On

OSTEOMALACIA.

Thesis presented for the Degree of

Doctor of Medicine

by

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SIX CASES OF OSTEOMALACIA.

Five in aged women.

During the time I was Resident Medical Officer in the Dundee Parochial Hospital, from September 1900 to January 1903, I had under my care four patients who appeared to be suffering from senile osteomalacia.

The fifth case occurred in the Dundee Western Poor House and was under the care of Dr. George Laurence, Dundee, who has kindly given me a short record of the illness.

For the history of the sixth case, where the disease occurred in a pregnant woman, I am indebted to Professor Kynoch, Professor of Midwifery, St. Andrews University, who has most kindly placed his notes at my disposal. I saw the patient frequently while studying in his wards in the Dundee Royal Infirmary.

CASE I. A. R. age 64. married, multipara, was admitted to Hospital from the General Poor House in January 1891, complaining of abdominal pain and weakness. She had a history of chronic cystitis, and suffered from frequent micturition, but the urine as examined in the routine of ward work showed no
abnormality. Its reaction was acid, Sp: Gr: 1024, Deposit mucus, no albumen. The abdomen was easily palpated, and prominence of the pubic bones was noted.

She had an attack of diarrhoea a few days after admission which readily yielded to treatment.

During her stay in Hospital she constantly complained of pains all over but particularly in the pelvis. The Circulatory and Respiratory Systems were healthy, her bent figure was ascribed to the feebleness of age and her constant complaining or "grumbling" to a "neurotic temperament." She was discharged to the House in April 1891. The following June she was readmitted still complaining of the same aching pains which appeared to be of obscure rheumatic origin, but were never typical of that disease. The pain was always worst in the lower part of the abdomen and in the pelvis. She lay all crumpled up in bed and the beaking of the pelvis was markedly increased. Examination of the pelvic organs showed extreme atrophy.

There appeared to have been cicatrization of the upper part of the vagina with adhesion of the anterior and posterior walls; the canal was only 1½ inches in length - the small uterus was felt per rectum.

Patient said she had suffered from a vaginal discharge three years before, and this is of interest as
it may account for the condition of the inguinal glands which were somewhat enlarged and indurated on both sides. The symptoms did not suggest malignant disease. She still complained of painful micturition and of pain in the region of the right kidney which was large and easily palpable. The urine was alkaline, no pus, no excess of phosphates.

The patient got gradually weaker and died 7th September 1901.

Unfortunately post-mortem examination was refused.

Remarks. The notes of this case are scanty. The patient was married and had had children, but no further particulars as to her pregnancies were sought.

The case was not recognised as osteomalacia, but all along impressed the writer as being an unusual illness with symptoms which could not be accounted for and its similarity to the subsequent cases in which the disease was verified post-mortem leaves little doubt as to its having been a true case of osteomalacia. The general symptoms and appearance, the constant pain in the pelvis, back and ribs, the difficulty and pain in moving and the beaking of the pelvis which increased, all point in the same direction.
CASE II. S. H. age 61, unmarried.

This woman was admitted in March 1899. She then complained of oppression in the chest and swelling of the feet. The report says that she was very thin, the muscles of the upper extremities being very much wasted. Her gait was feeble, she kept her left leg partly flexed at the knee and supported the thigh with her hand. Her steps were short and her weight was lent principally on the right limb. There was flat foot which was specially marked on the left, and on examination there was slight rigidity of the left knee-joint. Tapping the rectus tendon produced several jerky contractions of the whole lower limb and also of the left arm. The left grasp was weaker than the right and there was slight flattening of the naso-labial fold. There was increase of the heart's dulness, a mitral systolic murmur and atheroma of the radial vessels.

History. Patient said that she had a shock when 33 years of age which produced unconsciousness, and that she was insensible for several days. When she recovered consciousness she found that she was unable to move but that gradually "power came back all over her body." She did not return to her work as a weaver for three months, but from that time till a
short time before coming to Hospital she worked more or less regularly. The onset of weakness in her legs was gradual for a few months before admission. Her Mother corroborated the above and added that she had always been delicate and nervous since the attack when she was 33.

The family history was satisfactory.

When examined in November 1900 the patient was bedridden. She complained of pain in the right arm where there was a nodular thickening on the ulna at the junction of the upper and middle thirds. A similar though smaller node was observed on the left ulna, and several could be felt on the left tibia.

Patient said she had only noticed the swelling on her right arm lately but that the pain had troubled her for months. On testing the muscle reflexes of the arms the extensor muscles of the right hand alone gave response. There was great wasting of the thigh and calf muscles especially of the left limb and coarse tremors were observed when it was moved. The skin over the front of the legs was glazed.

From this time the disease made steady progress. In May 1901 she had slight gastric disturbance and in June she complained of great pain over the upper part of the chest and developed broncho-pneumonia. From this she recovered but her mind appeared to be
affected. Marked broadening of the finger tips was observed and both bones of the right forearm began to bend at the junction of the upper and middle thirds, with tenderness and increase of the thickening already noted. The flexibility was such that the arm could be fairly well straightened. About two inches from the lower end of the right radius marked thickening was observed. Splints were applied but as they did no good and caused the patient discomfort they were abandoned. Both clavicles began to bend and appeared as if they were incompletely fractured, being bent acutely between the outer and middle thirds, the direction being upwards and backwards; and within a fortnight thickening was noted in the inner and middle third of the left.

There were incomplete fractures of the upper ribs on both sides and all of these bones were soft and easily bent; the ensiform was also soft and pliable. The knee jerks were present, the left being slightly increased. The left tibia appeared to be bending. The patient was given

\[ \text{R Syr: Calci Lactophos: } \]
\[ \text{Ol: Morrh:} \]
\[ \text{Liq: Calcis.} \]

\[ \text{Sig: } \]
\[ \text{t.i.d.-} \]
Towards the end of September there was swelling and oedema of the left foot and ankle. The urine was again examined. This had not been done since the date of the patient's admission when the note on the case sheet was as follows:

"Pale straw, sp: gr: 1015, Neutral. Deposit, (which is not described) Albumen absent."

Patient never complained of renal or bladder trouble.

Examination of urine. Odour of stale shellfish, pale amber colour, mucin cloud at bottom of glass. No albumen, sugar, bile or blood. Deposit by microscope showed numerous rounded fatty cells and fatty debris, a few normal nucleated renal cells, a few fatty casts, numerous distinctly and actively mobile segmented (or sporulating) bacilli showing undulating and gliding movements. Professor Sutherland, Professor of Pathology, St. Andrews University, kindly examined these organisms and reported as follows. - "Mobile bacilli are larger and longer than B. coli and give a different appearance in culture. They are decolourized by Gram. They have not the character of any pathological organism save probably accidental or putrifactive." Seven months afterwards, shortly before patient's death, a specimen of
her urine was obtained by catheter and these microorganisms were abundant in the pellicle on the surface, they were not found in the urine below, but were plentiful in the deposit at the bottom of the glass.

In October she had vomiting; this was the second attack and was followed by a third during the same month. The vomited matter was dark and tarry looking. From then till May she was rather better, though she had diarrhoea occasionally.

In November the second and third phalanges of the second and third fingers of the left hand softened and could be bent from side to side. The deformity of the thorax also became more marked. Owing to the flexibility of the clavicles the upper part of the chest was contracted and narrowed; there was scoliosis of the dorsal vertebrae and the margins of the scapulae seemed to cause indenting of the ribs but no fracture. The thorax was sunk into the abdomen so that in May 1902 it was noted, "there is practically no space between the ribs and the iliac crests."

On the 5th of May patient again vomited black coffee ground matter, and continued to do so at intervals until she died. She also had diarrhoea,
the motions being mixed with blood, and mucus in shreds and pieces. These symptoms increased. She grew gradually weaker and died May 12th 1902.

Shortly before her death the blood was examined and was found to be normal as to Haemoglobin and the number and shape of the corpuscles. The vomit when examined showed the presence of free HCl.

Autopsy. The deformities already described were noted. Beyond slight hyperaemia of the lungs there was nothing worthy of special note in the thoracic organs.

Abdomen.—Stomach showed hyperaemia of the mucous-membrane and evidence of catarrh, and contained dark coffee ground matter. The intestines showed here and there marked congestion with evidence of fine haemorrhages. In the lower part of the large intestine on the unattached border were numerous pouchings or diverticulae, capable of containing a small marble. These areas were deeply congested.

The other organs, with the exception of the kidneys, showed no abnormality.

The right kidney was small and granular, the capsule being adherent in places.
On section the pelvis contained a calculus, irregular in outline, about 1 inch long by \( \frac{1}{4} \) to \( \frac{1}{2} \) inch at the broadest part.

There was also a stone in one of the calices about the size of a split pea. The left kidney was not granular; on section it also was found to contain a phosphatic calculus but of much smaller size than the first. Further examination showed that the largest stone was principally composed of calcium phosphate, the inner portion being oxalate. The smaller stone was oxalate of calcium. The stone in the left kidney was a phosphatic calculus.

Supra renals were normal.

Pelvis. The bladder was somewhat larger than normal. The mucous membrane had a pale greenish grey appearance and was hyperaemic in patches while all over the surface were small black specks and rings about \( \frac{1}{4} \) to \( \frac{1}{2} \) inch apart. The size is best shown in the accompanying diagram. These specks could be scraped off with the upper layer of epithelium. It was hoped that an attempt might have been made to grow cultures from the scrapings, but
circumstances made this impossible. The uterus and ovaries were normal though not showing such advanced atrophy as is sometimes seen in old age.

Osseous System. The whole skeleton showed evidence of the disease. The sternum was soft and easily cut, the ribs could be bent and showed numerous fractures and nodular thickenings. There was deformity of the vertebral column both in the lateral and in the antero-posterior directions. The brim of the pelvis was triradiate, the sacrum was displaced almost directly backwards and curved forwards, having much the appearance of a hook.

The diagrams, which are copied from Fehlings' paper on Osteomalacia in Arch: f. Gyn: Berlin 1895 exactly represent these deformities. See also photographs I and II. page 145.

These bones and those of the vertebrae and ribs could be easily cut with a scalpel. In some places they were so soft that the least pressure broke through the thin paper-like shell and great care had to be taken in preparing them. In fixing the bones together—no difficulty was experienced in pushing a soft wire through them in any direction, the feeling being
much that of pushing it through rotten wood, and wherever pieces were cut or broken off the trabeculae were seen forming a coarse fenestration, the spaces filled with pulpy-looking very fatty marrow. The porous appearance of the pubic and ischial bones is well seen in Fig: 1, page 115.

Of the long bones, the clavicles and bones of the forearms showed the greatest degree of deformity. (See Fig: 4, page 116.), while Fig: 3, page 116, gives a clearer idea of the degenerative changes in the femora than any description can do. In the shaft there was a thin outer crust of bone not yet decalcified.

Remarks. The points of special interest in this case are (1) The association of osteomalacia with slight hemiplegia and the question as to whether this nerve lesion had to do with the changes in the osseous system. (2) This woman had never been pregnant and yet the most marked deformity and greatest progress of the disease were shown in the pelvic bones which are not usually the first to be affected in senile osteomalacia. (3) The presence of phosphatic calculi in the kidneys. (4) The occurrence of diarrhoea with slight intestinal and gastric haemorrhages. (5) The broadening of the finger tips which appears similar to a deformity of the third phalanges noted by Charcot as being frequently present in these cases.
CASE III. M. Mc. aged 67, unmarried, was admitted to Hospital in February 1899. The notes on the case sheet record that this patient had been in hospital for some months, two years previously, suffering from chronic rheumatism in the right knee. The pain and stiffness were still present in this joint. Beyond this she complained only of general debility, and on examination nothing abnormal was made out. The systems were healthy and there was no paralysis. The urine was straw coloured, Sp: gr: 1027, reaction alkaline, there was a slight white deposit and a trace of albumen.

On July 7th, it is noted that the legs were both flexed, the left very acutely, the right in a lesser degree. The muscles of both thighs and of both calves were very much wasted. The plantar reflex on the right side gave an extensor response. On the left side no plantar reflex could be elicited. The sensory functions were apparently unaltered. She complained greatly of pain in the left knee and the left shoulder.

In July 1900 it is reported on the case sheet that the patient was in a lamentable condition. The left knee was completely flexed. She complained of pain in the left leg and chest, and also in the left hand. This she said had been bad since "the shock" but she could not say when that had taken place. Her
breathing was rapid. She had congestion at the base of the right lung, and was sweating profusely. In September the contractures were increased, as was the pain, which she said was all over, but especially bad in the left leg, side and shoulder. Her mind remained clear, and from then till she died on November 29th, she had constant and increasing pain.

The post-mortem report describes the contractures thus: the right thigh is flexed on the abdomen and the leg on the thigh. The left knee is just under the axilla and the left leg lies closely on the thigh throughout. The bones are very brittle and fractured when the limbs were straightened. The thorax is deformed. There is marked inward bulging of the lateral regions. The ribs show thickenings on their internal aspects; this is most marked on the first to the seventh on the right, and in the second to the tenth on the left side. There are nodular thickenings at the vertebral attachments as if from old fractures. There is a sigmoid curvature of the spine to the left, in the upper dorsal, to the right, in the lower dorsal and lumbar regions.
The bones of the spine, skull and ribs are very soft, the spinous processes are easily cut with scissors. The membrane of the bones is cancelled. The ribs show abundant chocolate coloured marrow. The brain shows an old lesion. There is an area of softening, in colour red and yellow. It is situated in the region of the optic thalamus and encroaches on the internal capsule. It measures 1 inch by \( \frac{1}{8} \) inch and is \( \frac{1}{8} \) inch in depth. The vessels supplying this side of the brain are atheromatous. The further examination of the organs shows nothing of special interest.

Remarks. (1) The softening of the bones was in this case associated with a cerebral lesion of which there were certainly no distinct symptoms on admission, the only sign of a cord lesion being the extensor response to stimulation of the plantar reflex. (2) In July 1900 the case was diagnosed as hemiplegia and nothing further was sought, to account for the pain which far exceeded that, associated with ordinary paralytic contractures. (3) The pelvic bones were not markedly affected, which is in accordance with no history of pregnancy. (4) The white deposit in an alkaline urine suggests the presence of earthy phosphates.
CASE IV. H. M. aged 80, married.

This old woman had been in the Poorhouse for several years before she was admitted to Hospital in December 1900. When first seen she was suffering from a slight attack of bronchitis. The heart was enlarged and there was a faint systolic murmur in the mitral area. She was a feeble old woman but was fit to be discharged from Hospital in May 1901. From this time she was under more or less constant observation either in the Poorhouse or Hospital yet the true nature of her illness was not recognized until six weeks before she died. When asked as to the onset of her illness the patient was perfectly definite in dating it from a fall three years before, saying that she never had "the pains" from which she now suffered before that. She said that she had fallen on her face and that her shoulder was broken, but no sign of the injury remained.

She had been married at eighteen and had had eight pregnancies. All were healthy and her labours in every way normal. Menstruation was irregular when she was a girl and she could give no data regarding the menopause. She complained continually of pain in her back and sides especially in the left and she had difficulty in walking. There was marked
Kyphosis in the upper dorsal region, the thorax was narrowed laterally and greatly increased in the antero-posterior diameter. During the last months the weakness and pain increased and she frequently complained of a feeling of suffocation and said she could not breathe. During her last illness she usually lay on her left side and generally with her knees drawn up. She complained of great pain and tenderness when being moved or examined. The kyphosis increased, the head was sunk between the shoulders and bent towards the prominent sternum. There was narrowing of the thorax between the shoulders which seemed to fall towards each other. The lower ribs were bent inwards at the sides, the intercostal spaces were narrowed and the distance between the ribs and the iliac crests was greatly diminished. Figure 5, page 117, shows the deformity to some extent. There was what appeared to be a fatty tumour on the left side over the lower ribs in the posterior axillary line. When examined post-mortem it was found to consist of muscle-tissue, which is interesting, as the patient said it was the result of a strain. There was slight flattening of the ilia and prominence of the pubis. The patient could abduct the
thighs though not to the full extent. Examined per vaginum there was narrowing between the rami of the pubis, and the vagina, uterus and cervix were found to be greatly atrophied. There was no deformity of the lower limbs save a thickening on the lower third of the right tibia which patient said was the result of an accident when she was a comparatively young woman. The knee jerk could not be elicited on either side. There was no ankle clonus and the plantar reflexes were normal. Sensation was unimpaired. Beyond the emaciation and breathlessness, pain and tenderness which was specially marked when the chest was examined or pressure made over the ribs, this patient had no symptoms and died of asthenia March 12th 1903.

The urine was frequently examined by the charge nurse and only once showed the presence of phosphates, but the examination was not very reliable and arrangements were being made to have it systematically analysed when the patient died.

The blood was carefully examined. The Haemoglobin was over 97 per cent, and the red blood corpuscles normal in number and size. Of the white corpuscles the polymorphonuclear equalled 69.5 per cent, the lymphocytes 25.5 per cent, the large hyaline 4 per cent, and the eosinophiles 1 per cent.
Post-mortem examination was made 24 hours after death. The lateral deformities of the thorax and bulging inwards of the ribs were marked as was the prominence of the sternum. The ribs could easily be bent inwards, and had a certain amount of elasticity, but fractured if pushed too far. The clavicles were bent backwards and upwards and appeared less resistant than normal but were not removed. The pelvis (see Fig: below) which was removed along with the heads and upper parts of the femora, is heart shaped. The bones showed softening in places. Here and there through the ilia, were, what at first sight appeared to be thickenings in the bone, but which were due to separation of the bony surfaces, the spaces between being filled with spongy-like material. The sacrum was pushed backwards and unduly concave. Both pelvis and sacrum resembled the accompanying outlines which are copied from Fehling's paper.

Fig. 1.

The periosteum was thickened and the most striking thing in dissecting these bones was the abnormal blood supply.

All the vessels supplying the bones and periosteum, and in the tissues attached to the bones, were engorged with dark blood. The openings in the bones
for the nutrient vessels were larger than normal and in some places like stomata with everted lips.

The femora showed no marked change; the bones were hard, though the shell was thin; and the medullary canal was large in proportion. The marrow was greyish in colour and of the consistency of thick gruel. The ribs were flexible and cut easily with a scalpel and were full of reddish brown marrow. Parts of two were removed.

The left side of the heart was greatly hypertrophied. The valves showed no lesion and the lower part of the ascending aorta which alone was examined, was free from atheroma and calcification. In contrast to this, the lower part of the abdominal aorta and the iliac vessels were full of calcareous plates. The left kidney was hydropnephrotic, the kidney tissue being almost entirely replaced by large simple cysts, the largest being somewhat bigger than a duck's egg. The ureter as it left the pelvis was dilated. There were no calculi. The right kidney was normal. The uterus and ovaries showed senile atrophy, the latter to an extreme degree. The other organs presented nothing remarkable. The head was not examined.

Remarks. The disease began in extreme old age and the patient ascribed its onset to a fall.
CASE V. M. B., aged 62, married, nullipara. This woman was an inmate of the West Poorhouse for five years. During the greater part of that time, she was confined to bed and complained of general weakness rather than of acute pain. Her skin was darkly pigmented and there were also pigmented areas in the mucous membrane of the mouth. She was considered to be suffering from Addison's Disease and was treated with Adrenal extract, but did not improve. She died of broncho-pneumonia early in April of this year (1903).

Post-mortem Examination. The description of the external appearance is as follows:- The stature is short and there is great emaciation. There is a generalised brownish yellow pigmentation of the skin. There is marked deformity of the thorax and vertebral column. The former is increased in the antero-posterior diameters and the lateral margins are flattened in their upper half and concave in their lower. The whole framework is elastic. Individual ribs from the fifth to the ninth are deformed, all are unduly elastic, friable and soft. The bone is easily cut with an ordinary pair of scissors. There is an extreme degree of spinal curvature; the most pronounced deformity being in the lower dorsal and lumbar regions. Here there is marked convexity to the left, the bodies of the lower lumbar vertebrae
actually being in contact with the posterior part of the left iliac crest. In the upper part of the spine there are marked compensatory curves. The vertebrae are unduly soft, the pelvis is not markedly deformed, the bones are extremely soft, it being easy to cut out wedges with a knife. The clavicles are unduly bent, but there is no deformity of the long bones.

The Heart shows marked fatty degeneration of the muscle.

The Kidneys are small and hyperaemic.

The Adrenals are normal and there is no matting round the solar plexus. Stomach mucous membrane showed evidence of catarrh. The intestines are normal the mesentery and omentum are almost devoid of fat.

The ovaries are somewhat small, but the structure appears normal. The uterus shows two small myomata on its anterior surface. The other organs present nothing noteworthy.
CASE VI.  Mrs A.  age 36. (Fig. 6 page 14)

A native of the North of Scotland and one of a family of fourteen. Menstruation began when she was 15 and was regular. She was healthy as a girl and married when she was 20. Her surroundings had always been fairly comfortable and she had been able to procure good food. She had had 10 full-time living children, 1. premature birth and 5 abortions, 3 of these having been induced on account of the disease. On two of these occasions, in 1894 and in 1896, she was an inmate of the Edinburgh Royal Infirmary and was there advised to have her ovaries removed. When first seen by Dr. Kynoch, she complained of difficulty in walking and in moving, and of pains through her body, which she dated from a confinement 7 years before.

On examination the ribs and pelvis were found to be very tender to pressure. Her gait was waddling and she had great difficulty in raising her feet from the ground. There was marked lordosis in the lumbar region, also narrowing of the lower intercostal spaces and the thorax had so sunk that there was little space left between the ribs and the iliac crests. She had lost considerably in height during the preceding seven years. As she lay in bed the thighs
were strongly adducted and flexed. The knee jerk and abdominal reflexes were increased, but ankle clonus was present but not marked. There was double dislocation of the hips on to the ilia, but no external sign of pelvic contracture, nor was the pelvis unduly prominent. There was no pushing inwards of the pelvic wall nor diminution of the inter-trochanteric measurement.

The urine at no time showed any great increase of phosphates.

The Patient was treated with Cod Liver Oil, Chemical Food and was given Phosphorus in the form of Oil of Phosphorus; in almond oil beginning with 3 and increasing to 5 minims daily. After four months of this treatment she was able to go about and do her household work. About a year afterwards she became pregnant but aborted at the third month. During pregnancy she was confined to bed on account of severe pain and tenderness of the bones, greatly increased by pressure and necessitating large doses of morphia. After abortion the pains began to diminish and she was removed to the Dundee Royal Infirmary for further treatment. While there she had attacks of vomiting which seemed to be associated with a large ventral hernia. This was operated upon by Professor McEwan and at the same time the ovaries were removed. The left was
closely bound down by adhesions to the pelvic wall and was somewhat difficult to remove. Microscopic examination showed considerable thickening of the walls of the blood vessels, of the nature which Fehling considers characteristic of this disease. For the first four weeks, the pain on pressure continued, but three and a half months after the operation they had completely ceased and the patient was again able to resume her household duties.

It is now more than two years since this patient was operated upon. For some months after Professor Kynoch described the case, Mrs A. was seen from time to time, and her progress was continuous. She then left Dundee and in spite of numerous enquiries, it has been impossible to trace her.

Remarks. The points of special interest in this case are: (1) The pelvis showed practically no deformity, possibly owing to the dislocation of the hips. (2) That the spinal column was affected as shown by the patient's diminished height and by the sinking downwards of the thorax. Professor Kynoch in his notes refers to a similar case described by Latzko.
OSTEOMALACIA or MOLLITIES OSSUM.

is a disease, characterized as the name implies, by softening of the bones. It is usually accompanied by deformities and fractures and is due to decalcification and removal of the earthy constituents from various parts of the skeleton. It appears to have been known in early times. Dr. Ritchie of Edinburgh in his monograph on osteomalacia refers to the story of Gschuzius, an Arabian physician who was described as having no bones except in his hands. Since then cases have from time to time been recorded, but the older writers including Kilian, who first described the puerperal forms in 1857, Schwaagman, Rokitansky, and Beylard who wrote in 1852, appear to have drawn no distinct line between osteomalacia, osteoporosis, fragilitas ossium and rickets, some even considering them stages in the same disease. Moers-Muck first differentiated between osteomalacia and senile atrophy of the bones. Pommer considers they are perfectly distinct but that they may be found side by side in the same patient. Cornil and Ranvier under the heading of senile osteomalacia describe a rarefaction of the bones with an increase of the medullary spaces which are filled with marrow bearing a certain
resemblance to the marrow of osteomalacic bones, but they consider the condition rather that of a senile osteoporosis than of true osteomalacia. Councilman speaks of a senile form which should be distinguished from the true. In it the bones became thin and fragile from absorption and are easily fractured, but the yielding character is not present, and the pelvis is not affected. It attacks men and women equally. Fothergill also mentions this type, but the description seems to apply rather to fragilitas ossium than to osteomalacia. Charcot and Vulpian first recognized clinically the existence of bony softening in aged patients, and Paul Bouley in his treatise on osteomalacia in men and animals (quoted by Demange), while pointing out, that in these senile cases there was not the same tendency to steady progress and generalization through the skeleton which is characteristic of the disease in adults, there was yet such similarity between the symptoms in these and in true osteomalacia that we are bound to consider them two clinically different forms of the same malady. Demange made careful observations in two senile cases: one a woman, aged 61, in whom the disease had made rapid progress and whose pelvis showed typical deformity; the other, a man of 80, where the symptoms
were not so marked. In both he found anatomical and microscopic changes in the bones similar to those seen in adult cases. His conclusions are as follows: that true osteomalacia may develop in the aged as well as in adults; that the lesions are identical, and are perfectly distinct from the changes seen in osteoporosis and that they are principally localized in the vertebral column, the thorax and in the pelvis. Grajon arrives at the same conclusions, and states as his opinion that true osteomalacia in the aged is one and the same as that seen in pregnant women. In his monograph on senile osteomalacia he says that he was first led to study the disease by observing one or two patients in the Hospital Andral, whose symptoms were severe and obscure and did not seem satisfactorily accounted for by the supposed diagnosis. He has collected notes of 25 cases, in almost all of which the disease was verified post-mortem. Among these are included the two cases described by Demange, and also four which are fully recorded by Walch in the British Medical Journal 1891. These four cases occurred in Wakefield Asylum and in many respects resembled those seen by the writer. All the patients were over 50 years of age; in one the disease advanced very rapidly, in all the symptoms were well
marked. In three the disease was verified post-mortem, the fourth being alive when the cases were recorded.

Durham, in his list of 145 cases, mentions that 50 were over 50 years of age. Lane gives the history of an old woman who had softening of the bones and says that he has noted softening of the ribs coincident with loss of teeth in the aged, and Von Velitz in 9 non-senile cases, noted caries of the teeth in 6. Von Spath operated on a woman of 70, and Bleuler and Sternberg each records improvement under phosphorus treatment in senile cases. Gelpke, Gull, Raschkes, Schlichthaar and others have all reported one or more cases and Rindfleisch goes as far as to suggest that osteomalacia is, in all cases, a premature senile change.

As already mentioned, the older writers also confused osteomalacia with rickets and Trousseau, following the classification of Stanski, who considered osteomalacia and rickets to be stages in the same disease, described the case of a woman of 66 who had softening of the bones, as suffering from "senile rickets." He said that osteomalacia was simply rickets in the adult or aged. Lobstein, Ziegler and Birch-Hirschfeld held that they were two distinct diseases,
and their view is generally accepted, but Cohnheim,\(^{(24)}\) Pommer and Kassowitz consider that in osteomalacia there is a process somewhat akin to that seen in rickets: that in the former there is, along with the process of resorption, a laying down of new bone which is poor in lime salts and that the changes are principally due to this.

With regard to the occurrence of osteomalacia in childhood, considerable discussion has arisen as to whether the cases recorded were not rather severe and advanced rickets; Vierordt\(^{(36)}\), among others, considering that osteomalacia had not been demonstrated in a child. There appears however to be sufficient evidence to warrant our coming to the conclusion that the disease may develop in early life. Rehn\(^{(27)}\) of Frankfort in 1877 described a case which occurred in a female child of 16 months old, where osteomalacic changes were present in some of the bones and rachitic in others. These bones were examined by Von Recklinghausen who found similar changes in the bones of an infant of 13 months in the Frankfort Museum. His has lately published the results of a series of clinical observations in the case of a child 2\(\frac{1}{2}\) years of age, where he believes the changes in the skeleton to be of true osteomalacic origin. Siegert gives a list of three
cases which he found in literature where the disease occurred in childhood and was verified post-mortem, and to these he adds one of his own aged 15. He holds that although these cases are rarely seen, still osteomalacia may exist before or at the period of full bony formation of the skeleton.

Dressbach records a case where Caesarian section was performed on a woman aged 37, but where the disease had begun at 8 years of age. Davies Colley gives the history of a girl who was first noticed to walk badly when she was 9, after which the disease progressed steadily in spite of treatment. In this case, among other symptoms, he noticed swellings on the lower jaw which increased and softened for months before fractures took place. The post-mortem examination in this case in some ways suggested advanced rickets but Colley argues in favour of osteomalacia. During last year Achmatieu and Postolowski each recorded a case of the disease in a child.

Statistics have proved that osteomalacia is most commonly seen in women, comparatively seldom in men, and the fact that the greatest number of recorded cases were in women between 20 and 30 years of age, during the period of active sexual life, and that the onset was frequently associated with child-bearing led to the belief that the disease was closely related to, if not dependent upon pregnancy. This
greatly tended to emphasize the idea that there was a distinct difference between the puerperal and senile forms of the disease. Ribbers\(^{(43)}\) and others have pointed out that in puerperal cases the disease begins in the pelvis, and in non-puerperal in the spine, but this alone is not sufficient foundation on which to base the argument that the pathology is different at different ages. Fehling\(^{(3)}\) found the pelvis affected in **nulliparae** and Grajon\(^{(44)}\) found these bones involved in eleven of his cases, two being men. Ritchie\(^{(2)}\) has reproduced in his monograph a photograph of two male pelves, in which the disease is well marked. Though few cases have been recorded of the disease occurring in men, there is yet a sufficient number to prove that osteomalacia is not restricted to the female sex. Siegert\(^{(28)}\) observed a case in a male child. Berner\(^{(45)}\) and Burgess\(^{(46)}\) have each described a case in men of 20. In the first the disease advanced rapidly and all remedies were useless. P. Berger\(^{(47)}\), Burani\(^{(48)}\), Kahan\(^{(49)}\), Moses\(^{(50)}\), Rigby\(^{(51)}\), Strauscheid\(^{(52)}\), Weismayr\(^{(53)}\), Ringel\(^{(54)}\) and others have published similar cases. We therefore conclude that osteomalacia while most common in adult life has been recognized in childhood, in youth and in old age - and in men as well as in women.
Symptoms and Progress. The onset is obscure, the usual complaint being of pain and lassitude. From first to last, pain is a constant symptom; it may be acute, but is generally of a dull aching character, and has frequently led to the disease being mistaken for chronic rheumatism. It may be localized in the sacrum and pelvis, or felt in the back and lower limbs, or described as "pains all over." The gait becomes waddling or rolling, the toes may be turned inwards, and owing to the difficulty in lifting the feet, the patient is apt to stumble. This is due to muscular weakness which is often accompanied by tremors, and in most cases by markedly diminished power of abducting the thighs. The knee jerk is usually increased and there may be ankle clonus. Rissmann in two cases, gives as the initial symptoms (1) hypersensitiveness of the epiphyses; (2) paresis of the upper thigh muscles, flexor and adductors, and later, a subjective feeling of weight in the legs with nocturnal pains and muscular tremors. Deformities become apparent; these vary in kind and degree according to the bones affected and to the stage of the illness. In pregnant women, where the disease usually begins in the pelvis, undue prominence of the pubis and increased lordosis will probably be observed, while in the senile, an
exaggeration of the kyphosis of age, often accompanied by scoliosis, marked prominence of the sternum, bending inwards or fracture of the ribs and sinking downwards of the head, commonly mark the progress of the illness. Fractures are of frequent occurrence.

As the disease advances, there is increasing tenderness in the bones, pressure especially on the ribs and pelvis causing great pain. Walking becomes more and more difficult until at last the patient becomes completely bedridden, and even movement of a limb or of the bedclothes occasions acute suffering.

Another most distressing symptom in the later stages is difficult respiration. The patient complains of inability to breathe, and a feeling of suffocation. Durham ascribes death in one of his cases to Asphyxia combined with weakness, the softened and deformed chest wall being no longer able to resist external pressure.

Diarrhoea of an intractable nature has been noted by several observers, including Grajon and Demange, as a frequent symptom, especially towards the end. Korczynski considers that the watery stools are probably due to the excess of sulphates which
are present in the intestines and faeces, and that an explanation of this excess might be discovered if careful estimation were made of the S. along with the Ca and P2O5 elimination in the urine and faeces.

We shall now consider the symptoms and deformities somewhat more in detail. The diminished power of abducting the thighs is, by some observers, including von Braun, held to be due to changes in the bones, that in consequence of the deformities, the origins and insertions of the muscles of the thighs are approximated, and their ability to act is thereby diminished - that it is due, rather to diminished power of the abductors, than to contraction of the adductors. Latzko, on the contrary, considers the adductor contraction characteristic of the disease, and lays weight on the pseudo-spinal paralysis. He observed the condition under anaesthesia, and found that the limbs could be abducted to a much greater degree, though not to the full normal extent. He therefore holds that the diminished capacity for movement is not entirely due to mechanical hindrance, but to active muscle opposition, and that the shortening of the adductors is the result of long continued inactivity. The remaining opposition under narcosis, he considers
due to the shallowing of the acetabulum and to changes in the angle of the neck of the femur, with shrinking of the capsule. If this be so, the pain caused by movement may account for the disuse of these muscles.

That there is more or less disturbance of the nervous system is shown by the excitability of the muscles. The increased knee jerk, the presence of ankle clonus, the involuntary jerking of a limb, and the frequent tremors, which are so commonly met with in osteomalacia cases, point to a nerve lesion. The tremors at times resemble those of insular sclerosis, for which the disease has occasionally been treated. Velitz, who found them present in half of his cases, considered they were probably due to involvement of the intervertebral ganglia. Sensation is not affected, except as regards the pain and tenderness. The insane have, by some writers, been believed to be more liable to the disease, but the cases recorded in asylum practice, have been far too few to justify our coming to this conclusion.

The disease may begin in any part of the skeleton, as in a case recorded by Allison, in a girl aged 19. The bones of the right leg were first affected, then the left, the pelvis not until ten
years afterwards, and the bones of the trunk still 
later, but, as already stated, it usually first 
appears in the pelvis in pregnant women, and if not 
arrested, attacks the spinal column and thorax, the 
long bones being the last to suffer. In non-pregnant 
or senile cases, and in men, it commonly begins in 
the spinal column and spreads to the ribs; the pelvis 
may be involved, but frequently escapes, while the 
long bones are seldom affected. Cases are on record 
where the bones of the skull became softened, but 
these are few.

The characteristic deformities in the pelvis 
are caused by the weight of the body, and the upward 
and inward pressure of the femora on the softened 
bones. In pregnancy, the deformity is probably 
increased by the altered centre of gravity, and the 
attitude of woman assumes. There is narrowing 
of the inter-trichanteric space and prominence of 
the symphysis pubis. The ratio of distance between 
the iliac crests and between the anterior-superior 
spines is increased; the sacrum is pushed back-
wards and doubled on itself, so that the tip of the 
coccyx approaches the promontory. The deformity 
may be of any degree; the brim may be heart-shaped, 
but in the typical osteomalacic pelvis, is triradiate,
and the outlet may be so narrowed, as in a case described by Fehling," as to make it seem almost impossible for conception to have taken place. Cases have been recorded where the bones were so soft as to allow of their being pushed aside by the accoucheur's hand, and a full time child being delivered.

As the deformities are caused by pressure and muscle strain, the softening of the vertebrae results in curvatures of the spinal column and a narrowing of the intercostal spaces with a general sinking of the thorax on to the plane of the iliac crests, while the ribs may be so easily bent that the arms have been described by one writer as lying by the sides as in a trough. Durham records a case in which the lower limbs, as shown by illustration, were twisted and distorted to an inconceivable degree, and could be bent in any direction. Chambers writes of a woman of 26, whose bones were so soft that she could be rolled up like an ill-stuffed bolster, and Grajon describes a man in whom the disease was far advanced, as being so deformed that he resembled a frog. On the other hand, a considerable degree of softening has been found post-mortem, where no deformity was apparent. Fractures are exceedingly common and the ease with which they occur is often
the first indication of the disease. Durham\textsuperscript{(15)} instances a case where fracture of the femur resulted from the patient slipping to the floor from the bed on which she was seated, while at a later stage the other femur gave way while the nurse was changing the bedclothes. Banks records a somewhat similar case in which nearly all the long bones fractured spontaneously, while the patient was lying in bed. Fractures of the ribs are frequent. Renard\textsuperscript{(61)} in one case, counted 80 in the ribs alone, but in this and other cases quoted by Beylard, the question of senile atrophy has to be remembered. Reparative action is slow and imperfect, and in many instances there is no union. Rindfleisch considered union did not take place, or only imperfectly. Ranvier\textsuperscript{(63)} believed it only occurred where the osteomalacic process was undergoing cure. Pommier\textsuperscript{(6)} and Volkmann\textsuperscript{(62)} hold opposite views, believing that normal union does occur.

Göbel found osteomalacic bones were in some cases faintly seen by Rontgen Rays, in others not at all. P. Berger\textsuperscript{(47)} also found them transparent.

Kidneys. As might be expected when it was understood that in osteomalacia there is a disappearance of lime salts, attention was directed to the kidneys as the organs by which they would be eliminated. The urine has therefore been carefully
analysed by many observers with varying results. Neumann, in 1894, published a paper in which he summarized the observations of 29 clinicians including Solly, Jones, McIntyre, Leitzmann, Collineau, Fingelburg, Durham, Weber, Rowley, who all found the excretion of Lime Salts increased. Kier found the increase 10 times in excess of the normal. Schramm found it increased in early cases. Collineau, Dermarquay, Sommeiler, Roloff, Senator, Ascoli, Schultz, Allison, Schramm, Wulff, Höxter, Schützenberger and Truzzi noted little change or diminished excretion and the conclusion arrived at was, that the excretion of Ca. and Mg. salts varied according to the stage of the disease. The alkaline as well as the earthy phosphates are at times in excess and at times diminished. Fehling made careful determinations but found no constant result. In two cases he found the excretion of CaO and P₂O₅ less, and in a series of more complete examinations made before and after oophorectomy he found in two cases there was increased loss of lime salts after the operation. None of these observers had however considered the amount of Ca. P₂O₅ or of N. in the ingested food or the amount excreted in the faeces. This has been done by Neumann, Von Limbeck, Robin and Binet, Hie and Korczynski. Von Limbeck made examination in one
case and found the total Ca O excretion in six days was 2.6 gm: in excess of that taken in the food. Robin and Binet who examined Paul Berger's case found the total excretion of lime salts greatly increased, while that of P₂O₅ was lessened. In a case recorded by Senator the Ca O and P₂O₅ ratio was normal.

The observations made by Neumann, His and Korczynski are most interesting, and an abstract from their tables will be found on Page 118. While these examinations show, as is to be expected, a difference in the elimination of Ca, Mg, P₂O₅ and N. in the different cases, and also a variation in individual cases during the different periods and even during the same period, there are yet certain similarities emphasized which appear to be of special significance in this disease. Ca O and P₂O₅ are excreted in greater quantity during the progressive than during the healing stage; the normal ratio of the excretion of P₂O₅ in the urine and faeces is disturbed; and in some instances the ratio of Ca O to P₂O₅ is also abnormal.

*In health, with a mixed diet 85% and with a meat diet 95% of the excreted P₂O₅ appears in the urine, the rest in the faeces. Of Ca O. in health, more is excreted in the faeces than in the urine.*

Korczynski.
In 1895 Neumann first made a careful series of examinations in an advanced case of a woman aged 37 who came under observation six weeks after her ninth confinement. She was carefully dieted and the Ca. Mg. \( \text{P}_2\text{O}_5 \) determined in the food ingested, also in the urine and faeces, during two periods each of seven days. The first began nine days after admission, the second a month later after improvement was established. During each of these periods more Ca O was injected than was excreted, there was therefore retention of lime salts by the system. During the first period more Mg: was excreted than was ingested, but during the second period less was excreted than was taken - there was, therefore, a balance in favour of the patient during the second period. Of \( \text{P}_2\text{O}_5 \), during the first period more was lost than was ingested, there was therefore a negative balance, and the normal relation of the quantity excreted by the urine and faeces was disturbed, the percentage in the faeces being increased. During the second period, there was a retention of \( \text{P}_2\text{O}_5 \) and the ratio of elimination between urine and faeces was normal. In 1896 Neumann again made a series of examinations in three cases. The examinations were made for periods, each of five days with the exception
of Case II, when the onset of pneumonia necessitated cutting short the first examination at four days, an average being taken and the estimation calculated for five days. In each case the examinations were made before operation and again after. In Case I, two examinations were made, in Case II, three, and in Case III, four.

Case I. Patient aged 36. VI.- para and an early case. Two examinations were made, the first before, the second after hysterectomy. The excretion of Ca O was in excess of that ingested during the first period, but the balance rose to 5.78 grm: during the second, in favour of the patient. There was also a slight retention of Mg O during this period while there had been a loss during the first. P2O5 showed a negative balance of 6.00 in the first, which changed to a positive balance of 6.31 in the second period, and the ratio of the quantity in urine and faeces became more normal. The elimination of N which was markedly in excess of the amount ingested during the first period, showed a positive balance in the second. In Case II, aged 36, a IV.- para and an advanced case, examinations were made during three periods, twice before operation,
the second of these being after Chloroform narcosis, and the third after castration. The examinations showed a slight retention of Ca O in each period. The Mg. O. balance was negative in each period though less markedly so during the last. P₂O₅, though it showed on each occasion a balance in favour of the patient, fell from 4.09 grm: which were retained during the first period to 3.20 in the second, and to 1.56 in the third and along with this the elimination of N greatly increased. During the first period there was a negative balance of 0.17, which increased to 6.88 in the second and to 9.56 in the third period. This seems to point to great tissue waste. The examinations were made too long after the attack of pneumonia to be associated with it.

In Case III. four examinations were made, two at an early period, the third shortly before, and the fourth after hysterectomy. The patient was aged 34 a IX - para and pregnant. In this case, while Ca O balance was positive on each occasion, it yet showed a steady fall from 3.9 in the first to 1.9 in the fourth period. Mg O on the contrary steadily increased in favour of retention. The elimination of P₂O₅ varied. In the two earlier examinations it
showed a negative balance of 11.54 in the first which became a positive balance of 10.34 in the second period. In the examination made before operation it showed a positive balance of 1.44 which rose to 3.37 after hysterectomy. These variations are striking and suggest that other factors than the generative organs may influence this disease. N. was not determined in the two first examinations, but the negative balance of 1.17 before, was changed to 8.89 of a positive balance after the operation.

His carried out his examinations in the case of a child of 2½ years of age in whom he had diagnosed osteomalacia. He examined his case during three periods; the first of eleven days, the second of ten days during which time 1 mg. of phosphorous in oil was given daily in addition to constant mixed diet, while during the third period of seven days no phosphorous was given. During the first period, CaO was excreted in excess of the quantity ingested; during the second, there was retention, while during the third the elimination was greater than during the first. The P₂O₅, though it showed a positive balance in each period, steadily decreased from 4.43 to 1.58. His observed that the proportion of Ca O varied greatly in the faeces, as well as according to
the amount of faeces, and he also lays stress on the occasional disturbance of the Ca O and P$_2$O$_5$ ratio, and says that the possible explanation may be that, in spite of the progressive loss of lime by the bones, a formation of albumen may occur in whose production P$_2$O$_5$ is required.

Korczyński made his observations in two cases; the first, a woman of 41 years of age, a VI-para who had suffered for 5 years. The second was aged 20, and had never been pregnant. The examinations were carried out in the first case for five periods, and in the second for four periods, each of five days. In both cases careful estimation of the Ca O, P$_2$O$_5$ and N in the food was made. During the first period in each case, a diet rich in nitrogen was given, during the second, begetable diet, while during the succeeding periods, ordinary mixed diet was given, with, in addition during the last period, 6-9 ovarian tabloids, (Burrough & Wellcome) each equal to .25 grm.

In Case I. the Ca O balance shows a steady fall during each period, from a slight positive balance in the first, to a negative in the last. The P$_2$O$_5$ shows great variations in the different periods, though the balance is always positive; the figures
being 6.32 in the first; 1.77 in the second; 0.01 in the third; 4.06 in the fourth and 0.53 in the fifth period. The N also varied considerably though there is always retention. During the first period with meat diet, the balance was 8.8 in favour of the patient, but it fell during the second to 1.53, and rose in the third period to 1.53. In this case the normal ratio of $P_2O_5$ in the urine and faeces was disturbed, far more appearing in the faeces than in the urine. The Ca O. excretion in the urine and faeces remained normal to each other, most being in the faeces.

In Case II. the diet was similar, ovarian tab- 
loids being given the last period. The Ca O balance was negative during the first, second, and fourth periods, while it showed a slight balance in favour of retention during the third. The $P_2O_5$ showed, as in the first case, a positive balance with considerable variations, being 1.65 in the first, 0.69 in the second, 4.75 in the third and 3.31 in the fourth period. The amount lost in the urine during the second period was under 50 per cent, while it was increased in the faeces. With regard to the N. it showed a slight positive balance during the first two periods and a slight negative during the third and
fourth. In discussing the elimination of $P_2O_5$ by the kidneys, (which in his second case varied from 50 to 70 per cent,) Korczynski says that a similar condition is seen in plant-eaters where, by reason of the large number of bases ingested, of which Ca. forms a large proportion, the $P_2O_5$ is combined and is eliminated in the faeces. He says that this has also been observed in men on a strictly vegetable diet, and argues, that if, with increased ingestion of alkalies especially of Ca, more $P_2O_5$ is excreted by the faeces, the same should hold good if less $P_2O_5$ be ingested. He therefore concludes that the disturbance of the ratio is the fault of the relative $P_2O_5$ deficiency. Though qualitatively the elimination of CaO is normal, most being separated in the faeces, the total quantity may vary considerably. In Case I, during the first two periods, the excretion was almost normal in the urine, while in the last days of the third and in the fourth and fifth periods it sank to almost half of the normal physiological value. In the second case the increased excretion of CaO was coincident with the increase of $P_2O_5$ in the faeces and the correspondingly low percentage found in the urine. The following is a short summary of Korczynski's conclusions:
1. During the progress of the disease the consumption and elimination of the N.-containing bodies goes on unequally.

2. The amount excreted varies from day to day during the periods, and also the periods vary between themselves.

3. The average excretion of Uric Acid is within physiological limits, though on some days it is markedly increased.

4. In cases which are not too far advanced, which are progressing slowly and in which there is not great cachexia there is retention of P₂O₅.

5. The excretion of P₂O₅ differs from normal in that more is excreted in the faeces, considerably less in the urine.

6. Ca O is markedly increased in the faeces and varies in the urine, at times being greatly below normal.

7. The total excretion of Ca O is very often in excess of that ingested and there is therefore a negative balance. In these circumstances the amount excreted in the urine is lessened, while that in the faeces is increased. This usually follows the increased separation of P₂O₅ in the faeces along with its marked diminution in the urine.

The elimination of N. has by most writers been
considered in terms of urea, and the results of the examinations show great variations in the amount of its excretion, though, as Neumann has pointed out, the stage of the illness during which the observations were made has not always been recorded. Latzko and Warschauer found the excretion of urea increased, Schrumm in a severe case found it normal. Fehling, in his cases, found it variable, but more frequently observations have shown it to be diminished. Barnes from an examination of Letheby's cases considered the excretion lessened; Wulff in a male case found an absolute diminution; Höxter found the amount lessened; in one severe case, after treatment for a considerable time with Calcium Phosphate, the elimination showed an increase though never up to the normal standard. Chambers, in an advanced case in which the muscles were almost entirely degenerated, found marked diminution of urea excretion and Truzzi, who took N as the basis of his observations, considered the nutritive changes, in women suffering from osteomalacia to be very low.

Albumoses were found in the urine by Kuhne, Raschke, and Ascoli, each of whom record a case; Langendorff and Mommson found traces while in the cases examined by Fleischer and Von Jaksch they were
absent. Kahler considers they are only found where osteomalacia is associated with myelomata; but Jochmann and Schrumm who found them in the urine, of an osteomalacic patient of 36 regard their presence as of no value for differential diagnosis between osteomalacia and sarcoma.

Petrone found Nitrites in the urine of one patient in whose blood he found the nitrifying organism of Winogradsky. Other observers have discovered nitrites in osteomalacic patients but say that they are at times present in the urine of those suffering from other diseases.

The presence of Lactic Acid was demonstrated in the urine by O. Weber, Moers-Muck, Langendorff, Hermann and by Ascoli in one case; Hofmann did not find it definitely, while Schmutziger, Heuss, Höxter and Warschauer did not find it at all.

**Blood.** The blood has been carefully examined during the last few years, but as in the other systems, no constant pathological variation has been recognized or one which has not also been observed in other diseases. Von Jaksch, Winckel and Eisenhart noted diminished alkalinity but Von Lübeck and many other observers have found the reaction to be normal as regards Alkalescence. When we consider that
diminished alkalinity has been observed in such varied diseases as Cholera, Diabetes, Rheumatism and Gout, its presence cannot be regarded as of diagnostic value, though Eisenhart\(^\text{90}\) considers that puerperal osteomalacia is closely related to it. In one case which he observed closely and where the diminished alkalinity was greatly marked, he found that with recovery it rose to normal.

The haemoglobin percentage appears to be fairly normal, though Seeligmann\(^6\) records a case which, at the time of operation (oophorectomy), it was reduced to 41\%, after that, it rose to 49\%, to 72\% and as the improvement was continued, to over 100\% and the red blood corpuscles were also above normal in number while the white were diminished. He held there is a casual relation between the blood and the bones.

Neusser\(^\text{62}\) noted an increase in eosinophile cells, and the presence of myelocytes, except in a senile case, where there was no increase of the former but where the latter were present. Ascoli\(^\text{66}\), Ritchie\(^3\) and Cabot\(^\text{93}\) confirm Neusser in the increase of eosinophile and Ritchie found the young leucocytes more numerous than normal. Fehling\(^1\), Chrobak\(^\text{94}\) and Sternberg\(^\text{95}\) failed to find any increase of the eosinophiles. Tschistowitsch\(^\text{65}\) found the lymphocytes and mononuclear
leucocytes increased. He also found myelocytes and the red corpuscles poor in haemoglobin, in this resembling the case noted by Seeligmann. Dr Lovell Gulland of Edinburgh has kindly allowed me to record that during the last two years he has examined the blood of three osteomalacic patients, two of whom were aged. In the senile cases the blood was practically normal in every way, while in the puerperal case there was an increase of the eosinophile cells. Virchow found microphiles and nucleated red blood corpuscles in a patient aged 37 on whom oophorectomy had no effect. With regard to the increase in the eosinophiles, Cabot has observed their increase in osteomyelitis and other diseases. Neusser also found them increased in many diseases, including leukaemia, nervous and skin diseases and diseases of the male and female generative organs. Castor found them diminished during digestion and in certain morbid conditions. With regard to the presence of myelocytes in the circulating blood, Cabot considers that their presence is always to be regarded as pathological, but the fact of their having been found in osteomalacia, only seems to link it to grave diseases, such as malignant disease, anaemia, &c.

Pathology and Morbid Anatomy.

Though the pathology has not yet been fully worked
out, and our knowledge of the morbid anatomy is imperfect and unsatisfactory, it appears certain that this disease is one which affects the whole organism and is not restricted to the skeleton, though it shows itself chiefly in the decalcification of the bones with disappearance of the lime salts and, at a later stage, a certain amount of absorption of their organic constituents. To use the words of Pommer, "there is no pathological condition in osteomalacia which is common to, and descriptive of all cases." One change which is frequently mentioned as being present in the tissues, especially of senile cases, is that of fatty degeneration, and this is seen in patients who are markedly emaciated.

Bones. Seen after death the bones are soft, porous and light, so that they may float in water and may be easily cut with a knife or scissors. The periosteum is greatly thickened and extremely vascular. Grajon describes it as very slightly adherent, generally thickened, its osteogenetic layer more fluid, pulpy and gelatinous than normal and at times coloured by blood effusions. Proesch also describes it as being thick and only slightly adherent, while Beylard, Kilian, Stansky, Bouley-Hanot and Winkel found it thickened and very adherent.
Lobstein\(^{33}\) on the contrary found it dense, but thin. In one case described by Shattock\(^{10}\), it was increased to a one line in thickness and formed the only casing of the femur, the bone being entirely replaced by soft, reddish, fatty material. Another writer says that in severe cases, the bony structure may disappear and soft, greyish, mucoid material take its place, or the bone be like connective tissue. These are exceptions, as the disease begins from the endostial surface, and rarely attacks the sub-periostial outer lamellae. Even in advanced cases, where the greater part of the bone has disappeared, there is a thin outer shell, which is comparatively healthy and hard.

Thickenings are common, and have to be distinguished from the formation of callus round the seat of a fracture. They are most often seen on the ribs, and are clearly described by Grajon\(^{24}\), but they may develop on any bone, and were well-marked on the bones of the forearm, in case II, vide Fig: 4. They appear to mark a spot at which the disease is rapidly advancing. Lane\(^{8}\) observed them on the lower jaw in one of his cases.

Cysts, filled with clear fluid or viscid, brownish red material, due to broken down blood cells are not uncommon in these thickened areas,
especially when these occur in the flat bones. Fractures are sometimes found surrounded by a layer of thickened periosteum, with or without a limited formation of bone. It may act as a ferule round the ununited ends which are in some cases rounded and thickened from the faulty deposition of new bone. The callus is soft and porous and is not replaced by true bone, so that even when there is union it is of an imperfect nature.

Reylard\(^9\) describes the varieties in the healing process as follows:

1. An osseous ferule as in ordinary cases.
2. Callus invisible externally but forming an osseous layer which obliterates more or less the medullary cavity and serves to unite the fragments.
3. Fibrous tissue which unites the ends and forms a pseudo-arthrosis. Renard\(^6\) describes the process of repair in almost singular terms, but in contradiction to the above descriptions, it must be remembered that Pommer\(^9\), Volkmann\(^6\) and Ranvier\(^6\) consider normal union may and does occur.

On section, the bones show spaces of varying size, instead of the normal cancellated structure. (Vide Fig: 4, Page \_\_\_\_). These spaces in the ribs and flat bones are filled with reddish or chocolate coloured marrow. In the long bones, the marrow is more frequently of a greyish yellow colour, more fluid
than normal, and with a great excess of fat.

The softening of the bones is due to removal of the earthy constituents. In normal bone the proportion of inorganic to organic matter is 68 to 32, or rather more than 2 to 1. In osteomalacia, the reverse is the case, but the results of analysis vary according to the stage of the disease.

Ritchie gives the following table, compiled from various authors. -

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Durham. -

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Kehrre. -

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Lehmann. (average of 4 analyses)

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<th>Normal</th>
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<tbody>
<tr>
<td>Inorganic</td>
<td>24.40</td>
<td></td>
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<tr>
<td>Organic</td>
<td>75.60</td>
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Weber. (average of 3 analyses)

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<tr>
<td>Inorganic</td>
<td>49.94</td>
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<tr>
<td>Organic</td>
<td>50.06</td>
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Most writers agree that there is increased vascularity in the bones and that this precedes decalcification and bony absorption. As the disease advances, the minute vessels become congested and tend to rupture. The larger vessels increase in size and their canals and foraminae appear more patent. Grajon notices this specially in one of his cases where the channels for the meningeal arteries were greatly deepened. The disintegrating process begins in the Haversian canals. The bony matter is first seen to be opaque and less uniform than normal, the earthy salts are unequally distributed through the laminae, these become less distinct and the neighboring Haversian systems fuse and the lacunae become wider. Along with the destructive process, there may be seen formation of new bone, but as the regeneration is feeble, the disease advances till there is little left, save a few irregular trabeculae with large or small spaces between.

As seen by the microscope, the areas of decalcification are clearly marked; the bony trabeculae surrounding the Haversian canals, and the medullary spaces, instead of having, as in the normal state, a homogeneous opaque appearance, show at their peripheries, a transparent zone, in which the bone corpuscles are visible. Coats, Frey and Rindfleisch
describe the appearance of the parts as precisely that of bone artificially decalcified by acid. If the section be stained with carmine, the decalcified areas are more plainly seen as the unaffected bone remains unstained. This is the carmine zone spoken of by Virchow, Cohnheim and Ribbers. From the description of Lamb, Steiner, Hirschfeld, Rindfleisch, Mommsen, Bouley and Ranvier (quoted by Schlichthaar), the limeless zones are more or less transparent and finely striated. Von Recklinghausen found them strobly refractive. Bone corpuscles are usually seen, though Bouley-Hanot, Rindfleisch and Ribbert have noted their absence. Their appearance varies greatly. Moore and Frey described them as enlarged, Lamb as oblong and irregular. Their canaliculi are indistinct, shortened, irregular or absent, (V. Recklinghausen, O. Weber, Coats). Litzmann describes them as broad and irregular and containing fat drops. This is considered by Virchow and Dalrymple to be a secondary change.

The dividing line between the decalcified and lime-holding areas is well marked and has been described by various writers as straight, dark, broad and wavy, irregular or serrated. (Bouley-Hanot, Recklinghausen, Steiner, Kassowitz). The lime-holding structure was found to be normal by Rindfleisch and Birch-Hirschfeld, while O. Weber and
Durham found the canaliculi widened and the bone corpuscles enlarged. Frey, Roloff and Kassowitz found the lime in some parts irregularly distributed. Grajon found in the vertebrae that although the very thin osseous trabeculae always showed the same characters as in the other bones, the intermediate substance had a different appearance. It consisted of a fasciculated connective tissue which stained faintly with carmine and filled all the spaces. In the centre of this tissue were embyronic cells and in places, the large cells described by Kolliker (osteoclasts) who attributes to them an important role in osteomalacia. He also found these cells in the ribs. Meyer described a case in which the disease appeared, in the vertebrae, to be proceeding from the periphery of the bones instead of from the centre, and where the microscopic changes differed from those usually seen in osteomalacia.

As has been said, the marrow may be dark red, or pale and fatty. Ranvier described it, in the second stage of the disease, as resembling spleen pulp. Virchow considers that it is blood red during the early progressive stage of the disease, becoming fatty and jelly like towards the end. He also described it as resembling foetal marrow. Lammel compares it to granulation tissue, with haemorrhages and spindle cells. Litzmann and Kassowitz say that
owing to frequent haemorrhages, it is difficult to follow the course of the vessels. Small round cells, suggestive of an inflammatory process, have been observed; fat cells, spindle cells and osteoclasts have been described by Pommer and Bouley-Hanot. Embryonic cells are frequently seen and crystals of triple phosphates were found by Beylard in the fluid marrow. V. Recklinghausen described the cells as of varying shapes and sizes, many being filled with fat. Rindfleisch, on the contrary, found the cells in the gelatinous looking ground-substance, few in number and large and considered that they resembled epithelial cells.
Ribber considers that in senile osteomalacia the marrow differs greatly from foetal and young marrow and describes it, under the microscope, as being a dark blue red pulpy mass, containing, along with normal fat cells, closely packed marrow cells with a large number of red blood corpuscles in all stages of degeneration. Crajon as already stated, found embryonic cells in an old woman, aged 71.

Observers differ as to how the process of disintegration and removal of the calcareous matter is brought about. Pommer, Cohnheim, and Kassowitz believed it to be due to absorption of the bone without previous decalcification, that along with the destruction there is a continual process of bone formation, or regeneration, but that there is not always, with this new formation, a normal laying down of lime salts. Lobstein, Virchow, Kilian, Guerin, Klebs, Ziegler, V. Winkel, Ribbert, and Rindfleisch, on the contrary, consider it a process of decalcification, followed at a later stage, by absorption of the animal matter. Durham, in his most interesting paper, supports this view, and observes, with regard to the changes that there is:

1. A change in the proportion of organic to inorganic matter.

2. The relation which the organic bears to the inorganic is altered. That along with the physiological
change the chemical union is disturbed, the earthy matter being much more readily dissolved out of osteomalacic bone.

(3) The constituents are in themselves changed. The minerals vary much in nature and in relative proportions. In normal bone, the carbonates and phosphates bear a tolerably constant proportion while in osteomalacia, the proportion of carbonates to phosphates is diminished.

The animal constituents consist of more fat and less nitrogenous matter than is found in normal bone. The fat is more liquid, freer, and less confined to cell membrane. The nitrogenised matter is so far altered in character that comparatively little gelatine or chordin is to be obtained by the ordinary process. Levy on the contrary, considers the organic substance has no qualitative change.

Hermann, who found lactic acid in the bones, advanced the theory that the decalcification is due to its action. Gertsner, Driven, and Moers-Muck appear to favour this view. Schmidt, Weber, Lehmann, and Goblet in their examinations, found the bones more frequently acid, but sometimes neutral and cases have been examined where lactic acid was not present. The reaction is believed by some observers, to be due to post-mortem changes. Levy considers that the decalcification is not due to lactic acid because normal bone treated with this acid loses more CO₂.
and phosphoric acid, but here we are met by the
difficulty of post-mortem examinations versus changes
taking place in living tissue. Schmidt held the
changes were due to phosphoric acid. Rindfleisch suggests that owing to the congestion and partial
stasis in the blood vessels, there may be an accumula-
tion of CO₂ in the tissues which may act as the solvent.

Kidneys. Few lesions have been recognised in
these organs, but cases have been reported where
they were cystic, granular or enlarged. Phosphatic
Calculi have in some instances been found. Durham notes the presence of a small renal calculus in
one of his cases. Davies Colley found, post-mortem,
in the case of a girl of 15, that all the organs
were normal except the kidneys which were enlarged.
The pelvis of the right contained a number of angular
stones, the largest being about the size of a common
nut. In this case the urine had contained triple-
phosphates, and before death she had passed phosphatic
calculi. Towards the end, the excretion of P₂O₅
had been markedly diminished, while CaO was increased.
Shattock, in one case, found a large phosphatic calcul-
us, where the urine before death had contained an ex-
cess of earthy phosphates. Eulenburg records having
found concretions in the pelvis and cortex of the
kidneys. Bouley-Hanot found deposits in the kidneys,
ureters, and bladder, which by chemical analysis were shown to consist of bone salts. Pagenstecher\(^{(12)}\)
in a case where lime salts had diminished in the urine, found calcium deposits in the bronchi, and in the stomach. In cases II and III, as already noted, phosphatic calculi were found.

**Muscles.** The muscle change appears to be that of fatty degeneration. Chambers\(^{(56)}\) records a case in a woman of 26, where, to the naked eye, the muscles appeared homogeneous, and under the microscope were found to have lost all trace of fibrous structure, and to show abundant fatty change. Grajon describes the muscle in the case of a woman of 61, as extremely pale and slightly yellow. In spite of the abundance of fat the fleshy masses were small. A great proportion of the muscle fibre had disappeared and was replaced by fatty tissue, which was seen between the finest fibres. Friedreich found multiplication of the nuclei of the muscle fibres and changes resembling those of progressive muscular atrophy. Weber\(^{(83)}\) mentions an old man of 71 whose muscles showed marked fatty changes. Köppen\(^{(123)}\) found slight microscopic changes, and believes that in the early stages, they are of a chemical nature. Stieda considered that in osteomalacia, the changes were rather in the muscles than in the nerves.
Nervous System. When we consider how constant are the nervous symptoms in osteomalacia, that in the early stages, it has frequently been diagnosed as neuritis, tabes, insular sclerosis or one of the diseases which are associated with a distinct nerve lesion, and when we find among those who have made careful observations, writers who consider the disease to be of nervous origin, it is surprising that so few investigations have been made as to any morbid condition of the brain, spinal cord or peripheral nerves, and also that in the few instances where examination has been made, how little of a pathological nature has been discovered. Grajon\(^a\) in one advanced case in which there had been great suffering, found the sciatic, median, radial, vagus and intercostal nerves normal, save that the tissue separating the fibres was so invaded by fat that their volume was increased in size. The cerebral substance, in this case, was usually firm. In another case where the vertebral column was so soft that the cord could be removed without the aid of a saw, examination of the cord and nerve roots showed no pathological change, either to the naked eye, or microscopically. In the case of a lunatic, where the bones were "like rotten wood", the brain
showed no lesion save a slight degree of atrophy of the convolutions at one part. The cord was smaller than usual, and the vessels more dilated in proportion to those of the brain. At the level of the cervical and dorsal regions the nerve cells of the anterior horns showed changes on both sides but differing from each other. This man in life had contractures of the lower limbs, and the question is, were the changes in the bones coincident with or in any sense dependent on the cerebral lesion?

Pommer and Renz, by histological methods, found distinct, though slight changes in the cord.

**Ovaries.** On account of the influence which the ovaries have been supposed to exercise in osteomalacia, and also on account of the opportunities which oophorectomy has afforded, these organs have been examined with a perseverance which is only equalled by the neglect of the other viscera. The conclusion to be drawn from the literature on the subject is, that pathological changes have commonly been observed, though many writers consider these changes are not peculiar to osteomalacia. The changes most frequently present, and which are, by Fehling, considered characteristic of the disease are increased vascularity, (the vessels in the hilum and cortex being increased in number) along with hyaline
degeneration in their walls. In many cases this degeneration is also present in the parenchyma, either throughout or in patches. Eisenhart, Rossier, v. Velitz, Heyse and Poppe have observed these changes. Orthmann considers hyaline degeneration characteristic of the disease, but only in 8 of his cases, was congestion, or increased vascularity present.

In some cases an atrophic condition has been found.

V. Velitz examined the ovaries of 24 cases, and found:

- In 4......degenerative conditions.
- 9......increase of vessels of the hilum.
- 6......Do. Do. and in central ovarian tissue.
- 1......atrophy of ovarian stroma.
- 4......normal.

Löhlein in 5 cases, found:

- In 1......both ovaries atrophied.
- 1......1 cystic and small, the other large and vascular.
- 2......normal.

Schnell, between 1889 and 1898, had 32 cases under his care, and considers that the greater the degree of ovarian disease, the greater will be the osteomalacic changes. Neumann, out of 4 cases,
found the ovaries normal in two. Although he says these observations are too few to allow of positive conclusions, he yet considers that there is no ovarian change which is characteristic of the disease. This opinion is shared by Kleinwachter and Winkel.

Schottländer examined the ovaries from 3 cases, and found in two, that they were larger than normal, and in one, smaller. He observed, along with the other changes, loss of germinal epithelium, and small cystic degeneration of the Graafian follicles. He considers that these changes are not characteristic of osteomalacia, but are the result of the hyperaemia, and venous stasis and says that a similar condition is seen in such diseases as tumours, pruritus, etc. Many other observers, including Stein, Seeligmann and Bulius, found no changes.

Ferroni compared the ovaries from two cases of osteomalacia with those from two cases of rickets. In rickets, he found the cortex normal, but in the stroma changes similar to those seen in osteomalacia.

Scharfe examined the ovaries from three cases, in one of which they had been removed by Caesarian section at full time. In one case, there was cystic degeneration, in another evidence of tubercle. (This is the only case in which we have noticed tubercle to be associated with osteomalacia).
In the third, there was a trace of hyaline degeneration. He examined two cases where the ovaries had been removed from patients who were not suffering from osteomalacia, and found changes so similar that he says it is doubtful if we have a right to speak of osteomalacic ovaries.

Researches in Animals.- Among animals, osteomalacia, or a disease very closely resembling it, is known, and it is believed by V. Winckel, Hennig, Casati and others to be analogous to that occurring in man. Roloff says that it is endemic in a well-defined area in Asbrettangen, near Augsburg, that it chiefly affects milk cows, rarely oxen, and that when the sick animals are sent out of the district they quickly recover. It was well known in Bohemia in the years 1863 to 1866 when, owing to bad climatic conditions, the food stuffs were poor in phosphorus and in lime salts. It prevails, more or less each winter, in the districts of Hinschofen, in Villigen and Baden. In Norway, in the year 1869, there were 2142 cases of which 448 had to be slaughtered. The animals are characterised by stiffness of the limbs and pain on moving, and there is deformity often accompanied with fractures. V. Recklinghausen considered the anatomical conditions to be the same as...
those occurring in man. Attempts have been made to
induce the disease in animals by feeding. Roloff
and Haubner fed cows on food stuffs, poor in lime
salts, and in a month they became affected, but re-
covered on the addition to their food of phosphate
of lime. Three healthy cows were fed on hay from
an infected district and became affected, but were
also cured by the addition of lime phosphate to their
fodder. Four goats, fed on the same fodder, but who
had lime water to drink, were not affected, but lime
water has not always been found a cure. These
experiments point to lack of phosphate of lime as
being the cause of the disease. Stilling and V.
Mering fed a healthy bitch for 126 days on food,
poor in lime salts, the pups showed no sign of
rickets or osteomalacia, but the mother showed well-
marked changes in the bones of the spine and pelvis.
Seemann found changes in the bones after feeding
animals on foods rich in Potash Salts. He held
that these salts combine with the chlorine in the
plasma blood and that there is therefore
diminished formation of HCl and consequently faulty
digestion and therefore diminished absorption of
lime salts. Heitzmann made experiments by giving
lactic acid in the food, and also by injecting it
subcutaneously in a variety of animals, and found
changes resembling rickets and osteomalacia in the carnivora, while in the herbivora osteomalacia change alone. Siedamgrotske found a loss of lime salts in the bones of animals, treated in this way, but no evidence of rachitic changes. Hofmeister (149) made similar experiments with similar results, Heiss who gave lactic acid to dogs found no changes in the bones and Toussaint and Tripier also failed to produce softening. Gaspari and Zuntz found changes in the bones, especially in the pelvis, of pigs and rabbits after treatment with oxalic acid. Morpurgo gave a disease to white rats by inoculation, which appeared to be half-way between bone weakening and bone inflammation. Zurn found cocci in the marrow of affected animals, which he believed, caused the disease, but evidence of putrefaction was also present. Haubner quotes from Utz who had observed weakening and bending of the bones in animals, that had been confined in dark stalls during winter.

Predisposing Causes and Theories of Causation.-

Predisposing causes - constitutional. As far as we have been able to ascertain, osteomalacia is seldom associated with congenital disease or constitutional weakness, one of its characteristics
being that it attacks those who have previously been healthy. It has not, like so many degenerative conditions, been ascribed to the latent toxic after-effects of syphilis, alcohol, or of the zymotic diseases.

**Heredity.** The possible influence of heredity has been considered by more than one writer, but the recorded instances of more than one member of a family being affected are few. In 1788 V. Eckmann described a disease in one district in Norway, which was characterised by bending of the bones and fractures and which affected several members of a family, but Eisenhart considers some at least of these cases may have been rickets. Pommer records a case where a man of 19, the second son of an osteomalacic woman, developed marked symptoms of the disease. Meyer had a patient who belonged to a family in which bone diseases had been frequent, but the exact nature of these he could not discover. Fehling records an instance in which two sisters were affected, and Kehrre and Grapow each record a case where relatives in the preceding generation appear to have been affected. Fothergill records a case where the disease occurred in a woman who was of Polish descent, but who had lived for long in England, and whose surroundings had been healthy.
He considers in her case that there is the probability of inheritance, as Poland has been regarded as "a home" of osteomalacia, but the disease does not, from the history, appear to have been recognised in her relatives. Kehrer and Kleinwächter note the fact that in Bukowina where there were people of various nationalities, the Jewish women almost alone were affected.

Locality and Surroundings. Though comparatively few cases have been recorded in Britain, osteomalacia is frequently seen abroad, and is believed by Fehling, Kehrer, Kleinwächter and others to have geographical distribution, and to be endemic in certain districts. It is well known on the borders of the Rhine, and numerous cases come from the valleys of the Neckar, Main, Lahn and Ruhr-Cornil and Ranvier have described a form on the lower Rhine which begins in persons over 50 years of age. It is common in North Germany; Fehling says of Gummersbach that 50 years ago it was the classic ground of the disease, but that now it has almost disappeared, owing to the efforts and influence of V. Winkel Sen., which led to improved hygienic surroundings, and more comfortable dwellings, especially in doing away with dark, unhealthy, sleeping places, and to a better quality
of food. A similar disappearance of the disease has been observed in Sottegen in East Flanders. Biefel notes that it is now much less common in Schleswig, in Jutland, and in the Friesian Islands than it used to be, and this he attributes to the improved conditions of the dwellings. V. Velitz notes an occurrence in the Island of Schutt. In Baden, Wurtemberg, and Alsace, cases are often seen, and Kehrer records 45 in his clinics in Heidelberg. In Switzerland it is common in the Bergolzthal, and Fehling says was endemic in Basel. Cases have been recorded in Zurich and Berne. The Orlanathal in Lombardy, is a centre. Arcangeli and Fiocca record cases from the villages of Lazio and Abruzzo Aquilano in Central Italy, while in Calabria in the South, it is well known. In Austria, Hungary, and Bosnia, cases are frequently seen. Vrleanic, in four years, had under his care in Gospie, 29 women suffering from osteomalacia. "These all came from one district in South-west Croatia, where the climate is keen, dry and healthy, and the formation is chalk, but the inhabitants are poor; overcrowding and insanitary dwellings are the rule, their food is insufficient, and is largely composed of milk and starchy materials.
In the valleys, malaria and pellagra are common."
It is a striking fact that the disease should be so common in a district where the formation is chalk, and where milk is a staple article of food. It is common in Poland, though seldom seen in Russia proper.

Dr Rachel Mackenzie, who has lately returned from India, says the disease is not uncommon in Chamba in the Punjab. Chamba is 3,000 feet above the sea, but is in a hollow quite surrounded by mountains. Many of the women in the place are upper-class Hindus and strictly confined to their houses. Their food is like most native food, not very nourishing, but is no worse than that used by the people of the plains, among whom she has never seen a case. The cases are in young puerperal women. Nearly all observers, including Fehling, and V. Winkel, are agreed as to the influence which bad hygienic conditions, especially dark and airless sleeping places, and poor and insufficient food, have in predisposing to this disease, though there are instances where it has developed in patients whose surroundings were comfortable and healthy. Kubler and Schweening attributed its frequent occurrence in Bosnia to poverty and Corradi considers insufficient food to be the cause in Milan.
Pommer, on the contrary, does not consider it to be a disease of the proletariat.

**Trauma.** So far, there is little evidence to support there being a direct relation between injury and osteomalacia, but Theim, Durham, Demange and Grajon with others record cases similar to Case IV in which the patients ascribed the onset of the illness to a fall, and Demange asks "Is accident in these cases a simple coincidence, or does it play the part of a determining cause."

**Pregnancy.** Repeated and quickly succeeding pregnancies, especially when associated with the above mentioned conditions, have been regarded as a cause, and the fact that the onset of osteomalacia has frequently been coincident with pregnancy or labour seems rather to favour this view. Hennig, in 78 cases found the symptoms developed in 7 patients during the first pregnancy, and in 7 after the first labour. Eisenhart, as the result of observation in 97 cases concluded that the onset was generally during the first three pregnancies. Fehling, V. Velitz, Eisenhart and others consider increased fertility to be a symptom rather than a cause of the disease, and Fehling in support of this view contends that the congestion of the pelvic organs
may produce a greater susceptibility to impregnation. From notes of the cases of osteomalacia recorded in German literature from 1873 to 1890, Eisenhart found that 105 women had given birth to 673 children an average of 6.4. Rosenträger placed the average fertility at 8.2, Baumann at 6.8, V. Velitz at 6.7. Neumann, from 11 cases where the greatest number of births per patient has been 10, and the fewest 3, gives as an average 6.3. Fehling places it at 5.4 while the average per head, among child-bearing women in Germany, is 3.9. Letzko disputes there being an increased fertility and from the number of births in 50 cases, places the average at 4.9 before onset of illness, and 1.75 after. Neumann observes that in considering this question we must bear in mind that the average may be now somewhat lower, as in so many osteomalacic cases the ovaries have been removed while the women was still at the child-bearing age. We must also consider that in these statistics abortions have not been included and these have been noted as frequent in osteomalacic cases. Ritchie has collected the statistics of seven observers which shew the percentage of puerperal to non-puerperal cases and to cases occurring in men.
Litzmann in 131 cases found... 64.88 per cent puerperal
Hennig.......................... 68.2
Casati.............................. 64.9
Italian Statistics............... 61.0
Gelpke, of 19 cases............. 94.8

Hanau, in a series of examinations of pregnant women, found in every case changes in the osseous system similar to those which occur in osteomalacia, but in a much less degree and his conclusion is that a mild degree of osteomalacia is present in every pregnant woman. Ducrest recognised a certain degree of softening of the bones during pregnancy and Korczynski speaks of this change as being well-known in pregnant women under certain conditions. This being so, it is easy to understand that during pregnancy when a woman is particularly susceptible to any morbid process, she could be peculiarly so to osteomalacia. During the intervals between pregnancies, or if pregnancy be arrested, there is often marked improvement followed by grave relapse with each succeeding conception. In cases where oophorectomy has been performed the results have been distinctly satisfactory and many cures have been recorded, but the effect upon the system of the removal of the ovaries has to be considered as well
as prevention of conception. From the above it is plain that pregnancy has an effect upon osteomalacia; that in some cases it appears to be the determining factor of onset, and probably largely determines the primary seat of softening in the pelvic bones.

It may be that greater demands are being made upon the system which disturb the normal metabolism and prevent the building up of the tissues, while the foetus is being nourished, but the disease has too often been seen in nulliparae, in women who have passed the menopause, and in men, to allow us to admit that there is a closer relation between pregnancy and osteomalacia than is due to the lowering of the system from the increased physiological strain.

Lactation. Prolonged nursing may be included with pregnancy, as causing a drain upon the system, and in all probability a drain which will have a marked effect, owing to the N. P. and Ca present in the milk. But even considering this, prolonged lactation is of such common occurrence among the poor in districts where osteomalacia is practically unheard of, that it can hardly be looked upon as a cause. In Japan, the women nurse their children for 2 or 3 years and the disease is said to be unknown.
Menstruation. One or two writers have referred to the effect of menstruation on osteomalacia, but no observations appear to have been recorded as to whether menstruation be effected by the disease. If there be abnormal congestion of the pelvic vessels menorrhagia might be expected but is evidently not present. Collineau found in 52 cases that 14 had exacerbations at the menstrual periods; this is not common. Fehling reports similar cases, while V. Winkel denies that it has any such effect.

Mary Theories of Causation have been advanced, but they may be classed as -
1. Those which attribute the disease to a pathological condition of the ovaries.
2. Those which consider it due to a disturbance of metabolism.
3. Those which attribute it to bacterial infection.

Ovarian. Owing to the partial or complete recovery from osteomalacia which on repeated occasions followed Caesarian Section or Porro's operation, which had been necessitated, by the deformity of the pelvis, Fehling, in 1887 expressed his belief, which has since been widely accepted, that in some abnormal condition of the ovaries lay the cause of the disease and that in removal of these organs lay the greatest prospect of cure. Three principal
hypotheses have been advanced as to how the ovaries exert this influence, in all, they are regarded as being reflex-nervous centres.

Fehling's which is supported by Neumann, Hofmeier, Thorn, Ribber, Eisenhart and others, is the osteomalacia is a tropho-neurosis of the osseous system. That the ovaries they become a centre of reflex stimulation to the vaso-dilators of the bones and marrow, thereby causing passive hyperaemia, an accumulation of CO₂ in the tissues, and consequently resorption of the earthy salts.

Curatulo holds that the ovaries introduce into the blood a secretive product, the chemical constituents of which are unknown, but which is capable of facilitating the oxidation of phosphoric organic substances which supply the material for forming the salts for the bones. He worked it out by castrating bitches, and found that after the operation, with the same conditions as regards food, etc., the excretion of phosphoric anhydride fell from 9.93 to 0.75 grms, and Schottlander also believes in an internal ovarian secretion, which dissolves bone phosphates and carbonates and he says that this chemical substance exists normally, but is greatly increased in osteomalacia. To this secretion he ascribes the fact that the female skeleton is finer than the male.
Ascoli considers that the disease is due to a disturbance of nutrition which is caused by a nervous excitation starting from the genital organs, and which affects the blood and marrow.

Zweifel holds that the ovaries do not act as reflex centres on the sympathetic system and that their removal acts by diminishing sexual activity and with that, pelvic congestion. He considers that tying the tubes if sufficient treatment. The weight of argument is not sufficient to make any of these theories convincing, the fact that the disease has not always been arrested by castration, and also that so many cases are recorded of its occurring in the male, make it doubtful if a pathological condition of the ovaries be the primary cause, unless with regard to the occurrence in man it can be proved that there is a pathological condition of the testes or an internal secretion from these organs which is in any way analogous to that of the ovaries. There is no recorded case where the testes have been removed for this disease, though P. Berger proposed the operation to one of his patients.
Metabolic.

Many observers are agreed that the cause of the disease is entirely owing to faulty metabolism but each suggests a different theory as to how this is brought about and on what it depends. There are those already mentioned, who consider the disease due to poverty, or to defective food, both quantitatively or qualitatively deficient, especially in lime salts. It has been also suggested that gastric catarrh occurs in such conditions causing an abnormal formation of organic acids, especially of lactic, from the carbohydrates ingested. These may combine with the lime in the already insufficienlly supplied lime foods and may cause the increased lime excretion by the faeces (Winkel) or by passing directly into the blood may act as a destructive agent on the bones (Moers-Muck).

Pommer considers that owing to faulty metabolism certain acids and half way products are left in the blood, and suggests that the cause of this may lie in the central nervous system. Kraus considers the possibility of the diminished alkalinity of the blood being due to the destruction of the red blood corpuscles and by the consequent splitting up of their lecithin into cholin and distearoglucero-phosphoric acid. Kraus says it is an open question whether
other acid products may not be formed in the broken-down blood or whether similar splitting up may not occur in other tissues or whether acids be not formed in other ways. Bouchard holds that whether or no the marrow manufactures acids it certainly accumulates them in certain pathological conditions.

In health the organism is constantly fabricating acids which it burns up, but in certain pathological states the oxidation of these acids is diminished and they accumulate in the system. This acid dyscrasia is therefore, Bouchard concludes, a disturbance of general nutrition. Eisenhart asks if the strongly hyperaemic marrow may not liberate certain organic acids whereby the diminished alkalinity is caused. Tepling speaks of the changes in the bones possibly being secondary to a primary inflammatory hypertrophy of the marrow and consequent disintegration and he quotes as follows from Busch: "May it not be a fight between the bone and the marrow in which the latter prevails." Meyer also speaks of the increase of small cells in the marrow and their resemblance to those present in inflammatory conditions and goes on to say that Schroeder considered it as an osteomyelitis, V. Winckel as a periostitis going on to an остит. Pommer and others are absolutely opposed to its
being an inflammatory process. Korczynski believes it is caused by an auto-intoxication due to a disturbance of the metabolism of albuminoids which in turn depends upon increased biological activity.

He holds then in certain conditions, especially those of pregnancy and lactation, when great demands are being made upon the organism, that compensation is carried out in normal conditions but that when the strain has passed by and a certain limit compensation breaks down. He considers that the ovaries, marrow and the parotid gland may be the agents in this work of compensation, and refers to the morbid changes which have been observed in them as a proof of their increased functional activity. The observations regarding the parotid he quotes from a paper by Damsch.

This hyperactivity is the property of the protoplasm cells whose number, growth and subsequent destruction are naturally more rapid and energetic. The need therefore of regenerative and formative materials is increased. The demand for nuclein, the most important constituent of the cell nucleus is especially great; in other terms the need of the organism for Nitrogen, Potash, Phosphorus is vastly increased. These substances along with Lime and Magnesia form the most important constituents of bones.
When therefore increased activity demands larger quantities of the above mentioned substances the cells satisfy their needs by withdrawing them from the bones. Senator considers the nitrogen metabolism resembles that of a starved animal.

**Bacteria.** No distinctive micro-organism has so far been accepted as the cause of osteomalacia though the possibility of its being of bacterial origin has of late years been suspected. Kerker,\(^\text{190}\) who considered that it was endemic, as are diseases such as leprosy and beri-beri, believed it was due to osteolytic bacteria and Lohlein does not deny the possibility of this although he failed to find germs either in a piece of osteomalacic bone removed from an iliac crest or in the ovaries of the cases which he examined. Fischer and Levy found in some cases staphylococcus pyogenes aureus and albus in the blood and held that the disease is due to a mixed infection. Fraenkel found streptococci and the diplococcus pneumonii. Petrone believes that it is due to the fermentum-nitricum, a micro-organism which occurs in the soil and which produces an acid in the system capable of dissolving out the earthy constituents of the bones. He supported his theory by the discovery of Nitrites in the urine, vide
Page 174. He made pure cultures of the organism which he injected into dogs and succeeded in producing a disease similar to that seen in man. Truzzi found Staphylococci in the blood of a patient who was improving. Morpurgo's inoculation of white rats has already been described, - Page 148

Lately Arcangeli and Fiocca have published the results of their examinations of portions of bones excised from the ribs of six living osteomalacic women. All these patients were multiparæ and their ages varied from 26 to 42. The patient aged 26 had suffered for 8 years; another for 4; 2 for 3 years; 1 for 2; 1 for 1 year only. In all, the disease was well marked, two being advanced cases. The fragments of bone were inoculated on bouillon, agar and solidified blood serum. In five of these they found a micro-organism which was constant in appearance both microscopically and in culture growth. In the case in which the results were negative, Arcangeli considers the media may have been at fault. The organism is described as a diplococeus, rounded, 0.60 - 0.80 μ in size. It stains easily with ordinary watery and alcoholic anilin stains and is not decolourized by Gram. It has no capsule. In preparations made from bouillon culture the greatest
number are seen as isolated couples, sometimes tetrads, more rarely in chains of 6 to 7 elements. In seven preparations made from the marrow the diplococci were seen in couples or chains of a few elements and were distinctly larger than those grown in the media. At 31 - 35°C, development begins between 2 and 3 days; the turbidity is uniform, and after 4 to 5 days little flocculent masses are formed which are precipitated leaving the Supernatant liquid almost clear. Even after many days culture the alkaline reaction remains unchanged. On slope agar, the development begins from the 4th to the 7th day and becomes more rapid by successive passages. The plaque which forms on the surface is at times difficult to differentiate from the staphylococcus aureus. Decalcification appeared to go on very rapidly in the small pieces of bone round which a rich development of the micro-organism had taken place, so that after two or three months in agar they seemed to be soft and parchment-like. The organism liquifies gelatin and grows in anaerobic culture. Guinea-pigs, white rats and rabbits were inoculated, but none developed the disease. A link is therefore wanting in the chain of evidence led to prove that this organism is the prima-causa of osteomalacia, though Arcangeli considers its cultural characters closely resemble those of the bacteria.
found by Morpurgo in the osteomalacia of white rats. The resemblance between this organism and the staphylococcus aureus suggests the possibility of its being similar to those described by Fischer and Levy.

**Differential Diagnosis.** It has been generally accepted that osteomalacia is rarely seen in this country, but the question suggests itself as to whether it may not be more common among aged persons than is generally believed. May not some of the old decrepit women in our workhouses whose feebleness, pain and bedridden condition are ascribed to the "changes of age", "chronic rheumatism" or the deformities of hemiplegia, be in truth suffering from osteomalacia. If this be so, opportunities for research are lost, which might throw light on the etiology of his mysterious disease. Renz of Wildbad says that more than one half of the osteomalacic cases he has seen were sent to him with a mistaken diagnosis. Heddans and Wagner also considers it more frequent than is generally believed. The two bone diseases which offer most difficulty in diagnosis are those occurring at the two extremes of age, namely rickets and mollítes ossium, and as we have seen, osteomalacia has been found associated with both. In rickets, the epiphyses are affected and the bending is principally in the long bones,
though the thorax occasionally shews deformities not unlike those seen in senile, or advanced cases of osteomalacia. Differential diagnosis is difficult, but pain which is such a constant symptom in osteomalacia is much less severe, or is not present in rickets. Help might be gained by estimating the amount of Ca, Mg, P₂O₅ and N in the food and that eliminated by the urine and faeces. From mollities ossium the diagnosis should not be difficult, for though the former is characterised by extreme brittleness of the bones, the deformities and bending are never seen, nor are the extreme pain and tenderness present. Spinal diseases have to be excluded by careful examination of the various symptoms. Though at first the increased reflexes point to a nerve lesion the tenderness over the bones and gradual appearance of deformities should make the diagnosis unmistakeable.

Another disease from which it must be distinguished is malignant disease affecting the bones either as a primary or secondary condition. Though the lesions are easily distinguished post-mortem, the clinical symptoms present many features in common, but increased knee jerk, ankle clonus and spasmodic twitchings so frequent in osteomalacia, are generally absent and the history of a primary cancer should always create suspicion. (Ritchie)
Prognosis. The outlook is not now as it formerly was. During the last 20 years many cases are recorded as the result of treatment by drugs and also by castration. Spontaneous cures have been known, but are rare after the disease has become marked, though it is not uncommon to meet with cases in which there has been arrestment, followed by relapse with a succeeding pregnancy. This arrestment has, in some cases, been due to treatment or to improved surroundings; in others, no cause can be shown to account for it.
Treatment. We shall consider this part of the subject under two headings: Medical and Surgical.

**Medical.** The influence of surroundings has been already discussed under the heading of Locality, page...

The first step in treatment is to assure good hygienic conditions, with careful avoidance of damp houses, with abundance of fresh air and good food.

**Drugs.** Of drugs, tonics such as iron and quinine are helpful, but the really satisfactory results have been obtained by the use of Cod liver oil and the administration of Phosphorus. Trousseau first gave Cod liver oil on the recommendation of Schenk and Bretouneau who had found Cod liver oil of value in osteomalacia and rickets, and because according to de Jongh's and de Vrij's analysis, free phosphorus was found in it. He recorded improvement in some cases and complete cure in two. Sternberg collected 17 cases from the cliniques of Busch, Strumpell, Matterstock and Nothnagel, where Phosphorus was used successfully, and to these he adds four of his own. One was an advanced puerperal case, where there was great improvement even during pregnancy. In a woman of 22, a IV. para, and a severe case with fracture of the right femur, there was cure, though the deformities remained. In the
two other cases, one of which was senile, the results were equally good. He advocated that the drug be given in large doses and the earlier in the disease the better. Latzko in 1895 cites 26 cases of which 15 were cured, 10 improved, 1 unchanged. Von Winkel, Fehling, Bernstein, Stieda, Fowson and Vrleanic all testify to its value at least in some cases. Several observers have found it of greatest use in senile and non-pregnant cases and Neumann and Chrobak each reports two cases where after removal of the ovaries, there was improvement, followed by relapse or no improvement at all, and where this was marked after phosphorus was prescribed. Fothergill has described a case where improvement after Porro's operation was followed by severe and continued relapse during which most of the deformities other than the pelvis appeared, where recovery was marked after treatment with syrup of hypophosphites and Cod liver Oil. Kosminski reports 13 cases, two of whom had had the ovaries removed without improvement, and in all of these cases the result of treatment by phosphorus was good. One woman had a pregnancy later and no return of the osteomalacic symptoms. Fischer, Beylard, Littauer and Bernstein found benefit following its use, and Siegert regards it as a specific in osteomalacia. His, to whose
examinations and observations we have referred, found marked improvement during and after its administration. Schnell, between 1889 and 1898, saw 32 cases, - He divides them into 'slow' and 'rapidly progressive' forms, and says that the earlier the disease begins the sooner it takes on the progressive form. In the slow form it begins after pregnancy and its course may be remittent, or intermittent. It responds to treatment, and that rapidly, and he advises that large doses of phosphorus be given.

In the pregnant form, he found internal remedies were useless, and that castration offered the only hope of cure, and only records one case of spontaneous cure. Rissmann and Hofmeier also record good results from this form of internal treatment. Other observers have not found it so beneficial. Gelpke gave small doses and was not satisfied, and Fehling and Witzel record cases where it failed to act. Colchicum, atropine, and chloral hydrate have all been tried. Chloral hydrate has been credited with success by La Torre, but Fehling who also tried it, did not find it beneficial.

Chloroform narcosis was first recommended by Petrone who believed it acted as a germicide to nitrifying organism, which he contended was in the blood, and was the cause of the disease, but other
observers have found no benefit result even after prolonged anaesthesia.

Thyroid and Ovarian extracts have both been tried. Latzko records 5 cases associated with Basedow's disease, and advances the theory that there is an interchange between the internal secretion from the ovaries and that from the thyroid gland, and that therefore disturbance of the one may cause disturbance of the other. Senator found thyroid of no use, and that it increased (as is known) the elimination of nitrogen, and also that of the lime salts. The action of Ovarian extract he found to be much the same, but considers it worthy of further trial. Latzko and Schnitzer treated 5 cases with ovarian extract of cows and pigs, but with negative result. Bernstein found no good from its use. Allison in 1896 reported a case which improved after the administration of bone marrow, with the addition of bone salts. This patient was an advanced case and had suffered for 24 years. Korczynski, as shewn by his observations, on the elimination of nitrogen and lime salts (vide page 46), considered the administration of ovarian extract was beneficial.

Baths have been strongly advocated. Vierordt considered phosphorus of doubtful value, but found that a long continued, thoroughly carried out course of
salt baths gave good results. Pelezar treated 8 cases with baths while giving lime water internally. In all there was marked improvement. Löhlein, Hofmeier and others recommended their use. Weisz treated three cases with sulphur baths and records cure in two, while there was improvement in the third. R. Schmidt prescribed hot air baths and believed the good resulting from their use, was due to the distension of the superficial vessels which relieved the internal hyperaemia, and that the relief of pain was also owing to the diminished congestion of the periosteum and marrow.

Surgical.— As already stated Fehling first performed oophorectomy for the cure of osteomalacia but a sketch of the early history of the operation which led to his adopting this treatment may be of interest. Ritchie has collected the cases recording the early history of the operation and from him we quote.

The first recorded case where osteomalacia was a hindrance to delivery is noted by W. Cooper in a letter to Hunter in 1776. The first Caesarian section on account of the disease was performed by Stein Sen. in 1783. Von Winkel Sen., before 1861, had performed the operation thirteen times, with results favourable to the mother on six occasions. Von Späth and Von Braun each removed the uterus for this disease, but the cases ended fatally.
Kleinwächter and Sänger had recoveries from osteomalacia, which they ascribed to Porro's operation. Fehling, who had observed good results succeeding Porro's operation, which he had performed 24 times in cases of osteomalacia previous to 1888, believed that the benefit was due to the removal of the ovaries, and in 1887 he performed double oophorectomy for the first time for the cure of the disease, and in 1888, was again successful in two cases. Since then this operation has steadily gained in favour. Fehling, V. Winkel, Hofmeier, Poppe, Rossier, Schnell, Truzzi have all collected statistics, to which they have added their own cases, while Seeligmann, Preindlsberger, Siesburg, Polgar, Curatolo, Scharfe, Raschkes and others, have reported one or more cases where cure or improvement followed removal of the ovaries. In considering the following figures, we must bear in mind that there may be overlapping, as the cases of one operator have probably been included in the cases collected by another.

In 1892, V. Velitz recorded 27 cases with cure in all and hardening of the bones in some.

In 1893, Winkel collected 40 cases from Fehling, Chrobak, Lohlein, Gelpke and others with 18% of cures; 4 were improved, the result in others was uncertain.

In 1894, Truzzi collected particulars of 98 operations:
in 82 cases, the ovaries alone had been removed; in 8 there was in addition ventro-fixation for retroversion; in one case the tubes were also removed and in 6 the uterus. 52 of these patients were observed for a sufficiently long time to allow of accurate results being noted; 36 were completely cured; 4 almost cured; 3 cured after relapse; 3 slightly improved; no cure in 6 cases. Cures therefore equal 75 per cent. Fehling, in the same year records 14 cases, with 6 cures, 1 improved, 3 no improvement. The others died, or were lost sight of. In 1895 Poppe gave results of 113 cases of castration, all of which had been observed for one year at least, and he gives the results as follows: cures 69.2%, marked improvement, 14.5%, cure after relapse 4.3%, lasting relapse 9.6%, no change 1.6%. Neumann in 1896 recorded 9 cases with 3 cures, 3 improved, 2 lost sight of, and 1 no change. In 1887 Schottlander noted 3 cases, with cures, Fewson, Macedonio, Salowij and Ritchie are all among those who consider that oophorectomy should be undertaken after other treatment has been given a fair trial, without improvement.
CONCLUSIONS.

1. Osteomalacia is a generalised disease of which the bone condition is the expression.

2. True osteomalacia may attack children, adults or the aged.

3. Though the disease is pathologically the same in senile and adult cases, the primary seat of the lesion is usually found in old age, in the thorax, in adults, in the pelvis.

4. The results of oophorectomy indicate that the ovaries have an influence in the disease.

5. The etiology is unknown. It has yet to be proved whether it be of bacterial origin, or is due to anto-intoxication.

6. Early diagnosis is important.

7. Treatment by improved hygiene and phosphorus are of great value. Oophorectomy should be performed if these fail.
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**Notes:**
- PO: Patient's Occupation
- C. d.: Clinical data
- June: Month of observation

**Additional Information:**
- Case 1: Hospital Case (1836)
- Case 2: Hospital Case (1836)
I hereby certify that this
thesis is written by me. I
am indebted to Dr. Mackie
Whyte, Late Visiting Medical
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Dr. A. B. Stuart

Aberdeen

29th April 1903