms may have an arteriosclerotic basis also.

Spinal cord symptoms are more frequent. The pressure level is most often at the mid-thoracic region. Extensive proliferative deformities in the cervical and the lumbar regions of the spine do not as readily produce the symptoms: pressure on the cord at different levels is determined by the relative diameters of the spinal cord and the neural canal.

Symptoms vary [89] in magnitude, from mere weakness and paresis to complete paralysis both spastic and flaccid, and from indefinite sensory disturbance to complete loss of all sensations.

ASSOCIATION WITH OTHER DISEASES

Renal calculus:—As has already been noted, osteitis deformans is often diagnosed during an X-ray examination of the urinary tract for colic. The incidence of renal stone in Paget's disease is frequent. The reason [36] for such association lies in the arteriosclerotic back ground which produces the disease and causes kidney inefficiency; along with this there is the increased urinary calcium. Experimental observations in animals on low vitamin-A diet, have shown not only renal stone but also Pagetic changes in the bones.

Osteitis fibrosa cystica (von Recklinghausen).—SANTORO [87] reported in 1931 coexistence of this disease with osteitis deformans in the same patient. There was no histological proof. This, and other similar cases if any reported, are possibly instances of erroneous diagnosis.

Syphilis.—It is not usual to come across cases of osteitis deformans with associated syphilitic infection. When such occurs, diagnostic difficulty is increased by superaddition of syphilitic characters to the Pagetic in the bone changes.

DIFFERENTIAL DIAGNOSIS

Even with the great help from radiology, the diagnosis of Paget's disease is not always easy, and sometimes is impossible. Therefore whatever aid may come from other examinations, should be fully availed of. These accessory examinations are, the bio-chemical, serological, and pathological.

The difficulty is experienced not in the fully developed cases with the characteristic clinical picture, but in the mono-osseous types in the early porotic stage as in the skull, in the later sclerotic stages as in the pelvis, where differentiation from carcinomas may not be possible at times.

Differential diagnosis has to be made from the following :—

I. Osteitis fibrosa cystica (generalised).—Bone resorption as also bone apposition with alteration of the normal architecture of the bone are very marked in Paget's disease. In osteitis fibrosa cystica, resorption is the marked feature, and not apposition which is either absent, or is localised to only a segment of the affected bone.

There is no parathyroid enlargement, or adenoma, or increase of blood calcium in Paget's disease, whereas the opposite holds good in von Recklinghausen's. With respect to hypercalcaemia, it has to be noted that even in undoubted cases of the last disease the blood calcium may not increase [11] from want of sufficient vitamin D, wich would tend to lower the calcium although the parathyroid pathology may be trying to raise it.

In Paget's disease the bone changes are mono—, or, multi-osseous, but the unaffected bones, or unaffected portions of the involved bones are perfectly normal; the skull changes are characteristic and frequent. In von Recklinghausen's disease the entire skeleton is affected; the skull shows a miliary osteoporosis about which there is nothing characteristic.

II. Osteitis Fibrosa.—This term though frequently used by many authors [55] should not convey the impression that it is a distinct disease, which in fact it is not. It is really a histological change, and means *fibrosis in the bone*, a reaction to different kinds of stimuli or injuries to which the bone may be subjected. There is no parathyroid background to this condition, and it has no connection with osteitis deformans, with both of which it has been confused by more than one author.

In the mono-osteitic type of Paget's disease, no differentiation is possible either on clinical, histological, or radiological ground [26]. Presenile period of life, and multiple (perhaps symmetrical as well) occurrence of cyst-like rarefaction in many bones are in favour of Paget's disease.

III. Syphilis of Bone.—Cortical sclerosis, periosteal thickening, widening, coarse medullary structure, and cystic appearances, that is, all those changes that are met with in Paget's disease are found also in syphilis of bone. The differentiating points are :—In syphilis periosteal thickening is irregular; the lesion is present in one bone; the lesion is localised to the diaphyseal portion. A positive Wasserman reaction and response to anti-syphilitic treatments are of great value.

IV. Osteo-plastic Carcinoma.—Metastasis in the bone from a primary carcinoma in the prostate, pancreas or stomach constitutes a serious diagnostic difficulty. The sites of election of metastatic carcinoma in these cases are the lumbar spine and the pelvis. The same age incidence, presence of secondary anaemia in both, their accidental discovery in the course of a routine examination for some other suspected disease or condition, and sometimes absence of clinical evidence of the primary focus are responsible for the difficulty, especially if the Pagetic change is solely or chiefly of the osteo-lithic type of BRAILSFORD.

Absence of deformity, and expansion, presence of areas of cancellar destruction in some other part of the bone are points in favour of carcinoma of the plastic type. It has been said that in malignancy the sclerosed appearance in the film is due to calcium deposit in the meshes of normal cancelli, whereas in Paget's disease there is obliteration of trabecular structure, or the trabeculae, if detectable, are coarse. The chances for detection of these *minutiae* are small in actual practice. In doubtful cases, examination of the tibiae, the femora, and the skull may reveal a clue, that would clinch the diagnosis in favour of Paget's disease.

It is not my idea to suggest that attention to the points noted above will in the majority of cases ensure a correct diagnosis, when some experienced observer does not make a secret of his repeated failure to differentiate the sclerosis from metastasis in scirrhus carcinoma of the stomach, from the osteolithic type of Paget's disease of the pelvic bones.

V. Chronic fluorsois.—In the early stages of this condition there may be some difficulty in diagnosis, for the only bone change then showing is a "white fleecy" condition of the cancelli. A close enquiry into the

occupation, the residential surroundings, the water supply, and possibly the presence of "mottled teeth" in the patient will reveal the chances of fluorine intoxication.

Later on, very marked sclerosis--"milky white" and granular absence of deformity and destruction, and the presence of fuzzy outlines of the bones are pathognomonic.

VI. Hyperostosis Frontalis Interna. In Paget's disease of the skull where changes are limited to the frontal bone difficulty may sometimes arise from a failure to locate the sclerosis as definitely outside the cranial cavity. One clinical feature serves to differentiate the two, and that is impaired intelligence in Paget's disease as against the neuropsychiatric and neurologic symptoms of the other. The fat deposition the hirsute condition of the upper lip and the chin in females, are further points for hyperostosis frontalis interna.

VIII. Chronic osteomyelitis.—Even this most frequent and familiar condition of bone may at times be very confusing, especially when condensation of the compacta has been very heavy. Clinical history, distribution of the lesion in the skeleton and in the individual bone, presence of sequestra less frequent deformities are helpful points.

VIII. Myelomatosis.

IX. Osteo-clastic Carcinomatosis.

X. Kanthomatosis.

XI. Endothelial Myeloma, (Ewing).—All these require differentiation from osteoporosis circumscripta of the skull.

Numerous small punched out areas of rarefaction without any trabeculae (as against bigger dissolved out areas in the bone), presence of similar appearance possibly in the ribs and vertebrae, absence of Pagetic changes elsewhere. Bence-Jones's proteinuria, are points for *myelomatosis*. It is to be noted however, that at the onset osteoporosis circumscripta shows as multiple, small, round foci of decalcification.

Similar appearances but with a less defined outline and the presence of a primary focus in the thyroid or in the breast indicate *osteoclastic carcinoma*.

Incidence in childhood, affection of the other flat bones, and diabetes insipidus are in favour of *xanthomatosis*.

Earlier age incidence than Paget's disease, rapidity of course, moderate pyrexia, and leucocytosis speak for *endothelial myeloma*.

Some rare clinical conditions should be kept in mind, and due regard paid to the possibilities of their occurrence, when engaged in differential diagnosis: *osteopetrosis* or Albers-Schoenberg's disease, or melorheosis-Leri, *i.e. flowing hyperostosis* may be very confusing.

TREATMENT

Paget's disease might as well be called a disease of contradictions. There is no uniformity of experience about the results obtained by the different workers from the adoption of identical therapeutic measures. According to some no form of treatment is of any avail; others are optimistic, and consider that not only relief of pain but also partial restitution of the bony structure to *status quo ante* is possible under certain therapeutic regime. Remedial agents accredited with beneficial effect by some, are described as harmful by others.

Treatment may however, be considered under three sections.

I. Medical.--Supply of *calcium and vitamin D* forms the sheet anchor of medical therapy in this disease. It is interesting to note that monkeys afflicted with this disease have been seen to eat the plaster of the wall for lime [101], from instinct.

Gluconate of calcium has been recommended as the salt *par excellence*, since the acid radicles of the lactate, and the chloride are decalcifying, and hence may prove harmful [30]. Others [8] however do not appear to have experienced any special difficulty or disappointment from the decalcifying property of these radicles, for they also claim immense benefit to their patients by prolonged treatment with 90 grains of calcium lactate, 1½ pints of tomato juice, and 30 drops of irradiated sterol per day, on empty stomach. The same authors apprehended an exacerbation of symptoms if *parathormone* were given as that would augment the decalcification going on in the bone; this, they verified by actually placing some of their patients on parathyroid extract. And yet, counter-claim [83] of good results from parathyroid therapy are not wanting!

High calcium diet and *adrenal cortex extract* are reported to have produced good results [54, 83].

Pituitary extract (spraying the nasal mucous membrane with hypophyseal extract) has proved beneficial. [85]

Measured *carbohydrate diet* and *insulin* [64] have achieved striking results in the matter of quick relief from the bones, aches, and drop in blood phosphatase value. No claim is made as to the permanency of the immediate result, or of accruing of further benefits on prolonged treatment.

If phosphatase level is a measure of osteoblastic activity and if it be recognised that the later bone apposition is a stage of repair in Paget's disease, there can hardly be any rationality in adopting a procedure that checks the natural repair as manifested by a lowering of the index.

Diet with high vitamin A content [36] is also on the recommended list, because of renal calculus and Pagetic bone changes in animals on low vitamin A diet. No curative or palliative result is yet published.

Potassium Iodide-"bone morphia"-is successful in relieving the bone aches.

II. Radiations.—*X rays* have been used [59, 83] with remarkable success in relieving the pain both in the sarcomatous and non-sarcomatous Paget cases.

Both deep and semi-deep therapy techniques with small or moderate dosage at weekly intervals up to a total of four such appear to have achieved the object of giving relief from pain. The relief lasts for a considerable period—months. Sometimes the applications are to be repeated to attain the result.

Irradiation over the parathyroids under similar technique but at three-weekly intervals, up to 3 or 4 applications, is reported to be followed by relief of pain and decalcification of the sclerosed bone.

Along with subjective improvement objective improvement is also claimed in the shape of diminution of the swelling, calcification in porosis, and decalcification in sclerosis—that is, a measure of restoration to normal structure. The exact mechanism by which an almost intelligent elective action of the rays is brought to bear upon the disease process, may not be explicable but the fact remains that the percentage of success is very great—16 cases of a series of 17 were benefited [59].

Ultra violet rays:—Encouraging results [69, 86, 90] in the matter of relief from pain and return of the osseous structure to a more normal state, (and enduring over a considerable period) are recorded[69].

The radiation cases were not invariably on Calcium, Ergosterol, or Parathyroid extracts, yet practically all showed improvement more or less, in their clinical condition, and bone pathology.

(3) Surgical.—Lineal *osteotomy* is sometimes done to give relief in pain. *Bracings and splints* are used to prevent deformities, and complete transverse fractures when fissures are detected in the long bones. When a fracture has taken place the same conservative method of treatment should be followed. Operative treatment of fractures is contraindicated [100] in osteitis deformans, as the bones are too brittle for the pegs, screws and wires.

Amputations for malignant complications need not be considered, as the extreme predisposition to sarcoma militates against such procedure.

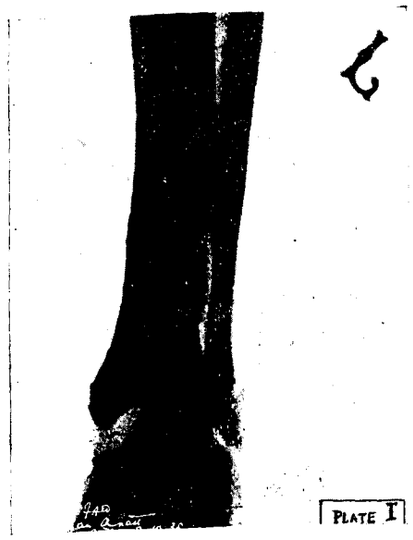
Laminectomy to relieve cord compression, has to be done. The reason and methods as to why and how arteriosclerosis is to be excluded have already been stated. Most of the symptoms disappear at once from

relief of pressure in the antero-posterior direction, but some remain which gradually though very slowly improve. There are increased operative risks and difficulties [89] from the state of the bones and the condition of the patient. Selective small resections are advocated, only at the sites of compression.

Sterilisation has been found useful in some cases of osteomalacia. From the identity of osteomalacia with osteitis deformans, *castration and Steinach operation* [80] though suggested as helpful measures. do not appear to have been adopted in practice.

REPORT OF A CASE

Mr. N.C.N., age 55, Bengali by



race. grocer by occupation, who had never been outside of Bengal (India), was referred to me about 9 years ago for an X-ray examination of the

left ankle, on account of an injury sustained 3 or 4 days previously, as the result of slipping on the road in trying to avoid an approaching automobile.

The ankle and the foot were swollen; both the legs above the ankles looked thicker than usual,—oedematous, pitting on pressure. No other abnormality was noted about the patient.

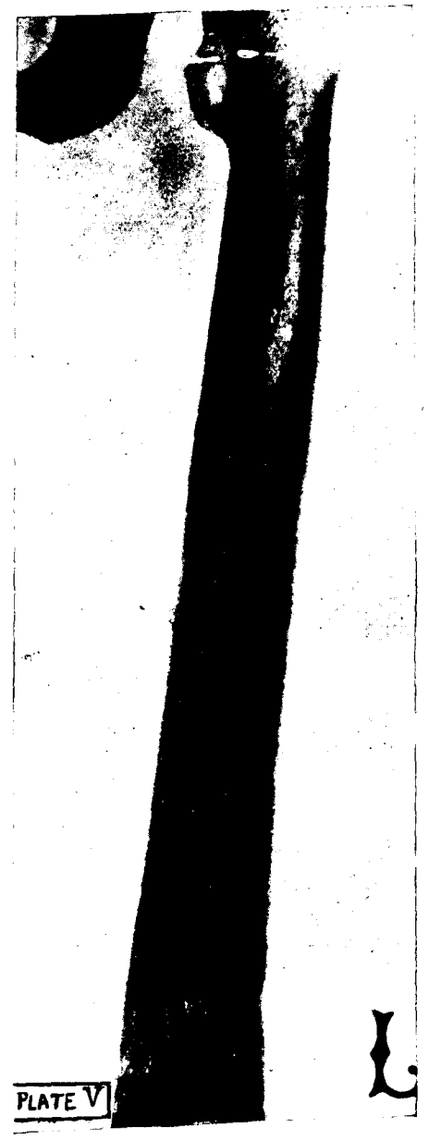
X-ray examination of the ankle showed besides fracture of the external malleolus, and displacement of the astragalus, remarkable structural alterations of the tibia, and to a lesser degree of the fibula. (Plates I and II.)

This led to a detailed investigation of the skeleton, (radiologically) and

focussed my attention to the past history of the patient.

In the long bones of the lower extremity, are seen expansion in girth, and other Pagetic changes described in the text above, as

"pseudo-cystic" or "litho-cystic" (BRAILSFORD). The disease is very



pronounced and extensive in the tibiae and the femora,—more so on the left. (Plates III, IV, and V) Both endosteal and periosteal changes are present, the latter prevailing. The left femur and the tibia show clearly some remnants from the original cortex (seen as dense irregular strands), and deposit of new periosteal or subperiosteal bone formation over them. The tibial plateaus on both sides show some cupping; on the left, the inner tibial plateau shows some roughening and small osseous spurs from the tibial spine(?). A tri-radiate incomplete fissure is present on the external aspect of the left tibia. Roughly, the upper two or three inches of the femora are normal in texture. (Plate VI). *(Vide page 172).*

In the pelvis, (Plate VI) the changes if any, are too insignificant. for a definite pronouncement,—probably nothing more than a suspicious "combing-out" of the cancellar structure of the iliac bones that is, a porotic state of the bone. The spondylolisthetic appearance of the sacral promontory is marked.

In the spinal column pronounced and extensive changes are noticeable in the lumbar and the lower dorsal vertebrae (Plates VII and VIII) *(Vide page 173 & 174)* slight affections in the bodies of isolated vertebrae in the upper and middle portions of the thoracic spine without any change in the regional spinal curvatures, are

present (Plates IX and X). (*Vide page 175 & 176*).

The changes noticed are:—deformities and minor degrees of flattening of the bodies: some increase in the size of the bodies in the antero-posterior and lateral diameters, as in the 2nd to 4th lumbar; diminution of the intervertebral space between the 3rd and the 4th lumbar with ossification of the disc; general porosis, irregular and coarse traculae, and isolated zones of sclerosis in the substance of the bodies; heavy interlocking osteophytes: ossification of the anterior common ligament over the 3rd and 4th lumbars, and between the 5th lumbar and 1st sacral vertebrae: scoliosis and a minor grade of spondylolisthesis[63] or correctly speaking[15] a very accentuated lumbo-sacral curve

PLATE VI.

(Plates VII and XI). (*Vide page 173 & 176*).

The clavicles are definitely thickened and dense from periosteal bone formation, the left more than the right (Plate IX).

In the skull, except for some thickening over the parietal and the occipital, and porosis over the lateral aspects of the frontal, and of the occipital about the occipito-parietal sutures, there is no characteristic Pagetic change. (Plates XII and XIII). (*Vide page 176.*) The porosis over the frontal in a film, is sometimes normal because of thinness of

the bone on its lateral aspects. Vascular markings and sutures are prominent.

Family and previous histories are essentially negative. Syphilis was absent. Except for stiffness of the back and aching pains in the legs with periodic exacerbations during the last 6 or 7 years, attributed to rheumatism, there was no history suggesting a previous osseous inflammation. The patient did not remember whether the stiffness in the back, or the aches in the legs started first.

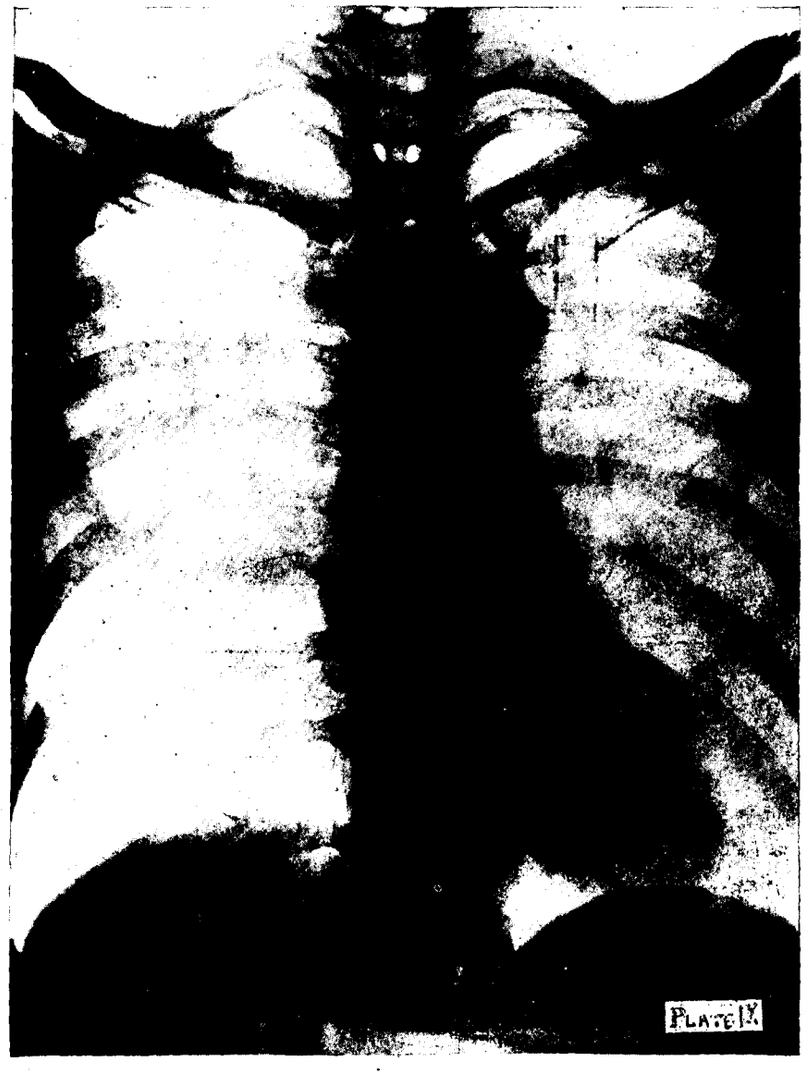
Results of other examinations :—*Urine.*—sp. gr, 1006; trace of albumen; no cast. Blood.—Wassermann reaction and Khan's test negative; coagulation time normal. Systemic.—Practically negative result, except for (?) accentuated second sound over the aortic area. The posture and gait could not be studied then because of the splints, and there was no opportunity for a follow up.

Diagnosis:—Osteitis Deformans (Paget's Disease of Bones).

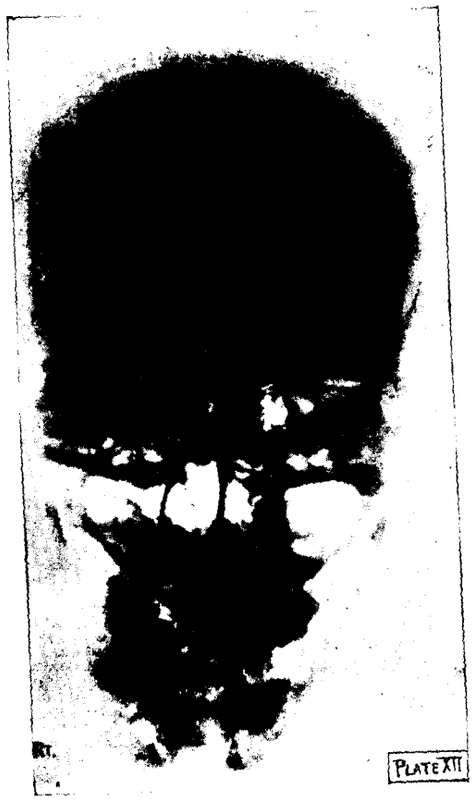
Criticism:—There is nothing to deny a Pagetic origin for the positive findings recorded. Absence of bowing deformity of the long bones, of more characteristic changes in the skull than what were present, and pelvic changes of a doubtful nature—all these though remarkable are not by any means impossible in a disease which as we have discussed above, is protean in its distribution, extent of involvement, and bony alteration. Incidence of deformity is controlled by rest, and also by acuteness and duration of the initial stage of softening in the bones. Apart from the "negro-hair" type of changes in the skull, other types are also present in osteitis deformans, and very delayed sclerotic change in the calvarium is only too frequent. Even if the pelvis, a site of election in this disease, were thoroughly exculpated from any involvement, that cannot constitute an evidence against the present case being one of Paget's disease of bone.

Diagnosis of bone syphilis, or of previous generalised osteomyelitis is at once excluded by the barren

history and negative blood tests, over and above the other points in the differential diagnosis that are also against them, or, any other alternative causation.



Therefore, disturbances in the texture and density of the bones as recorded and described, their well marked character and wide-spread distribution in some of the bones



which are not less favourite sites than the pelvis, the insidious onset, virtually asymptomatic course, age, sex, urinary findings pointing to a nephro-sclerosis, absence of syphilis or of previous osteomyelitis, and even the accidental discovery—all conforming to the accepted description of the disease by all the previous writers, are regarded by the present author to be in favour of a diagnosis of the case as one of Paget's Disease of Bones.

SCHEMA OF THE PRESENTATION

A departure has been made from the usual practice of summarising the paper, by inserting in its stead a schema which serves only as an index of the various aspects from which this disease has been considered, and also of the literature that has been consulted, and referred to, in the text.

I. *Introduction.*—Nature of the Contribution. General remarks on the conflicting opinions prevalent about this disease. Historical.

II. *Signs, Symptoms, and Clinical Course.*—A detailed account including explanation of the Bone aches, Prognosis.

III. *Etiology.*—Age. Class. Sex. Heredity. Occurrence in other members of the animal kingdom. Frequency of occurrence with special reference to its incidence in India.

IV. *Pathology.*—Pathogenesis. Theories of causation: inflammatory, toxic, syphilitic, neurotrophic, endocrino-metabolic, dietetic, vascular. Discussion of the theories. Presentation of a new theory as complementary to the vascular theory. Necessity of further proofs in support of the new theory: possible sources of such proofs. Morbid anatomy—macroscopic, and microscopic. Macroscopic: naked eye appearance of the bones, their weight, plasticity and fragility. Microscopic: essential features of the bone changes; endosteal and subperiosteal types; histo-pathologic changes; types of new bone formation in the reparative stage. Cyst formation in Paget's disease. Special features of Pagetic lesions. Production of curvatures and deformities. Radiographic appearance—descriptive terms. Bio-chemical findings in blood, bone, and urine.

V. *Distribution of lesions: Special pathology.*—Favourite sites. Frequency of involvement of the different bones. Difference in frequency according to the method of investigation. Cause of the difference. Consideration of the lesions in individual bones: Skull—usual changes and osteoporosis circumscripta. Bones of the face—leontiasis ossea. Nasal sinuses and teeth. Vertebral column. Pelvis—with special reference to the initial sclerosis. Femur. Tibia. Humerus.

Clavicle. Ribs and Sternum,Scapula. Small bones of the hand and foot. Calcification in the soft tissues.

VI. *Some observations on the reported pathology*.—The role of the periosteum in bone regeneration in Paget's disease. Mechanism of bone expansion.

VII. *Complications* — Fractures : complete and incomplete.

Complete :—Character ; special predisposition ; causes of increased fragility of the bones ; union of fractures in Paget's disease ; import of delay in union ; callus—a favourite site for sarcoma

Incomplete : fissures ; their nature, causation, and surgical importance.

SARCOMA: special liability to bone sarcomas ; statistics ; sites of origin; types of invasion, histological classification.

NEUROLOGICAL COMPLICATIONS.—Mechanism and frequency of causation ; factors influencing the evolution of nerve symptoms ; two alternative causes of the symptoms; how to differentiate the causation.

VIII. *Association with other diseases*.—Renal calculus ; osteitis fibrosa cystica (von Recklinghausen) ; syphilis.

IX. *Differential diagnosis*.—Observations on diagnostic difficulty. Points of differentiation from—osteitis fibrosa, osteitis fibrosa cystica (generalised), bone syphilis carcinoma (osteoplastic), chronic fluorisis, hyperostosis frontalis. interna, chronic osteomyelitis, myelomatosis, carcinoma (osteoclastic), xanthomatosis, endothelial myeloma (EWING), some very rare clinical conditions.

X. *Treatment*.—General observations on therapeutic efficacy.

MEDICAL : calcium vitamins, endocrines and diets.

RADIATIONS : X-Rays, ultra-violet rays.

SURGICAL : Palliative osteotomy. Conservative methods in prophylaxis and cure of fractures and correction of deformities. Amputation in malignancy. Laminectomy in neurological complications. Increased operative risks in Paget's disease and their remedies. Sterilisation operations.

XI. *Report of a case*,—History. Radiological findings. Results of other examinations. Diagnosis. Criticism.

XII. *Bibliography*.—105 publications—books and articles in the journals.

XIII. *Appendix*.—Table I, incidence in big general hospitals:

Table II, cases detected by Schmorl.

Table III, frequency of occurrence and of distribution (according to Schmorl).

Index to Schmorl's original papers (not included in the bibliograp

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(Titles of non-English papers have been translated into English.)

APPENDIX.

Table I—Admissions.

Hospitals.	Osteitis Deformans.	Annual Admissions.	Ratio.
John Hopkins... ...	3	30,000	1/10,000
Jefferson Medical College Hospital	3	38,000	1/12,666
Mayo Clinic	15	2,37,000	1/15,800
Massachusetts Genl. Hospital	7	2,85,000	1/40,715
Total ...	28	5,90,000	1/21,071
			(Approx. 1/21,000)

Table II.—Number of cases detected by Schmorl.

Before 1925, 25 cases detected by post mortem on 32,000 cadavers.

After 1925, within six months 18 cases in 650 post mortems.

By 1930 114 ,,
1931 150 ,,
1932 190 .,

Table III.—Frequency of occurrence and Distribution. (Schmorl.)

138 cases in 4,614 post mortems on persons over 40, *i.e* , 3'3% or, *approx*, *3%*.

Distribution in the Skeleton:—Sacrum 56%. Spine (most often lumbar) 50%. Rt. Femur 31%. Cranium 28%. Sternum 23%. Pelvis 21%. Lt. Femur 15%. Clavicle 13%. Tibia 8%. Ribs 7%. Humerus 4%.

Index to Schmorl's Papers :—

Verhandl. d. deutsch. path. Gesellsch., 1926, Vol. 21; 1930, Vol. 25.
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The

Indian Journal of Radiology

Vol. I. NOVEMBER, 1947 No. 4.

Editorial

DR. M. D. JOSHI, M.B.B.S., F.C.P.S., D.M.R.E., J.P.,
President, Indian Radiological Association, Bombay.

IT gives me great pleasure in presenting to the members the last quarterly issue for the year 1947, and in doing so, I take the liberty of cordially thanking such of my colleagues as have been materially helpful in making this periodical a great success.

I need not remind the members of the difficult days through which we are now passing. Launching of a periodical of this kind is not an easy matter. Great difficulties and impediments have got to be overcome.

To secure good Art Paper is difficult in these days. On account of shortage of supply, prices of art paper have gone up very high. Another difficulty is to secure the necessary quota of paper from the Central Government. I am happy to say that we have successfully overcome these difficulties and have secured the necessary quota of paper for our periodical. Our thanks are due to the Central and Provincial Governments for this.

The next difficulty is to find out a suitable Press which can cope with the printing of such a highly technical periodical. It is a fortunate circumstance that Dr. U. Krishna Rau, a member of our Radiological Association and who is the Printer and Editor of the medical journal "The Antiseptic" Madras, has come to our rescue and has been very helpful in facilitating the printing of this periodical with efficiency and accuracy.

The next difficulty, as is well-known in the case of such a periodical, is to invite and collect suitable articles from competent and well-known persons in the line. In this respect Rao Bahadur Dr. P. Rama Rau, Madras and Dr. K. M. Rai, Director of Bernard Institute of Radiology Madras have rendered invaluable assistance which it is

hard to over-rate. Not only have they subscribed excellent articles and taken the trouble of carefully revising and collecting the articles from other members, but also have made themselves responsible for the irksome task of preparing blocks of skiagrams and correcting proofs of articles from time to time. The high calibre of the articles which have hithertofore appeared in print will speak for itself and I sincerely hope that our members will fully appreciate the benefit of such articles.

I must not omit to render my sincere thanks to the subscribers of this Quarterly without whose help the Journal would not have been a success. My thanks are due to the firms who have been generous enough to patronise this periodical with their advertisements.

In conclusion, let me express the hope that the periodical which has started its existence only recently, will have a long and useful life and will serve the purpose for which it is intended by making a material contribution to the advancement of the Radiological Science.

NOTICE TO CONTRIBUTORS

Contributions are to be sent to one of the joint Editors, 'The Indian Journal of Radiology' Rao Bahadur Dr. P. Rama Rau, D.M.R. (Vienna), The Madras Radiological Institute, 155-157, Poonamallee High Road, Kilpauk, Madras 10, or Dr. K. Manjunath Rai, F.R.C.S. (Edin.), D.M.R (Lond.), Barnard Institute of Radiology, Govt. General Hospital, Madras.

Contributions should be typewritten on one side of the paper only. They are accepted on the understanding that they are sent exclusively to this Journal and a statement to that effect should accompany every contribution. Original Radiographic negatives should not be sent, but prints there from, or prints from reductions; adequate explanatory notes should be attached to each radiograph, diagram or sketch. Illustrations will be the Copyright of the 'Indian Journal of Radiology' and may not be published elsewhere without acknowledgement or permission. Rejected contributions will be returned only if accompanied by a stamped addressed envelope.

All communications regarding membership of the Association, subscription to the Journal and advertisements may be addressed to the General Secretary, The Indian Radiological Association, 155-157, Poonamallee High Road, Kilpauk, Madras, 10.

Greetings

from the

"British Journal of Radiology."

Our distinguished contemporary "The British Journal of Radiology" in their September 1947 issue review our publication thus:

"It is appropriate that in the year in which India assumes her independence, we welcome the first appearance of The Indian Journal of Radiology, the official organ of the Indian Radiological Association.

This is a quarterly journal, the first number of which appeared in Feb. 1947.

The President of the Association is Dr. M. D. Joshi, of Bombay, and the Joint Editors of the Journal are Rao Bahadur Dr. P. Rama Rau, of Madras and Dr. K. Manjunath Rai, also of Madras.

The Indian Journal of Radiology has a pleasing and dignified format and is printed in a bold and very legible type. The illustrations compare favourably with much that is found in the world's radiological literature.

From the world's oldest radiological journal go greetings and the hope that this enterprise will meet with the success it deserves."

List of Publications Received.

"British Journal of Radiology," August and September, 1947.

"International Medical Abstracts and Reviews," October, 1947.

"Medical Digest," September, 1947.

"Indian Physician," October, 1947.

"The Miscellany," September, 1947.

Programme of the 2nd Indian Congress of Radiology

Place.....**J. J. Hospital Compound**

Wednesday, 24th Dec. '47	
9 a.m. to 12 noon	Joint Inauguration of All Medical Conferences.
3 to 4 p.m.	Opening of Exhibition.
Thursday, 25th Dec. '47	
8-30 to 9 a.m.	Registration.
9 to 10-30 a.m.	Inauguration Session. I.R.A. 1. Chairman's Welcome. 2. I.R.A. President's Address : by Dr. M. D. Joshi. 3. Inaugural Address: by Dr. Jivraj N. Mehta. Director General of Health Services in India. 4. Induction of incoming President : by Dr. Jivraj N. Mehta. 5. Incoming President's Address—Dr. K. P. Mody. 6. Vote of Thanks by Dr. L. H. Athle. 7. Reception Committee Secretary's Announcement.
11 a.m. to 1 p.m.	Cenrtal Council Meeting. I.R.A. (Agenda will be posted separately).
1-30 p.m.	Lunch.
2.30 to 4.30 p.m.	General Body Meeting. I.R.A. Agenda (slip attached separately.)
4-30 to 6 p.m.	Inauguration of Obst. & Gynæ. Conference.
9-30 to 11-30 p.m.	Entertainment by medical students.
Friday, 26th Dec. '47	
Morning	Opening of Surgical & Medical Conferences.
2 to 5 p.m.	Scientific Session.—Surgical (Tumours).
9 p.m.	Boat Trip.
Saturday, 27th Dec. '47	
9 a.m. to 12 noon.	Symposium on functional Uterine Bleeding.
2-30 to 5-30 p.m.	Scientific Session. I.R.A.
8 30 p.m.	Subscription Dinner (if possible).
Sunday, 28th Dec. '47	
9-to 12 noon	To visit Hospitals & Medical Institutions.
2-30 to 5-30 p.m.	Scientific Session. I.R.A.
9 to 11-30 p.m.	Cinema Entertainment.
Monday, 29th Dec. '47	
9 to 12 noon	Symposium on Appendicitis.
2-30 to 6 p.m.	Scientific Session I.R.A.
6 to 7 p.m.	Concluding Session of All Conferences.
	Congress adjourns *sine die*.
	Meeting of the New Central Council.
Tuesday, 30th Dec. '47 8 a.m.	Trip to Elephanta Caves.

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