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Further Studies in Adult Rickets (Osteomalacia) and Fœtal Rickets

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NOTE.—This paper would have been impossible without the cordial coöperation and help of my colleagues in the Peiping Union Medical College who have allowed me to use the results of their work and have given me advice in various directions. My thanks are especially due to Dr. R. R. Hannon and Dr. S. H. Liu of the Department of Medicine; Dr. A. P. Black of the Division of Pediatrics; Dr. C. H. Hu and his colleagues of the Department of Pathology; Dr. C. K. Hsieh and his colleagues of the Department of Radiology; Drs. Miltner and Meng of the Division of Orthopædics; Miss Sophie Chen of the Dietetic Division, and the members, both doctors and nurses, of my own Staff. My thanks are also due to Mr. Wang for photographs and microphotographs, whilst Dr. Wolfe has made a special study of the teeth in cases of fœtal rickets. My thanks are also due to Professor H. M. Turnbull for his valuable advice.

OWING to the difficulty of obtaining autopsy permits in China at the present time, it has hitherto been impossible to obtain the tangible evidence of osteomalacia necessary to complete the demonstration of the Chinese cases, but one is now able to present the evidence afforded by specimens from two patients.

Through the kindness and enterprise of Dr. Wagner of Taiku, Shansi, a perfect specimen of a pelvis from a case of advanced osteomalacia was obtained, and he also supplied the notes of the case. (This pelvis is now in the Hunterian Museum of the Royal College of Surgeons.)

This is the first specimen of an osteomalacic pelvis obtained from China. It will be called the Shansi pelvis. In previous papers by the writer [1, 24] it has been pointed out that Shansi is one of the centres in which the disease is exhibited in its worst form.

Mrs. K. (fig. 1), aged 39, entered hospital when five months pregnant. She was of pure Chinese descent, and had lived all her life within a radius of a few miles from her birthplace. One sister-in-law had osteomalacia. She had no serious illnesses as a child, or in early married life. Beginning one month after the birth of her second child, fifteen years before admission to hospital, she began to suffer from pains in the arms, legs and lower part of the back. Three or four years later she noticed that her back was bending. Eight years ago she began to take cod-liver oil and took it for two years. For the last seven years her deformity had remained constant. She had been free of pain for the past three years. She was a slight short woman, with a marked kyphosis, bending forward at the hips so that she walked with the trunk almost horizontal, the head being raised as far as possible, so that the eyes could just see straight ahead. She walked with two canes, and moved very slowly with short steps. The left costal margin overlapped the iliac crest, the right costal margin approached to within two fingerbreadths of the iliac crest. Although there was a heavy fold of abdominal wall there, the abdominal contents did not distend it. The umbilicus was hidden in an inverted crease which sagged as an empty patulous fold in front of the symphysis.

The symphysis presented a broad face which looked upward and forward, and its superior margin was 3·5 cm. below the tip of the ensiform cartilage. The flattened hand could be passed over the right anterior superior iliac spine, and under the right costal margin a resistant rounded mass (the uterus) could be felt. Deeply pressing-in a stethoscope at this point the fœtal heart could be plainly heard. When the patient was standing, the buttocks appeared small and thrown together, the hips very narrow. When she was lying down, the thighs could not be extended beyond an angle of 35 degrees, nor abducted more than five degrees, save by flexion and internal rotation, and all movements were much limited.

Spine.—No lateral deviation. Both thoracic and lumbar spines presented a simple forward bend which brought the ensiform close to the symphysis, and the head several feet off the table, making a prone position impossible. The interspinous intervals were lost from the sixth dorsal to the fourth lumbar, but this latter interspace was plainly palpated, and was used for spinal anæsthesia.

Pelvic measurements:—

Interspinous	...	...	...	20·5 cm.
Intercristal ...	...	...	...	25·0 ,,
External conjugate	...	...	...	17·5 ,,
Bitrochanteric	...	...	...	22·0 ,,
Post-sagittal	...	...	...	4·0 ,,
Interischial	...	...	...	2·5 ,,

The finger could not be passed into the vagina in front of the ischial tuberosities.

The pregnancy was of about 5 months, and it was plainly impossible for her to carry to term, on account of lack of space in the abdomen, whilst it was equally impossible to deliver her through the vagina.

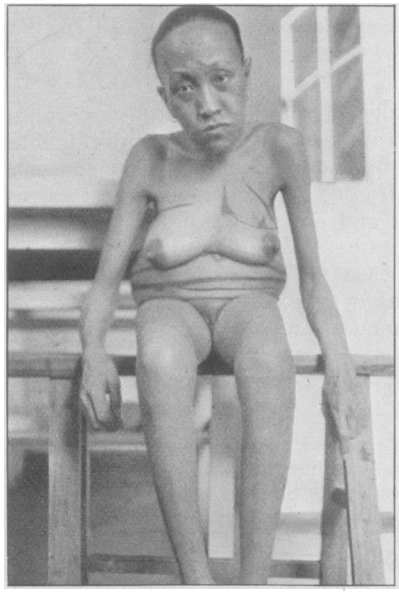

FIG. 1.

Dr. Wagner decided that it would be better to try to do a preliminary resection of ribs, and removed, on the right side, portions of the 7th, 8th, 9th, and 10th ribs with the costal cartilages and ensiform process. A small wound in the pleura was made and repaired, but the patient became cyanotic, and continued so for the next

five days. Unfortunately, four days after the first operation, she went into labour. An incision with local field-block was made parallel to the previous incision, and two inches below it. The uterus was incised through the fundus which could be brought into the incision. The uterine incision gaped widely and considerable difficulty was experienced in closing it. It was impossible to get at the lower uterine segment. The tubes were tied. In spite of transfusion, the patient became very cyanotic and died fourteen hours after operation.

A post-mortem examination showed marked pulmonary emphysema. There had been some extravasation of blood into the abdominal wall, apparently as a result of the first operation. Dr. Wagner considers that it would have been better to have tried to operate in one stage with heavy retraction of the ribs, but in any case there would have been considerable difficulty in getting any adequate exposure of the uterus.

The pelvis, which is shown in figures 2 to 5, is a most remarkable one, showing a healed osteomalacia with the typical deformities seen in a severe case of the disease.

These are the bony measurements of the specimen :—

Interspinous	19·5	cm.	
Intercristal	23·5	,,	
True conjugate...	8·0	,,	approx.
Available conjugate	6·0	,,	,,
Oblique	9·5	,,	
Interischial	2·25	,,	
Between the outer edge of the acetabula ...	15·75	,,	

Sacral index, 7·5 cm. by 8·5 cm. breadth.

The sacrum was firmly ossified to the ilia, and the transverse process of the last lumbar vertebra firmly joined by bone to the sacrum.

The lumbar vertebræ were ankylosed to each other by their transverse processes and spines, the ligaments having become ossified.

The second specimen is one from a woman who was admitted to the Peiping Union Medical College Hospital on July 3, 1933, having been in labour for three and a half days. She had active osteomalacia, and the deformity of the outlet was so severe that it was out of the question to deliver by that route. The child was dead, and pus was running from the uterus.

The details of this case are as follows :—

Mrs. L. C., aged 43, Hospital No. 40773, was admitted to the Peiping Union Medical College Hospital on July 3, 1933. She had been in labour for three and a half days. The membranes had ruptured on July 1, at 7 p.m., and she had been examined outside by an old-type midwife. The left leg had been swollen since labour began, and she was at term.

She had a history of pain in the back and legs, beginning when she was aged 38, i.e. three years after the birth of her last, and fifth, child. She had had typical osteomalacia symptoms. These became milder about the age of 40, but she was conscious of being shorter in height than before this illness. She had suffered from tetany from time to time during the disease. The abdomen was now distended, the bladder full, the fœtus dead, the os fully dilated, and there was purulent fluid exuding from the vagina, with the characteristic odour of gas bacillus infection. The left labium majus was much swollen.

The pelvic measurements were as follows :—

Interspinous	17·0	cm.
Intercristal	25·0	,,
External conjugate	18·0	,,
Interischial	4·5	,,

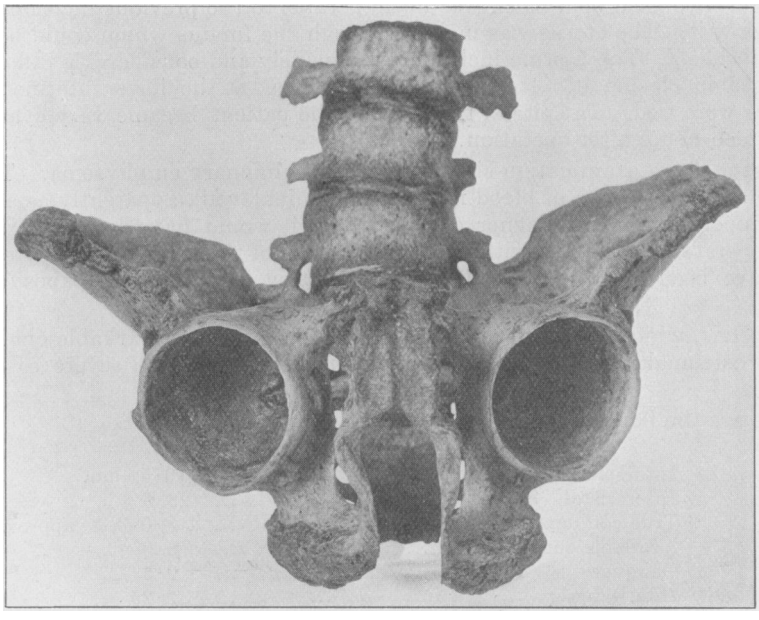

FIG. 2.—The Shansi pelvis: Front view.

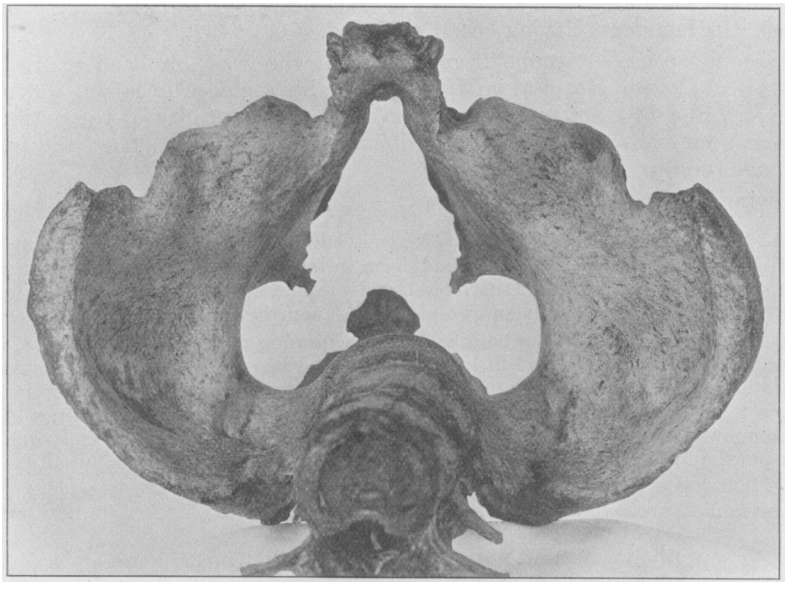

FIG. 3.—Superior strait.

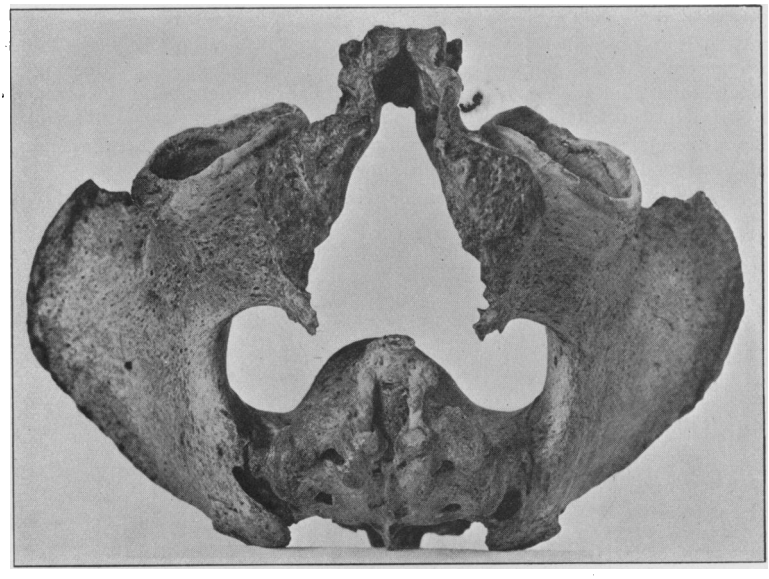

FIG. 4.—Inferior strait.

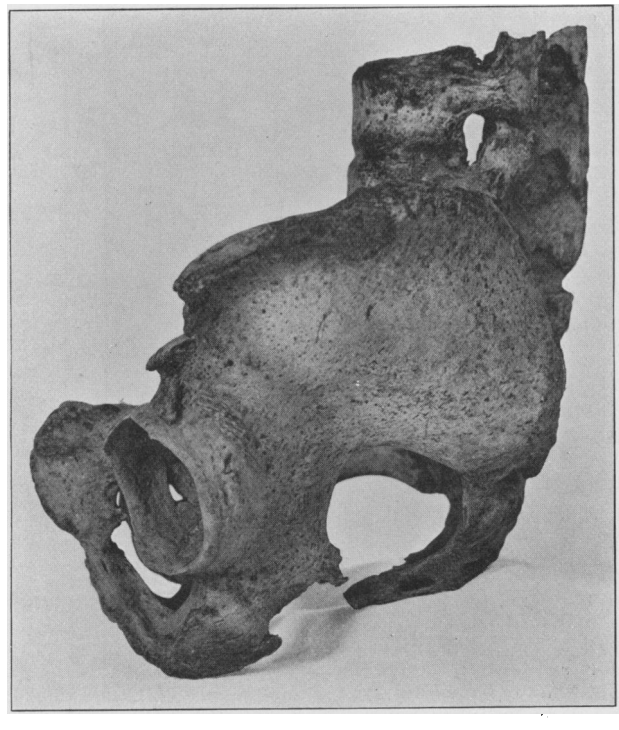

FIG. 5.—Side view.

It was manifestly impossible to deliver the fœtus per vaginam, and the uterus was in tetanic contraction.

The patient was anæsthetized with open ether at 8.30 p.m. on July 3, 1933, and a rapid Cæsarean hysterectomy was performed, the abdomen being drained by five cigarette drains. Gas bubbles were felt under the peritoneum of the broad ligaments and the back of the uterus. She went on fairly well till July 6, when she rapidly sank and died of acute septicæmia.

Her blood calcium on the early morning of July 4 was 7·32 mgm. per 100 c.c. of serum, and her blood phosphorus 3·16 mgm. per 100 c.c. of serum.

The X-ray examination showed deformity with fractures of the pelvis and osteoporosis.

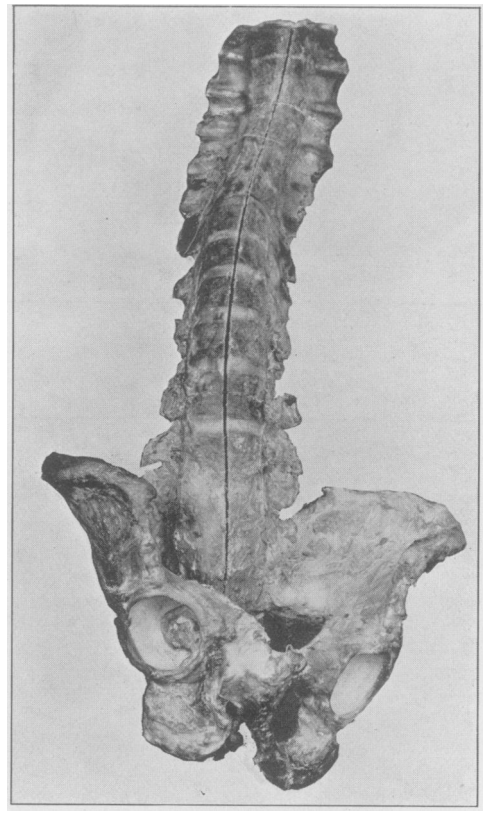

FIG. 6.—The Peiping pelvis and spine.

Dr. C. H. Hu made a very careful autopsy and secured the pelvis and spine (figs. 6, 7, and 8).

The following extracts are made from his autopsy report:—

Bones: In the middle of the following ribs, a degree of swelling, representing healed fractures, is noted on their inner surfaces. These ribs are the left 5th, 6th, 7th, 8th, 9th, and 10th, and the right 3rd, 4th, 5th. The pelvic bones are markedly deformed; the right half of the pelvis is pushed forward beyond the midline and the angle formed by the pubic bones becomes very narrow and admits only two fingers. Bone-marrow of femur moderately hyperplastic. The spinal column shows marked lumbar lordosis and left thoracic scoliosis. Longitudinal section of the vertebral column shows marked thickening of the central portions of the

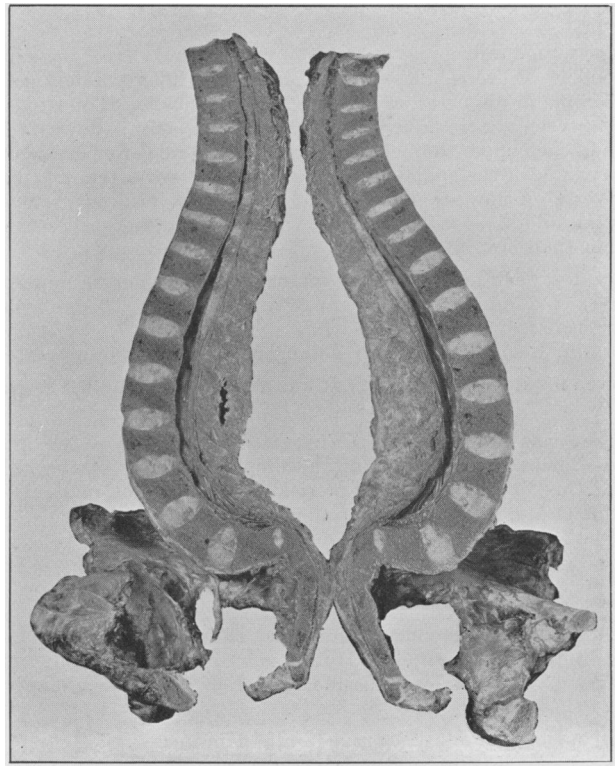

FIG. 7.—Antero-posterior Section.

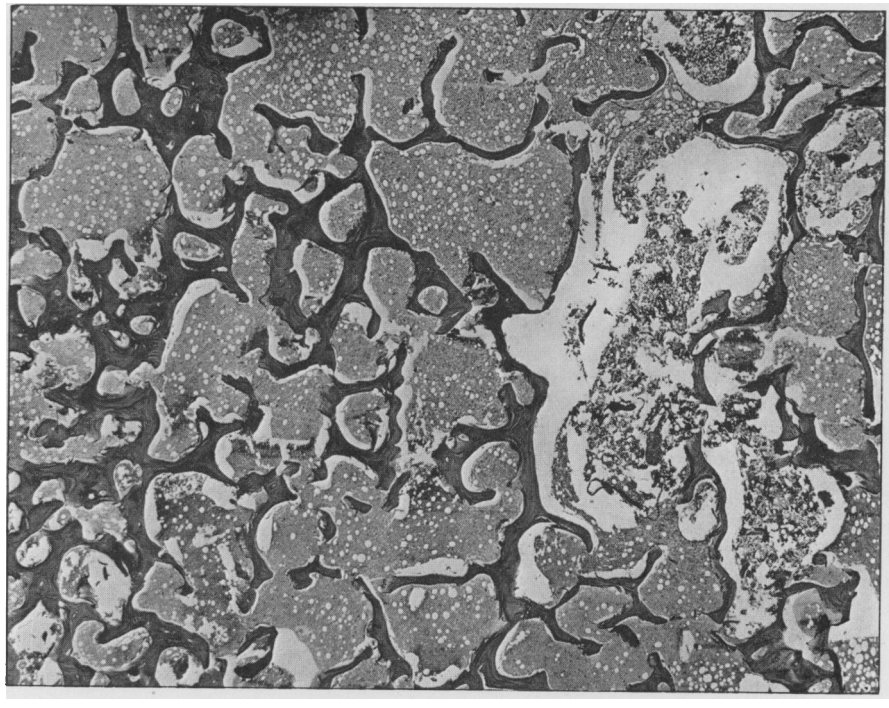

FIG. 8.—Microscopic Section of Vertebra.

intervertebral discs in the lumbar region with increased concavity of the superior and inferior surfaces of the bodies of vertebræ. Small irregular honeycombed cavities or spaces, measuring up to 5 mm. in diameter, are found in the cancellous bone of practically all the thoracic and lumbar vertebræ removed at autopsy (from 4th T. down). These spaces are present, one or two in each upper thoracic vertebra, situated midway between the intervertebral discs, on the concave side of the spinal column, close to the periosteum. In the lower thoracic and upper lumbar vertebræ they are present in large numbers, forming a zone extending anteroposteriorly across the middle of the vertebræ. In between these spaces the bone trabeculæ appear to be thinner than normal.

Microscopically, the bone-marrow of the femur showed moderate hyperplasia. The bone-marrow of the body of a lumbar vertebra was very cellular. The trabeculæ in the central portion were very thin; in many places they were absent. In addition a few irregular large spaces containing a small amount of homogeneous pink staining material were found.

The fœtus showed fœtal rickets (fig. 9). It was a male, weighing 3,000 grammes (Hospital No. 40777).

The X-ray report was as follows:—"*Extremities*: Evidence of osteoporosis at the ends of the long bones. There is irregularity of the epiphyseal ends of the radii, ulnæ, femora, tibiæ and fibulæ. This finding is typical of rickets, though not marked. *Ribs*: There is definite, though moderate, enlargement of the sternal ends of the ribs. Flaring of ribs noticed on both sides."

Dr. Hu's report of the autopsy contained the following notes:—

"The parathyroids could not be found.

Bones: Ribs. The costochondral junctions show slight enlargement, with slight broadening of the lines of ossification. Humerus, radius, ulna, femur, tibia and fibula are longitudinally cut open. Their lines of ossification show no visible change to the naked eye that is indicative of rickets."

But the microscopical examination proved quite definite:—

"*Ribs*: The line of ossification is very irregular, due to the presence of large or small islands of cartilaginous tissue remaining uncalcified in the marrow cavity. The cartilage cells above the line of ossification show a rather disorderly arrangement. The blood-vessels in the ossifying zone show marked congestion. The bony trabeculæ, even a long way from the line of ossification, still show numerous areas of osteoid tissue. The bone-marrow of the rib is not remarkable. *Humerus*: The lower end of the humerus also shows a very irregular line of ossification. Broad or narrow tongue-like protrusions of cartilage are present in large numbers in between areas of myeloid tissue which is rather acellular, somewhat œdematous, and markedly congested. *Femur*: The upper end of the femur shows only slight irregularity of the line of ossification, there being only a few small areas of cartilage remaining incompletely ossified. The lower end of the femur, on the other hand, shows much less complete ossification of the cartilaginous tissue. Occasionally a small patch of degenerating cartilaginous tissue containing shrunken cartilage cells, the nuclei of some of which take a pinkish stain, is present. *Tibia*: The upper end of the tibia shows very marked irregularity of the line of ossification. Many long or large tongue-like processes of cartilaginous tissue are left behind, remaining uncalcified. The myeloid tissue in between these cartilaginous masses is intensely congested, and oftentimes markedly hæmorrhagic. There is a good deal of œdema, but the number of myeloid cells is small. The lower end of the tibia also shows well-marked disturbance in ossification. The change is similar to that found in the upper end of the same bone. *Vertebra*: A horizontal section of the vertebra also shows slight irregularity of the line of ossification."

The spine of this mother with osteomalacia shows well the bulging of the intervertebral discs into the osteoporotic bodies. This is a characteristic feature of osteomalacia, and the characteristic spinal deformity is in part due to it. The condition has been well described by Beadle [2] in his monograph on "The Intervertebral Discs." The spaces in the vertebræ described by Dr. C. H. Hu in the autopsy report have been noted by Schmidt [26] as occurring in sections of a rib

from a case of osteomalacia, but as far as one knows they have not been described as being found in the vertebræ.

It will be noted that this paper is entitled: "Adult Rickets (Osteomalacia)." The time has come when it should be frankly recognized that these are one and the same disease.

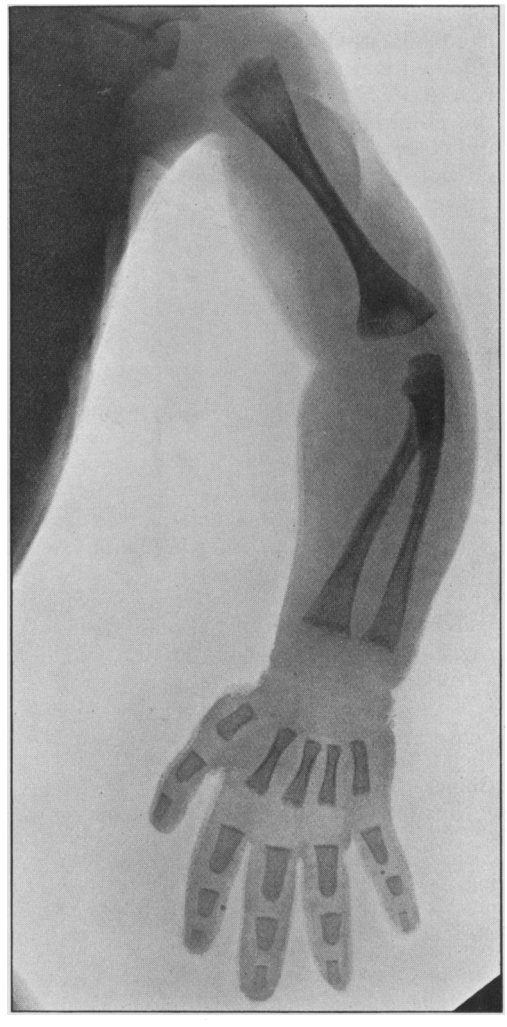

FIG. 9.

It is now possible, as will be seen later on, to bring out more clearly than before the intimate connexion between adult rickets, fœtal rickets, infantile rickets and late rickets. Granted that the mere fact that an osteomalacic mother has a child with fœtal rickets does not prove the identity of the disease, the evidence of the intimate connexion of the two has become so full as to make it extremely unlikely that they have no causal connexion.

In fact the evidence is such as to make it very doubtful in some cases whether the disease should be classified under late rickets or osteomalacia, and it is clear that what one previously considered as classifying points between osteomalacia and rickets can no longer be maintained.

Take an example. The typical deformity of the pelvis in a case of rickets consists in the flattening of the pelvis, the outstanding alteration in the sacrum being an increase in the transverse convexity, whereas the typical deformity of the pelvis in a case of osteomalacia shows itself in the marked concavity which the sacrum acquires, and in the marked narrowing of the outlet, and in the formation of what is practically a triradiate pelvis. But Ogata [3] has pointed out that whereas in Europe the children are kept on their backs previous to walking, in Japan they sit in straw baskets or are carried on the back in a sitting posture, and in these cases you do not get the typical flat pelvis, but one which approximates to what one has called the osteomalacia type.

With regard to these deformities, Park [4] also writes as follows:—

"I wish to point out that the deformities caused by rickets follow different patterns at different age-periods, depending entirely on the time in the child's life when the rickets develops and flourishes. . . . Indeed, from the fifth year on, rickets bears an increasingly close resemblance to osteomalacia."

Further experience in the clinical signs and symptoms of the disease has revealed a very marked difference, which I have noted in previous papers [1, 24], in the severity with which the affection attacks various parts of the body. There is also a very great difference as to the amount of suffering experienced by various patients.

Here is a patient aged 29. Her disease commenced at the end of a prolonged lactation (four years) with the onset of another pregnancy. During this pregnancy the disease progressed rapidly, causing severe deformity of the chest, but not affecting the pelvis to any marked degree till after the spontaneous birth of the full-term child, when the pelvis began to be affected, and in less than two months was fractured and so deformed that a spontaneous labour would have been out of the question. And except in the last two months she seems to have suffered surprisingly little from pain.

The details of this case are as follows:—

Mrs. P. J., aged 29, Chinese, Hosp. No. 42452, married at the age of 23. She bore a full term, healthy baby when she was 24. Nursed the baby for four years. One month later impairment of appetite. January 1933, she had some respiratory difficulty. February 1933, deformity of chest and shortening of stature were noticed. April 1933, pain in legs and difficulty in walking. On September 6, 1933, a full-term child was born without assistance, and the patient was able to get up and walk in a month. Her milk was abundant but of poor quality, the calcium content being very low, 17·7 mgm. per 100 c.c., and the fat content deficient. Her blood calcium on admission was 7·3 mgm. per 100 c.c. of serum, and blood phosphorus 4·0 mgm. per 100 c.c. of serum. She was admitted on November 11, 1933. The baby was puny, the subject of rickets, almost certainly fœtal, and died twenty-four hours after admission. Measurements of mother's pelvis:—

Interspinous ...	...	...	23·5 cm.
Intercristal ...	...	...	25·5 ,,
External conjugate	...	...	15·5 ,,
Interischial ...	...	...	5·5 ,,

Marked kyphosis and scoliosis.

The pelvis shows deformity and fractures which have come on since September 6, 1933.

According to Schmorl [5], the chronological sequence of rickety manifestations is as follows:—

Costochondral articulations.

Lower epiphysis of femur.

Upper epiphysis of humerus, tibia and fibula.

Lower epiphyses of radius and ulna.

Upper epiphyses of femur, metatarsus and phalanges of feet.

But one sees no reason why the deformity in adults should fall on the chest before the pelvis. Ballin [6] points out that in hyperparathyroidism there is the same uncertainty as to the localization of the bony changes.

Looking at these facts about the genesis of rickety deformities of the pelvis one is led at once to the consideration of another form of deformity, i.e. that of the "funnel" pelvis. In one of my earlier papers [24] on osteomalacia, I hinted that it was possible that some, if not most, of these pelves were really due to mild forms of osteomalacia.

I would now propose to go further and reclassify the flat pelvis, the funnel pelvis, the osteomalacic pelvis and the pseudo-osteomalacic rickety pelvis in the following way:—

Deformities of the pelvis due to rickets:

(1) *Flat pelves* due to rickets in infancy, before walking has commenced and where the child has been kept on its back.

(2) *Triradiate pelves* due to rickets in infancy when, instead of lying down, the the child is carried about in a sitting posture.

(3) *Funnel pelves* due to rickets in childhood or adolescence.

(4) *Triradiate pelves* due to adult rickets, i.e. osteomalacia.

Of course a deformity due to rickets may also be grafted on any of the congenital forms of deformity of the pelvis, such as a small round pelvis, and the rickety deformity of the pelvis may be modified by the development of scoliosis or kyphosis.

It may be asked what evidence there is for so definitely classifying the funnel pelvis amongst those whose genesis is due to rickets, because the characteristic form of the pubic arch after infantile rickets is a very wide arch.

(1) During the last few months two foreign patients have come to me, neither of whom was aware that there was anything wrong with the pelvis. Both of them are marked examples of funnel pelvis, the interischial diameter being below 7 cm. in each case, and the posterior sagittal diameter being also somewhat diminished. In the one case there was a frank history of rickets in childhood, and the patient has a moderate amount of bow leg. In the other case the patient did not walk till she was sixteen months old, and then very unsteadily for another year. And her mother, who knew what rickets was, having suffered from it herself, was of the opinion that the surmise that her daughter had had rickets was correct.

In these cases, as a rule, the infantile rickets has not been very severe, and although in several other cases in the last ten years I have been able to elicit a history which pointed to rickets, as a rule the patients know little about their past history in this respect.

(2) Twice in patients who were developing osteomalacia, I have seen the interischial diameter diminish whilst under treatment, so that when cured they were left with what, were it not for the history, would be deemed a typical funnel pelvis.

(3) Here is another woman, a Chinese, whose three previous labours were normal, and who came for her fourth labour with a typical funnel pelvis, needing a

hard and difficult forceps extraction in which the child nearly died. She had a blood-calcium of 8·5 mgm. per 100 c.c. of serum, and it was clear that she had a mild osteomalacia.

In these cases there is little if any alteration in the measurements of the inlet, and from the point of treatment it is imperative that they should be diagnosed early; for the majority, if at all marked, need a delivery by Cæsarean section. Otherwise not only does one run the risk of having to end the labour by a perforation, but even where a child has been delivered through the vagina, the pelvic floor and possibly rectum are apt to be seriously damaged, leading to lifelong disability.

Another interesting clinical phenomenon in rickets is that of the development of Harrison's groove. This is "a furrow or concavity which runs horizontally across the lower plane of the thoracic wall at the level of the diaphragm and extends anteriorly from the base of the ensiform cartilage to the posterior folds of the axilla. Generally it is less marked on the right than on the left side due to the underlying support of the liver" (Hess).

It may be noted in mild cases of rickets, and is supposed to be due to the tugging of the diaphragm on a weakened chest well.

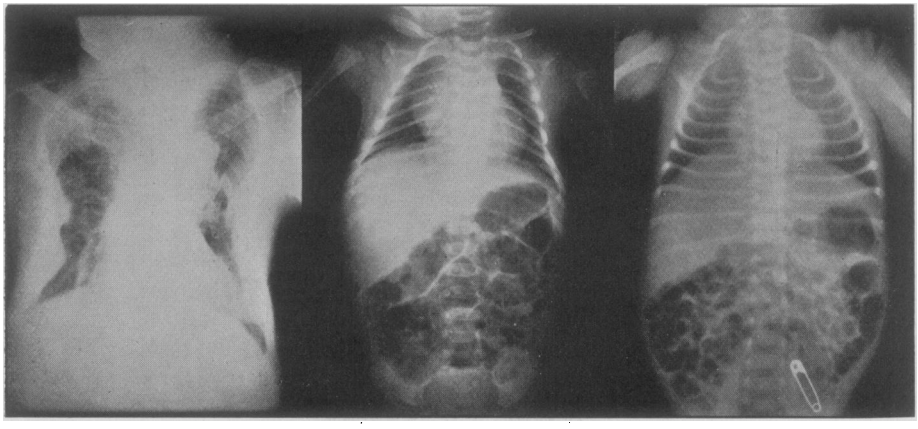

FIG. 10.—Harrison's groove in fœtal rickets and osteomalacia.

It is interesting to note the occurrence of this groove not only in infantile rickets, but both in fœtal rickets and in osteomalacia. Whether it develops before breathing commences is difficult to say, but as will be seen by fig. 10 it develops, not merely immediately after birth as in the case of antenatal rickets, but is also found in marked cases of osteomalacia. Its genesis is not perfectly clear and in our cases the groove appears to be a little high up on the chest.

Hess [7] has well shown the fallacy of the old reports on the question of the coexistence of osteomalacia and rickets. In the first place it is clear that many of the older reports on the non-coexistence of osteomalacia and rickets in regions where the former disease is common were inexact, due to the fact that the latter disease was not properly sought by skilled observers and that its milder symptoms were missed. Rickets was judged to be practically absent in North China, but the work of Ernest Tso [8] and the experience of the Pediatric Department of the Peiping Union Medical College Hospital has shown that so far from this being the case, it is very common in this locality.

We have also Green-Armytage's dictum [9] as regards the connexion between osteomalacia and rickets in India. He says: "Moreover, all babies born of osteomalacia mothers later tend to develop rickets. We have seen a great number of these children with typical rachitic phenomena between the years of one and eight." Finally, Ogata [3] in his second report on osteomalacia in the district of Toyama, Japan, gives figures to show that rickets was found plentifully in children in this region.

And in considering this question one has to remember the nature of the environment in the regions where osteomalacia is present in the Far East. The sun's rays are not filtered by the smoke of large cities, the amount of clothing worn by infants and young children varies immensely from practically nothing to full clothing, and an outdoor life is the usual thing for those who survive the heavy neonatal mortality which eliminates a large number of those most likely to develop rickets.

And when one comes to the question of late rickets and its relation to osteomalacia, our knowledge on this point has been materially advanced by the work of Stapleton [10] and of Wilson and her associates [11] in India. They have shown most conclusively that the two diseases blend into one another.

That the same is true, as regards China, is well shown by the following three cases:—

Miss W. H. H., aged 16, Hosp. No. 37244, was seen on July 15, 1933, in the Peiping Union Medical College Hospital.

She had been limping for four to six months. Coming from a poor family, at the age of 12 she became a maidservant. Her food had been mainly rice and vegetable. At about that age she had noticed a slight disability in walking, but it had not really troubled her till four months previously. Two months previously she had noticed that the left leg was adducted in walking. She has had little pain, but when present it was dull in character and in the bones. Menstruation had been present for three months. Her legs were bowed outwards to right, the right exhibiting a condition of bow leg, the left exhibiting a condition of knock the knee. On admission her blood calcium was 10·3 and phosphorus 3·1. Her interischial diameter measured 6·75 cm.

The report on the roentgenograms contained the following paragraphs:—

Legs: There is a mild anterior bowing of the right femur and mild bowing of the distal third of the right tibia. Periosteal new bone is seen along the medial aspect of the distal third of the right femur. The right leg shows marked deviation with the right ankle pointing toward the left foot; this deformity is more of an angulation of the leg at about the knee-joint, apparently due to maldevelopment of the proximal epiphysis and metaphysis of the right tibia. The metaphyses of the bones of both legs show localized absorption, slight expansion and irregularity. Along the shaft of the fibula at the junction of the middle and distal thirds there is some localized periosteal thickening.

Wrists: There is mild, but definite, generalized osteoporosis of the bones of the wrists and hands. The metacarpals appear shortened. The spectacular changes are in the metaphyses of the ulna and radius in both wrists—localized absorption, slight expansion and irregular outline, characteristics of adolescent rickets.

Pelvis: Generalized osteoporosis of the bones of the pelvis and both femurs. The trabeculæ of the bones are very coarse. There is marked, localized decalcification of the pubis and to certain extent the ischia. Mild but definite approximation of the acetabula is noted as in cases of mild osteomalacia.

The impression was that the findings in the metaphyses suggested adolescent rickets whilst the deformity of the pelvis suggested osteomalacia (*see* figs. 11 and 12, p. 14).

The second case is that of Miss C. C., aged 18, Hosp. No. 38581, admitted to the Peiping Union Medical College Hospital on December 20, 1932.

About March 1931, patient found herself getting weak, and she was seized by attacks of sharp pain, intermittent and radiating, starting from the middle of the left inguinal region and passing down the left leg. Two months later pain started in the left knee. In July

1931, the right inguinal region began to give pain, and shortly after the right knee also started. Since July 1932, she has been limping and found it difficult to assume the erect posture.

Her diet has consisted of two meals a day, flour, rice, and vegetable, no meat, eggs or fish.

Her pelvis showed contraction of the interischial diameter, slight rostration and she had typical pain and spasm of the adductors of the thigh.

Her blood calcium was 8·4 mgm. per 100 c.c. of serum and blood phosphorus 2·9 mgm. per 100 c.c. of serum. Chovstek's sign positive.

There was a distinct tendency to pigeon chest, and the costochondral junctions were somewhat enlarged. There was a definite knock knee (see figs. 13 and 14).

The X-ray report may be summarized as follows: All the bones seen are osteoporotic and slightly washed out in appearance. The pelvis is about normal in shape with slight narrowing of the pelvic arch. An old fracture is noted about two inches below the head of the right fibula. The epiphyseal lines of the lower ends of both femora are clouded which is suggestive of remnants of old rickets. Slight medial angulation noted at both knee regions.

All the visualized vertebral bodies appeared osteoporotic. The skull was normal in shape but the cranial bones presented a washed-out appearance.

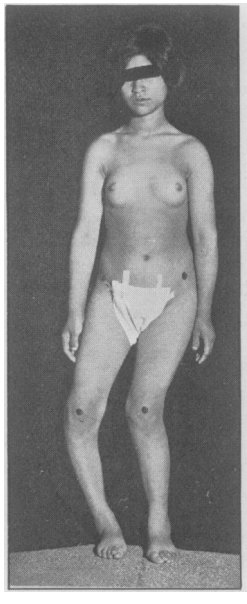

FIG. 11.

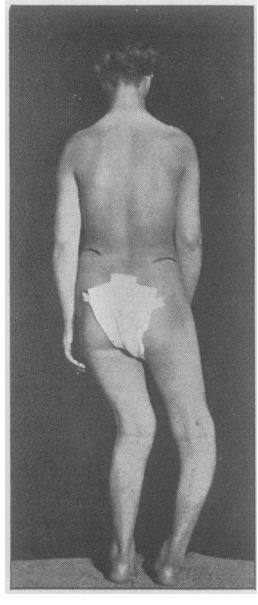

FIG. 12.

Late rickets (Case 1).

There is no doubt that in this case the pelvis illustrates the commencing deformity of an osteomalacia case, whilst the knock knee, and the epiphyseal lines of the radii and ulnæ, show the lesions one has been accustomed to associate with rickets.

The third case is the most remarkable of the three, for in it we see a complete sequence of late rickets, osteomalacia, and fœtal rickets.

Mrs. C. U. C., aged 30, Chinese, Hosp. No. 43815, was admitted to the Peiping Union Medical College Hospital as an emergency case in February 1934. She was in the thirty-eighth week of her first pregnancy; the membranes ruptured seven hours before admission,

labour having lasted about nine hours. Delivery of a living child from below was impossible, and the fœtus, though alive, was in distress, and died just as the Cæsarean section was starting. Her history was as follows: Menstruation started at the age of fourteen, and about three months later she began to suffer from pain in the thighs and later on in the back. It was worse on walking, and especially on going up hill. This went on, better in the summer, and worse in the winter, till she was married at the age of twenty. After marriage the pain became somewhat worse, and at the age of twenty-three, while helping to carry a box, she had spontaneous fractures of the left clavicle and left forearm. Since pregnancy started she has been much worse. In the fourth month she had diarrhœa, and during the last six months she has had much pain and disability, walking being practically impossible during the last three months. Since the beginning of pregnancy she has been off her food, and this has been marked during the latter half of pregnancy.

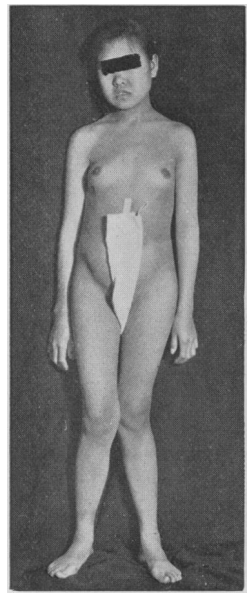

FIG. 13.

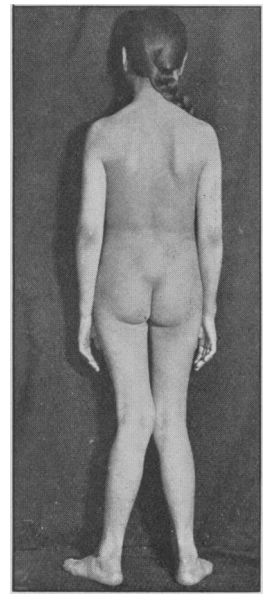

FIG. 14.

Late rickets (Case 2).

The diet during her girlhood was fair, but she was very little out of the house. After marriage the food was worse, and of late she has taken two meals a day of wheat-flour cakes, fried in sesame oil, rice gruel, maize cakes and a little celery cabbage.

Calculating the diet it works out as follows:—

Calories	1,146	
Protein	32·4	grm.
Fat	13·3	,,
Carbohydrates	223·6	,,
Calcium	0·06	,,
Phosphorus	0·276	,,
Vitamins	Poor	

Her blood calcium was 7·8 mgm., and her blood phosphorus 2·36 mgm. per 100 c.c. of serum.

She is short in stature with marked bow legs (fig. 15). The pelvis is deformed in the usual way (fig. 16), and the left clavicle and forearm show signs of old fractures (fig. 17).

The fœtus was a typical example of severe fœtal rickets, and its cord blood contained 8·83 mgm. of calcium per 100 c.c. of serum. The X-ray report on the fœtus was as follows:—

There is saw-like irregularity and fraying of the metaphyses of all the long bones of the extremities. The cortex of the bones is slightly thinned and osteoporotic. The sternal ends of the ribs show slight expansion. No periosteal changes seen (*see* figs. 18 and 19).

It may be justly said that this is a calcium rickets series. There is probably a phosphorus osteomalacia, but it is the rarer form, whilst in the West the usual form of rickets is the phosphorus deficiency one.

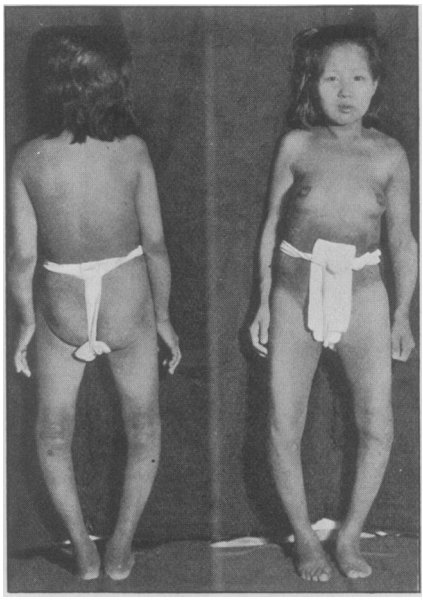

FIG. 15.—Late rickets (Case 3).

As Shipley, Park, McCollum and Simonds say [12] :—

" It must be remembered that rickets can be produced in the absence of vitamin D either by diminishing the phosphorus in the diet and supplying an optimum or excess of calcium, or by reducing the calcium and maintaining the phosphorus at or near optional concentration."

But it is a question whether the cause of rickets is merely a matter of absence of vitamin D and disturbance of the mineral balance.

The matter of the supply of calcium and phosphorus in the diet has been already mentioned and will be further discussed.

Dr. R. R. Hannon has pointed out to the writer that the question of the relation of the endocrine secretions to the causation and healing of rickets has still to be worked out. It is certain, for instance, that thyroid gland secretion plays its part in the matter, but whether by a direct action or by its influence in metabolic processes is not known. Rickets, like changes in the bone which will not be cured by cod-liver oil, may be associated with hypothyroidism, and it is possible that the secretion

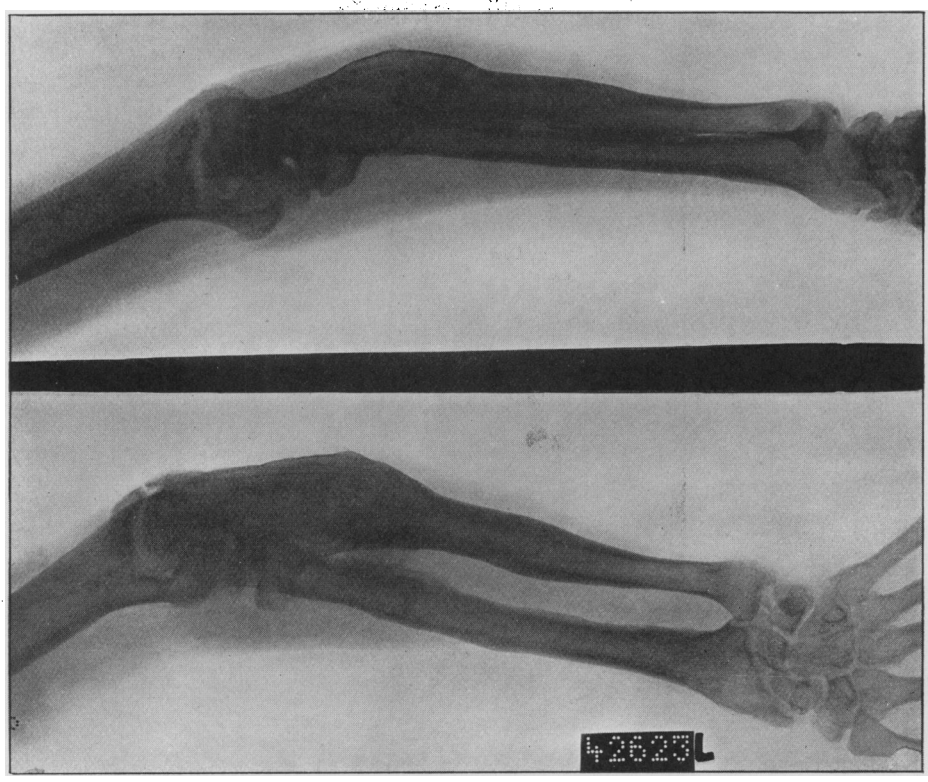

FIG. 17 (Case 3).

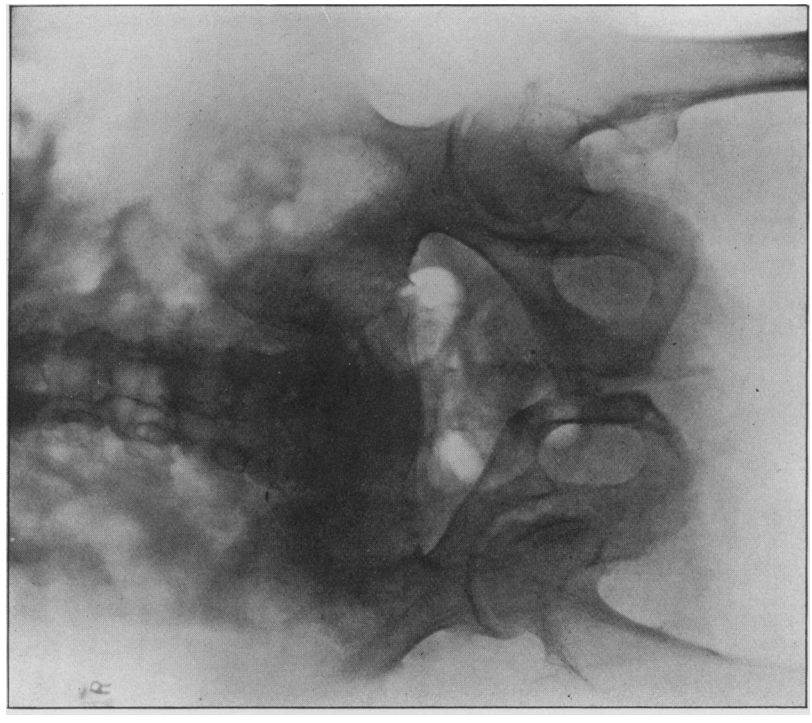

FIG. 16 (Case 3).

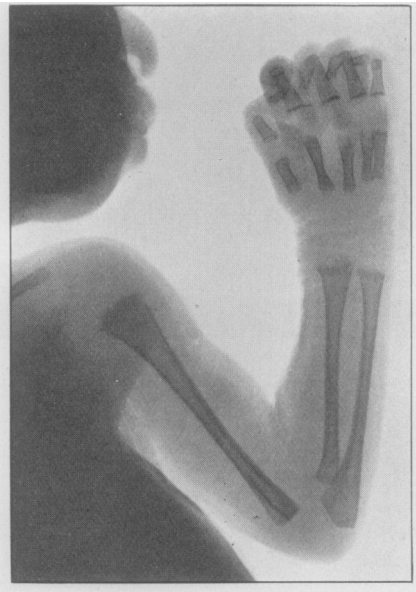

FIG. 18.

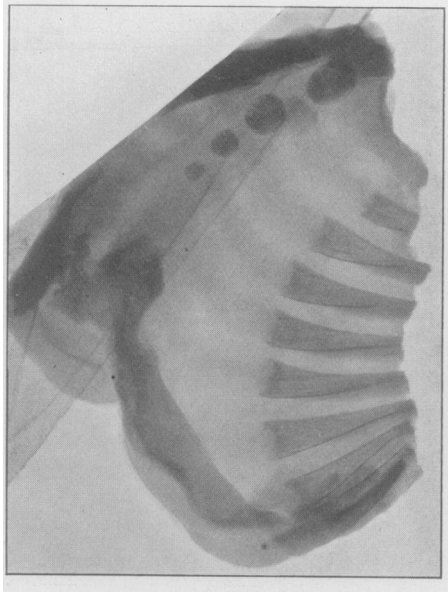

FIG. 19.

FIGS. 18 and 19.—Fœtal rickets (Case 3).

of the pituitary, adrenals and the parathyroids is not without its influence in the matter.

It must also be noted that tetany in babies born of osteomalacic mothers is by no means unknown.

Hess [7] says:—

"It has long been recognized that there is an intimate relationship between infantile tetany and infantile rickets. Indeed Kassovitz regarded tetany merely as a nervous manifestation of rickets, and Shipley, Park, and their colleagues refer to it as the low-calcium form of this disorder. Although tetany may occur occasionally in an infant free from rickets, from a clinical point of view it may be considered that practically all infants with signs of tetany, if followed long enough, are apt to develop rickets to some degree."

The question of the apparent absence of pain in the ordinary case of rickets has never yet been solved. But one has to remember that the majority of the cases of rickets in the West are apparently due to a phosphorus, rather than a calcium, deficiency. One also has to remember that the sensitiveness of an infant to pain is distinctly less than that of an older child or adult. Park and Eliot [13] note the occurrence of pain in the older child, and the occurrence of greenstick fractures, very similar to those one gets in osteomalacia.

Has any further evidence come forward which would modify our views as to the question of these diseases being due to a deficient diet, and in what respect does this deficient diet fail? In an article entitled "Osteomalacia and diet" [14] this question has been fully discussed. Here is a specimen diet which is representative of the food which Northern Chinese poor patients consume:—

Total calories	1,188
Protein	29·3 grm.
Fat	22·01 „
Carbohydrate	212·55 „
Calcium	0·249 „
Phosphorus	0·522 „
Vitamins	poor

This diet consists of varying quantities of corn bread, white flour, rice, millet, kaoliang and vegetables, with practically no meat, milk, eggs, or animal fats; sesame oil being mainly used for cooking.

Not only is the general caloric intake low, but the protein is of poor quality, the staple food is cereal, which is rachitogenic; the carbohydrate supplies 72·9% of the calories, the mineral supply is below the normal, and the supply of vitamins, especially vitamin D, is poor.

And in many of our osteomalacia cases the caloric intake is well below the figures given in this representative diet.

Compare this diet I have just given with that which Hamill's Report [15] lays down as containing the necessary requirements of a healthy working woman.

Total calories	2,500
Protein	90 grm.
Fat	75 grm. average (minimum 20 grm.)
Calcium	0·6 grm. minimum
Phosphorus	1-2 grm.

Carbohydrates may provide 50-70% of the calories, but if the percentage of calories derived from carbohydrates rises much above 66% the diet may be considered to be in need of improvement. Moreover, the protein should be first-class, and there is no first-class protein in the diet of these patients.

One of the interesting points about adult rickets (osteomalacia) is the early symptoms of the disease especially in pregnancy cases. It was pointed out in a previous communication [16] that excessive motion on the part of the fœtus was an early sign, and that under appropriate treatment with calcium and vitamin D these excessive movements would cease. Another of the early symptoms of a calcium vitamin shortage is pain in the back.

It is possible also that some patients who suffer badly from cramps in the legs towards the end of pregnancy are in a like condition, for occasionally a little irradiated ergosterol will entirely relieve this symptom. It may be argued that it does not follow that the medicine was the cause of the improvement, but it is certainly worth bearing in mind, for some of these so-called minor troubles give one's pregnant patients great discomfort.

To turn now to the question of fœtal rickets. Here are tables (Table I) showing the details of the first sixteen cases of the disease which have been diagnosed by us, and notes on three other cases (in Table II) which come very near to falling into the same classification. I think it is clear that, if sought, fœtal rickets will be found to be far from uncommon. It is certain that a very large number of pregnant women are living on the edge of a serious deficiency of vitamins and salts, as we have already demonstrated.

What are we to accept as the standard figures for calcium and phosphorus in the maternal blood stream and in the cord blood?

There is considerable variation in the figures given by Bogert and Plass [17, 18] and by Denis and King [19]. Peters and Van Slyke [20] place the average value between 9 mgm.-11·5 mgm. calcium per 100 c.c. of serum for normal individuals. Some workers, such as Bogert and Plass, give the figure for calcium at "term" at 9·1 mgm.; others such as Denis and King place it at 10-11 mgm. per 100 c.c. of serum. So that we shall not be far wrong if we average these latter figures and arrive at the following standard (mgm. per 100 c.c. of serum):—

Normal non-pregnant women:		
	Calcium	10·25
	Phosphorus	3·00
Pregnant women at term:		
	Calcium	9·50
	Phosphorus	3·10
Cord blood:		
	Calcium	10·90
	Phosphorus	4·50

Serum-calcium is supposed to be appreciably lowered in the later months of gestation in the mother and definitely raised in the newborn, though whether this is strictly physiological is not fully known. And so far there has been no adequate explanation given of the mechanism by which this concentration in the cord blood is carried out. The substances thus concentrated are those specially needed for the building up of new tissue in the fœtus. On the other hand, total plasma and serum proteins are lower in the pregnant and parturient woman than in the non-pregnant, and still lower in the fœtus at birth.

We have conducted extended investigations into the matter of the calcium and phosphorus figures in the blood-serum in our patients to see how far they correspond with the normal figures given above.

The calculations of the calcium have been made by Kramer and Tisdall's [21] method, and the calculations of the phosphorus by the Briggs' modification of the Bell-Doisy method [22]. Practically all have been done by one technician,

TABLE I.—FŒTAL RICKETS

Date and number	Age Mother	Ca Mother	P Mother	Para	Mother's condition	Week of delivery	Method	Evidence of Rickets	Cord Ca	Cord P	After-history of child.
(1) Dec. 1927	39	—	—	V	Osteomalacia. Pulm. tb. Died 2 months later.	Term	C. S.	X-ray and Sections	—	—	Weight 2,040 grm. Died 5th day, hæmorrhage
(2) *23871* April 1929	38	4·7 mgm.	1·8 mgm.	VII	Osteomalacia. Tetany.	Term	Normal labour	X-ray	4 days 10·16 mgm.	pp. 8·25 mgm.	Rickets healed 38 days. Well.
(3) *34053* Nov. 1931	34	4·5 mgm.	3·1 mgm.	II	Osteomalacia. Pulm. tb. Died 3rd day.	38th	C. S. Hysterectomy	X-ray	7·6 mgm.	—	Improved slowly.
(4) *30741* Jan. 1931	38	7·83 mgm.	—	VI	Osteomalacia. Pulm. and spinal tb. Died 14th day.	Term	C. S.	X-ray. Clinical evidence. Sections.	10·6 mgm.	—	Died 65 hours after birth. Hæmorrhage.
(5) *34611* Jan. 1932	26	—	—	V	Early osteomalacia. No pelvic deformity.	38th	Normal labour	X-ray	8·8 mgm.	—	Rickets improved slowly. Well.
(6) *35880* May 1932	19	5·4 mgm.	2·9 mgm.	I	Tetany on verge of osteomalacia.	Term	Normal labour	X-ray	8·1 mgm.	4·2 mgm.	Rickets improved slowly Jan. 1934, Teeth characteristic.
(7) Jan. 1933	31	—	—	III	Osteomalacia.	Term	C. S.	X-ray	—	—	Baby doing well.
(8) *38841* Jan. 1933	24	4·65 mgm.	3·15 mgm.	III	Osteomalacia.	38th	C. S.	X-ray. Sections.	5·6 mgm.	—	Died in utero just before birth.
(9) *36682* July 1932	39	7·8 mgm.	2·0 mgm.	II	Osteomalacia. Late rickets.	Term	C. S.	X-ray	9·3 mgm.	4·4 mgm.	—
(10) *37465* Sept. 1932	25	8·3 mgm.	2·2 mgm.	I	Osteomalacia. Funnel pelvis.	Term	Craniotomy	Sections	—	—	—

TABLE I.—FŒTAL RICKETS (*continued*)

Date and Age	Age Mother	Ca Mother	P Mother	Para	Mother's condition	Week of delivery	Method	Evidence of Rickets	Cord Ca	Cord P	After-history of child
(11) *39549* March 1933	33	9·1 mgm.	2·7 mgm.	IX	Osteomalacia.	37th	C. S.	X-ray	9·1 mgm.	3·3 mgm.	Unknown.
(12) *40777* July 1933	43	—	—	V	Osteomalacia. *B. welchii* infection.	Term	C. S. Hysterectomy	X-ray. Sections.	—	—	—
(13) *43773* Feb. 1934	27	8·35 mgm.	1·33 mgm.	IV	Osteomalacia.	36th	C. S.	X-ray. Clinical evidence.	10·8 mgm.	2·66 mgm.	Well.
(14) *43746* Feb. 1934	30	9·15 mgm.	2·0 mgm.	IV	Osteomalacia.	38th	C. S.	X-ray. Clinical evidence.	9·35 mgm.	—	Well.
(15) *43817* Feb. 1934	30	7·8 mgm.	2·36 mgm.	I	Osteomalacia. Late rickets.	38th	C. S.	X-ray. Sections.	8·83 mgm.	—	Stillborn.
(16) *43804* Feb. 1934	32	8·4 mgm.	3·16 mgm.	VII	Avitaminosis. Pt. apathetic; 5 children died of convulsions in childhood.	Term	Normal labour	Clinical evidence confirmed by X-ray	—	—	Well.

TABLE II.—FŒTAL RICKETS

The following cases are appended because their symptoms point so strongly to the presence of a pre-rickety fœtal condition, and it is noteworthy that all three are the low calcium type of rickets in contradistinction to the usual infantile type which is a low phosphorus rickets.

31260 (1) March 21, 1931	50 days old	Tetany commenced on the 45th day	Rickets suspected on admission	Confirmed by roentgenographic evidence	Ca 7·8 mgm. on admission.
36217 (2) June 6, 1932	Born in Hospital	Tetany commenced on the 21st day	Rickets suspected	Confirmed by roentgenographic evidence	Ca 7·8, P 8·8 on readmission.
		(Mother, on July 7th, 1932, Ca 8·5, P 4·1. Milk was calcium short.)			
36291 (3) June 13, 1932	77 days old	Tetany commenced on the 28th day	On admission marked rickets	Roentgenographic evidence of rickets	Ca 7·5, P 6·5 on admission.

Mr. Chuan, whose figures have been checked up from time to time by some of my staff, especially by Dr. S. W. Lee.

There has been no selection of patients except as noted below.

Obstetric cases: Chinese pregnant women, general average:—

(1,448 patients, calcium and phosphorus)
(110 patients, calcium only)

Calcium ...	9·43
Phosphorus	3·30

Omitting the above 110 cases, which were more or less a selected group, we have the following figures:—

Chinese pregnant women, 10th to 20th week. 20% of the cases:—

Calcium ...	9·70
Phosphorus	3·48

20th to 30th week. 24% of the cases:—

Calcium ...	9·64
Phosphorus	3·20

30th week to term. 56% of the cases:—

Calcium ...	9·64
Phosphorus	3·26

Foreign pregnant women (66 patients):—

Calcium ...	9·67
Phosphorus	3·28

Gynæcological cases: Chinese gynæcological patients (408 patients):—

Calcium ...	9·62
Phosphorus	3·40

Foreign gynæcological patients (36 patients):—

Calcium, average ...	10·13
Phosphorus, average	3·51

It will be noted that the whole of the figures run fairly parallel with the standard figures for the pregnant and non-pregnant women. But when one comes to deal with these cases more closely, it is found that 260 Chinese pregnant patients, or 16·68% of the total, had a blood calcium between 8·51 and 9·00. 85 Chinese patients, or 5·45%, had a blood calcium between 8·01 and 8·51, and in 38 Chinese patients, or 2·44%, the blood calcium was below 8 mgm. per 100 c.c. of serum.

Scrutinizing these last 38 cases, one finds that they classify themselves into:—

Cause unknown	7
Pregnancy and osteomalacia	7
„ „ accidental hæmorrhage	2
„ „ placenta prævia	3
„ „ eclampsia	2
„ „ cardiorenal disease	2
„ „ intestinal trouble (typhoid and dysentery complicating pregnancy)	2
„ „ pyelonephritis	2
„ „ anæmia	5
„ „ sepsis	2
„ „ tuberculosis	4

Turning to the cord blood figures, these are as follows:—
Chinese newborn infants (200):—

Calcium	... 10·71
Phosphorus	... 5·21

Foreign newborn infants (30):—

Calcium	... 10·9
Phosphorus	... 5·34

And again the figures bear a close resemblance to those obtained by other authors.

There is another interesting question. Is it possible that some of these infants have got a condition bordering on rickets, the signs of which might be visible in sections of the bones before one could obtain evidence by means of a roentgenogram? To try to settle this point a number of sections have been compared.

What does one understand as being the normal for such a section? Here is Turnbull's [23] summary of the position:—

"In a normal bone from a fœtus two main zones can be recognized in the cartilaginous epiphysis; an upper zone of resting cartilage and a lower zone of proliferating cartilage. The zone of proliferation itself shows three zones from above down: (1) A zone in which the multiplied cartilage-cells are arranged in groups which above are very small and round, but inferiorly increase in size and length; (2) a zone in which they are grouped in short, oval, vertical columns; and (3) a zone in which they are greatly swollen, and are arranged in long, wide columns. Zones (1) and (2) merge into each other, and are usually taken together as the zone of columns; zone (3) is the hypertrophic zone. The hypertrophic zone lies immediately above the epiphyseal line. The epiphyseal line is even and straight, except for one or more shallow upward indentations where relatively large vessels from the diaphysis anastomose with vertical chondral vessels. All the hypertrophic zone except a shallow strip in its upper part, is calcified, and constitutes the zone of provisional calcification."

The sections of the bones of fœtuses examined fall into three categories.

(*a*) Osteoporosis without any sign of fœtal rickets. A very good illustration of this was published in the paper by Maxwell and Miles on "Osteomalacia in China" [24]. The various zones spoken of above are all present, the epiphyseal line is even and straight, but the bone is markedly deficient in osseous tissue when compared with a normal specimen. The roentgenogram shows no sign of rickets. It is possible that in this case treatment of the mother before labour had modified the microscopical appearances.

(*b*) Fœtal rickets without any question. Both in sections and in the roentgenogram one has ample evidence of the affection.

(*c*) Early fœtal rickets, the roentgenogram showing no signs of the affection, but sections revealing a commencement of the disease. Here is an example of this class, there being probably many more existent, but undetected, as if the child lives and is properly fed healing takes place speedily. If not properly fed, the child will probably develop, early on, the signs of rickets.

Baby C. T. K., Hosp. No. 37465, was born dead on September 28, 1932. It had to be delivered by embryotomy.

The mother had osteomalacia. Her blood calcium and phosphorus figures were as follows:—

Calcium 8·3 mgm. per 100 c.c. of serum. Product 18·26.
Phosphorus 2·2 mgm. per 100 c.c. of serum.
On account of these a roentgenogram was taken of some of the baby's bones.

The report by Dr. T. S. Jung, of the X-ray Department, runs as follows :—

"On the whole the diaphyseal ends of the femur appear quite smooth and rounded. Slight tendency to floring is seen at one end of the humerus. Findings are not conclusive for fœtal rickets." But Dr. Ngai's report (Pathological Department) on these bones runs as follows :—

"The osteochondral junctions of these long bones show very slight irregularity in the line of ossification, especially the lower end of the femur and the upper end of the humerus. The costochondral junctions of the ribs are slightly enlarged, suggestive of a rosary, and show hazy and irregular lines of ossification. Microscopically : *Ribs*. The cartilaginous portion is not striking. The costochondral junction shows a moderate swelling. The line of ossification is irregular instead of being smooth and even as in the normal cases. Portions of the cartilage protrude into the narrow cavity for a considerable distance. In these cartilage protrusions blood capillaries are moderately abundant and are distended by red blood cells and calcification is not seen. In this zone, especially in the region near the cortex, the marrow cavities are slightly fibrotic, and contain few hæmatogenous cellular elements. The rest of the marrow cavities is normal except some post-mortem necrosis of the blood cells. The bony cortex and the trabeculæ also contain many foci of bluish cartilaginous masses, even for a considerable distance away from the metaphysis (*cf.* fig. 20, p. 26). *Humerus* : The upper end shows a slightly irregular line of ossification where a few cartilage tongues protrude toward the diaphysis. In these cartilage tongues the blood capillaries are much distended by red blood cells. The marrow cavities are not striking. *Femur* : The lower end shows the same type of change as above described, but the process is slightly more marked. In the epiphyseal cartilage portion, the small centre of ossification shows slight tendency to bone formation and calcification. The cartilaginous trabeculæ, which are in few places covered by thin layer of bone, project into the centre and often anastomose with one another."

So that I think it is justifiable to say that there are probably many cases of infants in whom, given an unfavourable environment, and improper food, rickets will develop very early.

On the other hand, judging from the fœtuses falling into the first category, is it not possible that there are a certain number of cases in which the deficiency is not one of avitaminosis, but of calcium starvation?

By the time the affection has advanced to the stage at which there is roentgenographic proof of rickets, it has become sufficiently stubborn to need considerable treatment—at least six weeks to two months—before the lesions can be seen to be healed.

Another point is raised by these tables. Is it possible to predict fœtal rickets before birth? Are the calcium and phosphorus figures of the mother's blood sufficient to suggest this possibility? Here are figures taken from the patients cited in Table I :—

FŒTAL RICKETS

Case II.	Mother's	Ca 4·7, P 1·8.	Product 8·46
,, III.	,,	Ca 4·5, P 3·1.	,, 13·95
,, VI.	,,	Ca 5·4, P 2·9.	,, 15·66
,, VIII.	,,	Ca 4·65, P 3·15.	,, 14·64
,, IX.	,,	Ca 7·8, P 2·0.	,, 15·60
,, X.	,,	Ca 8·3, P 2·2.	,, 18·26
,, XI.	,,	Ca 8·35, P 1·33.	,, 11·10
,, XII.	,,	Ca 9·15, P 2·00.	,, 18·30

It will be seen that in every case the product is under 20, and in the majority very much under this figure. But what of these figures? Are they really significant?

Whilst this table was being made out another osteomalacia case (Case XI) came in with obstructed labour. The mother's calcium was 8·35 mgm., and her phosphorus 1·33 mgm. per 100 c.c. of serum, making a product of 11·10. The

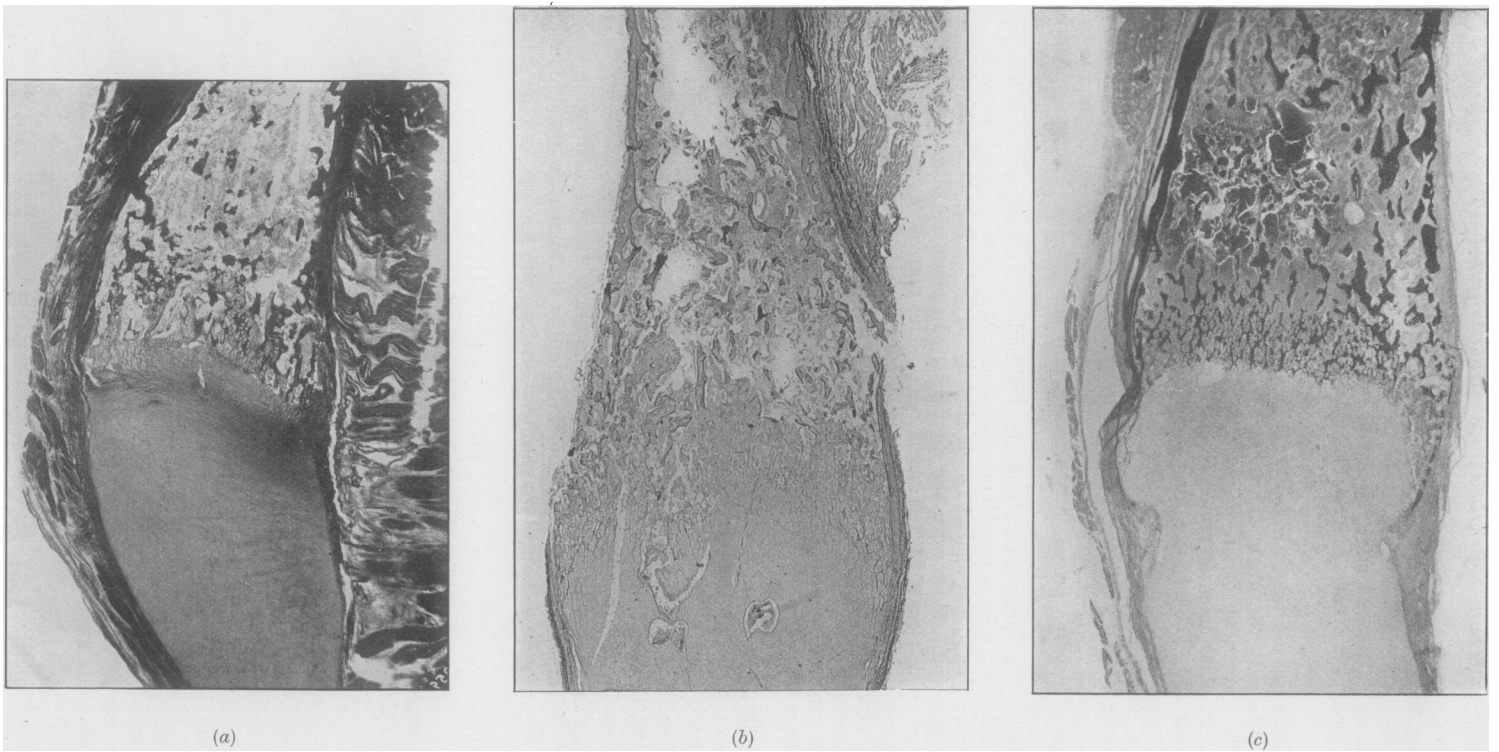

FIG. 20.—Osteochondral junction in (*a*) normal infant; (*b*) a case of very early fœtal rickets; (*c*) a case of marked fœtal rickets.

child's cord blood gave a calcium of 10·8 mgm., and a phosphorus of 2·66 mgm., or a product of 28·72. On these findings a diagnosis of fœtal rickets in the newborn was made and confirmed by roentgenograms.

Park in a paper on "Some Aspects of Rickets" [4] writes as follows:—

"Rickets is present or absent according to the relationship which prevails between the rate of lime-salt deposition and the rate of bone growth. If the latter just corresponds to the former, complete calcification prevails. If the latter exceeds the former, rickets develops."

If one expands the idea of bone growth to include bone replacement which goes on all through life, the dictum is also true of osteomalacia.

The practical result is that in his formula $\frac{Ca \times P}{\text{rate of bone growth}} = K_2$, if the rate of bone growth increases, the Ca × P must also increase for metabolism to be maintained at a constant figure.

It is possible that it would be a truer representation to translate the terms "bone growth" in the adult into "bone metabolism." It would explain the osteoporosis which one sometimes gets with hyperthyroidism, in terms of an attempt of the body to maintain the Ca × P figure to correspond with an increased metabolism. It would also explain the unwillingness of an osteomalacia patient to increase metabolism by movement as a desire on the part of the body to try to depress metabolic change to correspond with the calcium starvation.

What is the normal calcium figure in the serum in the adult? Park puts it as a more or less constant value of 10 ± 1 mgm. per 100 c.c. of serum, or a product (Ca × P) varying roughly between 20 to 37, but in any case not below 20.

In the very young the phosphorus figure is $5 \pm 0{\cdot}5$, and a factor of 50 may exist with evidence of rickets in premature and very young children.

So that one has to remember that Howland and Kramer's figure of 30 has to be accepted with caution in the very young. Below a figure of 30 you are certain to have rickets, but a figure over 40 does not, taken by itself, preclude its possibility.

Thus "the ætiology of rickets has two sides, so to speak, and some factors operate by affecting calcification and others by influencing growth."

I am inclined, however, to disagree with Park when he states: "If the patient is an adult, the calcium × phosphorus product under 30 does not have special significance."

Take for instance the following case:—

Mrs. C. L., aged 22, admitted to the Peiping Union Medical College Hospital on October 13, 1932, in great pain, bedridden, and four months pregnant.

Typical osteomalacia pelvis. Interischial diameter 6 cm.

	Ca and P	Product	Date
Bedridden and unwilling to move for the pain ...	Ca 8·8		
	P 1·6	14·08	Oct. 14
Pain improved, but still unwilling to move, walking round bed	Ca 8·5		
	P 2·5	21·25	Nov. 17
Still pain in chest and thighs but beginning to move about	Ca 9·0		
	P 2·3	20·70	Dec. 21
Walking about a little	Ca 8·6		
	P 3·4	29·24	Jan. 16
Walking well, pain all gone	Ca 8·8		
	P 3·8	33·44	Feb. 13
Condition good	Ca 9·0		
	P 4·2	37·80	Mar. 9

Cæsarean section on March 15, 1933.

Treatment throughout: Irradiated ergosterol, cod-liver oil, ultra-violet light and massage, calcium lactate 0·6 grm. daily.

As to the question of the possible prediction of fœtal rickets, it is certainly to be looked for in cases where the product of calcium and phosphorus in the mother's blood is below 20, and especially if the calcium factor is distinctly low. Where the calcium factor is high and the phosphorus figure low the probability is not so great.

Another question is raised by these findings: How far can one push back in antenatal life the roentgenographical appearances of rickets? It is not always easy to be actually sure of one's dates, but there was no doubt about the accuracy of the data in the ninth case in our list of cases of fœtal rickets (*see* Table I). In this case the baby was delivered by Cæsarean section shortly after the bursting of the waters. It was at least twenty-one days from term and the roentgenographic evidence of rickets was unequivocal. We have not yet definitely demonstrated fœtal rickets *in utero*, but in view of this evidence there is no doubt that there is a possibility of so doing, given a case with the fœtus lying so that a good view of the ends of the long bones could be obtained.

That there is little doubt about the genesis of these cases is proved by the history of two of our patients, whose children presented the signs of fœtal rickets, but in whom the avitaminosis and calcium starvation were arrested before they acquired the pelvic deformities of osteomalacia, so that there was no difficulty from the obstetrical standpoint in their having more children by the normal route.

Both these patients were treated, and were given instruction as to diet and the necessity of sunlight and movement, and both have subsequently borne children without any sign of fœtal rickets, though in the second case it is doubtful whether the child was not a weakling.

Here are the details of these two patients:—

Case I.—Mrs. C. C. S., aged 19, a primipara, was admitted to the Peiping Union Medical College Hospital on May 4, 1932, in labour.

She had been well till the seventh month, and then was ill in bed for six weeks without fever. She did not want to eat, and at the best she was getting a very deficient diet which worked out as follows:—

Total calories	963·0
Protein	33·1 grm.
Fat	17·9 ,,
Carbohydrates	166·3 ,,
Calcium	0·146 ,,
Phosphorus	0·649 ,,
Vitamins	Very poor

The baby weighed 2,200 grm. and its cord-blood calcium and phosphorus were 8·1 mgm. calcium, and 4·2 mgm. phosphorus per 100 c.c. of the serum. It presented unmistakeable signs of fœtal rickets. The mother's blood calcium was 5·4 mgm. per 100 c.c. of serum and phosphorus 2·9 mgm. per 100 c.c. of serum.

The mother had definite signs of a mild tetany but no clinical signs of osteomalacia. She had slight secondary anæmia (Hb. 66%). She was treated with irradiated ergosterol and good food, and by the time she left hospital her blood calcium was up to 10·2 mgm., and her blood phosphorus 4·2 mgm. per 100 c.c. of serum. After leaving hospital she took 25 mgm. of irradiated ergosterol spread over a month. Her diet was little improved, but she moved to a better and sunnier house and had no further illness. She also took care to eat what she could get. She was readmitted to hospital on July 12, 1933, and was delivered of a living female child weighing 2,315 grm., which showed no signs of rickets, and whose cord blood contained 11·0 mgm. of calcium and 5·16 mgm. of phosphorus. The mother's blood picture was normal and her calcium figure 9·51 mgm. per 100 c.c. of serum.

Case II.—Mrs. W. M. C., Hosp. No. 23784, a Chinese woman, first came to the Peiping Union Medical College Hospital in her fourth pregnancy and was delivered in April 1929 of a living, healthy child.

She came in again for another delivery in February 1932, having had several attacks of diarrhœa during the pregnancy, the last one being at eight months and lasting a month. It

was noticed when the child was born that the head was soft, with very large fontanelles. On an X-ray examination it was found to be suffering from fœtal rickets. It nearly died of melæna neonatorum, but recovered and, under treatment, was reared, but in 1933 still presented signs of healing rickets.

The patient came in again in September 1933. Her blood calcium was 8·9 mgm. and her blood phosphorus 1·54 mgm. per 100 c.c. of serum. On October 13, 1933, she was delivered spontaneously of a 2,635 grm. female child. Apparently the child was healthy, and roentgenograms showed no evidence of fœtal rickets. Its cord blood contained 10·5 mgm. calcium, and 3·63 mgm. phosphorus per 100 c.c. of serum. For a couple of days it did well, then rapidly failed, and died of an unknown cause. A very careful autopsy revealed no sign of rickets in the infant. The mother's diet had been poor, though not as bad as in the first case, and she was getting about 1,000 to 1,200 calories a day before the birth of her baby with fœtal rickets. Between this pregnancy and the last she had been taking more care about food and sunshine, though she was still not sufficiently alive to the dangers attending carelessness in this respect.

In both these cases we have women who have, in the matter of diet, been living near the starvation-line. In neither of them were there any frank osteomalacia symptoms, but in both cases the mother's blood figures for phosphorus and calcium had fallen considerably below the normal. Both of them, during the pregnancies

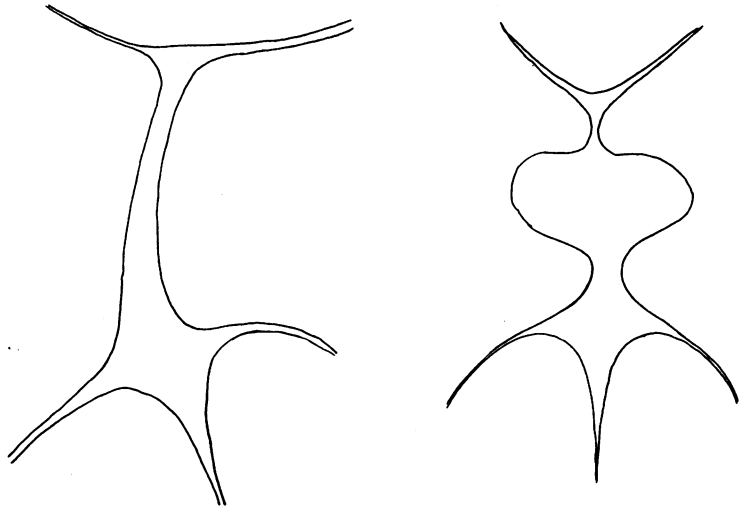

FIG. 21.—The fontanelles in two cases of fœtal rickets.

which resulted in the birth of a child suffering from antenatal rickets, had been troubled by attacks of diarrhœa and anorexia. And it raises a very definite question as to whether the diarrhœa was *due* to avitaminosis, or whether the diarrhœa interfered with the absorption of vitamin D. Probably both suppositions have an element of truth in them.

Do these children born with fœtal rickets present any special peculiarity about the cranial bones? In several of our cases we have had most striking enlargement of the fontanelles, so that the anterior and posterior fontanelles fuse. Two examples of this are shown from our cases of fœtal rickets (fig. 21). This is as it should be, for during the first six months of life the head is said to be specially affected in rickets.

There are two other physical peculiarities exhibited by newborn infants the subject of fœtal rickets, which Dr. A. P. Black has kindly pointed out to the writer.

The first of these concerns the shape of the chest. Compared to that of a normal infant, the chest in these children is markedly flattened at the sides, giving an almost box-shaped chest. This seems to be partially dependent on the want of rigidity which is present at the costochondral junction, and which allows the ends of the ribs to come forward more than is usual (fig. 22).

The second is one which concerns the lower end of the fibula. It has been pointed out that in infantile rickets the lateral outline of the malleolus is not even, but has a small hollow in it. This is due apparently to a hyperplasia at the place of junction of the epiphysis, and also to a prominence of the cartilage of the distal portion of the epiphysis. It is peculiar to rickets and is found in our cases of fœtal rickets.

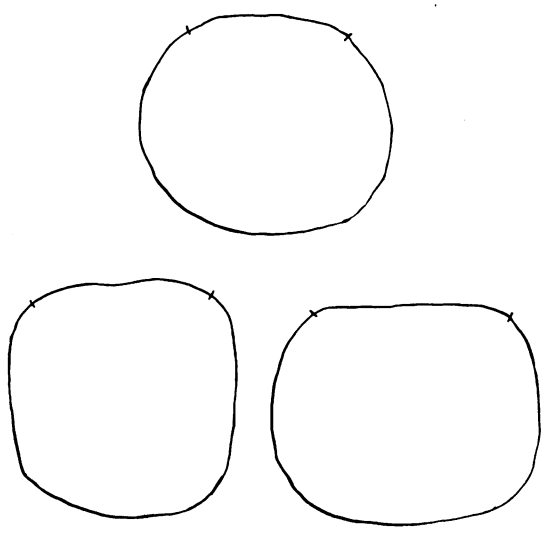

FIG. 22.

In the paper published in 1925 on "Osteomalacia in China" [24] some analyses of fœtal bones from children born to patients with osteomalacia were given. Fœtal rickets was not, apparently, present in these cases.

To compare with these figures, Dr. S. Wan, of the Department of Biochemistry has kindly analysed for me some bone from an infant with definite fœtal rickets, born dead by Cæsarean section from an active case of osteomalacia.

The figures work out as follows :—

	Fresh weight femur grm.	Dry weight femur grm.	Ash weight femur grm.
Normal (average) ...	19·34	5·80	2·53
Fœtal rickets case ...	19·34	5·24	2·04

	Moisture per thousand	Organic matter per thousand	Ash per thousand
Normal (average) ...	699·25	168·41	132·09
Fœtal rickets case ...	728·80	165·57	105·63

	Calcium per thousand of ash	Phosphorus per thousand of ash	Calcium per thousand of bone	Phosphorus per thousand of bone
Normal (average) ...	362·24	185·47	44·71	22·04
Fœtal rickets case ...	323·00	175·40	34·10	18·60

It will be noted that the figures for the case of fœtal rickets are all smaller, with the exception of the figure for moisture per thousand.

Tetany of the uterus.—This is not a question of the tetanic contraction which occurs in obstructed labour. Hess [7], in speaking of tetany speaks of what has been called cardiac tetany in infants and describes a case in which "the heart was found in systole and of the consistency of wood."

Tetany may also affect various involuntary muscles of the body, such as the muscle of the rectal wall and the sphincter ani.

But it appears from the following cases, that in patients with very low calcium and phosphorus, it is possible to get an actual condition of tetany of the uterus leading to the death of the fœtus *in utero*.

Mrs. C. T. L., Chinese, Hosp. No. 38644, was admitted to the Peiping Union Medical College Hospital on December 26, 1932, on account of very marked osteomalacia. She was pregnant, a month from term, and was in considerable distress from attacks of tetany. Blood calcium 4·65 mgm., blood phosphorus 3·15 mgm. per 100 c.c. of serum.

Her measurements were as follows:—

Interspinous	22·5 cm.	Fractures of pelvis and right femur.
Intercristal	26·5 „	
External conjugate	18·0 „	
Interischial	6·5 „	

It was clear that nothing except a Cæsarean section could be done.

Under calcium treatment the tetany diminished somewhat, and an injection of calcium gluconate was given. This procedure for some unexplained reason set up a sharp attack of tetany, and the child died after an hour or so in utero.

Cæsarean section was done about ten hours after the commencement of the attack, as it was thought from the feel of the uterus that an accidental hæmorrhage had occurred. The uterus was tense and tender, the fœtal parts could not be felt, and the patient was showing signs of shock.

On opening the abdomen the uterus presented. It was in a state of tetanic contraction, the waters unruptured.

The tension was so high that on opening the membranes, liquor amnii spurted out to a height of three to three and a half feet. The child was dead, the placenta in position and not detached. There was no accidental hæmorrhage. The incision in the uterus tended to gape, and was closed with a little difficulty. The tubes were cut and tied. The mother made a good recovery and under further treatment lost her pains; the calcium and phosphorus figures rose slowly to the normal, and she left hospital well.

Before this patient left hospital another patient came in:—

Mrs. W. C. C., Chinese, Hosp. No. 39506, in her third pregnancy, and in the seventh month. She was in considerable distress, and had a curious history of quasi-epileptic attacks. Two previous pregnancies had ended at the fifth and sixth months by the death of the child *in utero* during these attacks, and its subsequent delivery.

She had not got marked osteomalacia, but she had osteoporosis and possibly the commencing symptoms of osteomalacia. Under the care of Dr. S. H. Liu she steadily improved, and two months after began to show signs of coming into labour. On account of the findings she was again carefully measured, and it was found that in spite of her steady progress under treatment, pelvic contraction had been progressing and her transischial diameter had diminished from 9 cm. to 6 cm.

When she came in her blood calcium was 3·6 mgm. and her blood phosphorus 2·2 mgm. per 100 c.c. of serum. It was clear that she was suffering from severe tetany and it is likely that both of the previous miscarriages may have been due to tetany of the uterus. There was no other obvious cause for the death of the fœtuses and their being cast off. Under treatment she steadily improved and a living healthy child was delivered at full term by Cæsarean section. The child had no signs of fœtal rickets.

Special Note on the Teeth in Fœtal Rickets (*Dr. J. J. Wolfe*).

The material studied consists of teeth in the lower jaw of two cases of fœtal rickets which came to autopsy, and also teeth in a case of fœtal rickets which came into the Pediatric Ward at the age of 20 months.

This latter case will be dealt with first. It is the only instance, as far as is known, of a case of definite fœtal rickets in which one has had the opportunity of studying the teeth later on, and demonstrating the accuracy of the first diagnosis by the appearances of the erupted teeth (figs. 23 and 24).

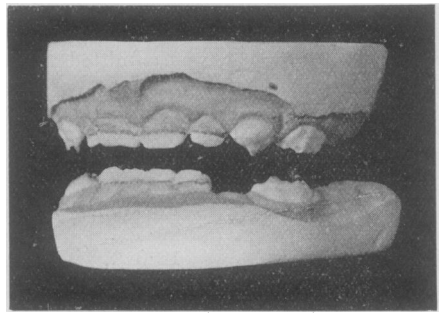

FIG. 23.

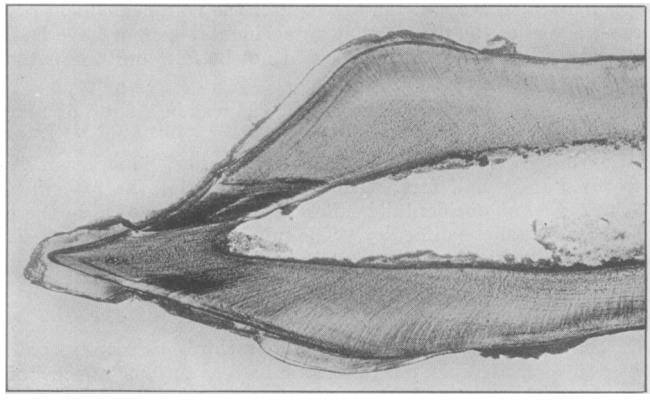

FIG. 24.—Fœtal rickets: section of affected tooth.

Models were made from the impressions of the teeth of Ching Ming (Hosp. No. 35880). They show that there is marked hypoplasia, almost aplasia, of the enamel of the occlusal surface of the molar, and tip of the the canine teeth. The tips of the central and lateral incisors are well formed, hence calcification apparently began normally at the seventeenth week (as is seen also in a section of the central incisor), and proceeded till about the twenty-third week of intra-uterine life. From this period until birth the calcification of the enamel, as manifested by the extreme hypoplasia, was extremely poor. The child was given adequate diet within the first few days of life, and the result is the formation of normal enamel onwards.

When one comes to look more closely at the microphotograph of a ground section of this central incisor, previously mentioned as having been extracted, one sees that normal enamel is present at the tip of the tooth merging gradually into an extremely defective structure. Normal enamel is seen to begin abruptly, however, on that part of the tooth which calcifies in the first month of life. This rapid response of the enamel organ to improvement in diet is in accord with the findings of Mellanby [27] in her experimental rickets in puppies. It can be prognosticated, moreover, that the first permanent molar teeth will show hypoplastic changes in the enamel of occlusal surfaces, and it is clear that the diagnosis of fœtal rickets made at birth was correct.

Secondly: When one studies the sections from cases of fœtal rickets who died at or shortly after birth, one finds the following significant appearances. In sections of the bone of the maxilla of Hosp. No. 37465, wide zones of osteoid tissue, typical of rickets, are seen. In a decalcified section of an incisor tooth from the same case the dentine is seen to be unevenly calcified throughout, the line of calcification is extremely irregular and the predentin layer is much wider than normal. Islands of calcoglobulin are seen scattered along the zone of calcification. In a tooth from Hosp. No. 38841, similar changes in the dentine are seen and in a ground section from the same case rows of interglobular spaces are seen beneath the enamel. The calcifying zone in the dentine is very irregular. Again, from these findings it is clear that the diagnosis of fœtal rickets is confirmed by the sections.

Taken together, these observations accord completely with the other clinical and microscopical findings proving the existence of true fœtal rickets.

(A fuller account of this work will be published in due time.)

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Discussion.—Professor EDWARD MELLANBY said that Mrs. Mellanby and himself had never been able to produce fœtal rickets in animals, but they had produced osteoporosis. There was no doubt that fœtal rickets, adult rickets and osteomalacia were the same disease in a sense, but the ætiology was rather different. For osteomalacia to occur there must be more than a deficiency of the calcified vitamins; there must be a real deficiency of phosphorus as well as of vitamin D.

Dr. DONALD HUNTER: In England to-day osteomalacia is a rare disease. Two types are found. The first is due to a diet deficient in vitamin D and calcium salts. It occurs as a result of the industrial depression in the North. One such woman, aged 33, was born in Darlington, Durham, and had always lived there. In 1922, immediately following her fourth pregnancy, she began to have pains in the left hip and back. By 1928 the total height had diminished by two inches, the limbs were bowed, the bones tender, and she was unable to walk unaided. The pelvic measurements were: interspinous 25·4 cm., intercristal 28 cm., external conjugate 16·5 cm., transverse diameter at outlet 2·5 cm. The serum calcium was 9·6 mgm. per 100 c.c., and the plasma phosphorus 1·5 mgm. per 100 c.c. The calcium output was estimated in the urine and fæces for three three-day periods, the patient being kept on a weighed diet of known low-calcium content. The calcium output in urine and fæces was slightly less than in the control. Radiograms of the bones showed definite diminution in density with multiple spontaneous fractures. The calvaria showed innumerable pale, rounded, mottled shadows, many of them more than 1 cm. in diameter. There was a greatly deformed tri-radiate pelvis with fracture of the superior ramus of the os pubis on each side. A piece of bone removed from the inner aspect of the right tibia showed the abnormally deep osteoid zones of osteomalacia, associated with great osteoporosis. She was given a diet of high calcium content, together with large doses of calcium lactate and tablets containing vitamin D. Within three months the pain disappeared from the bones and she began to walk. Within six months she was able to get about the house, to climb the stairs unaided, and to do her usual household duties. Radiograms of the bones showed union of many of the fractures, and complete healing of the defects in the calvaria.[1]

The other cause of osteomalacia is idiopathic steatorrhœa (Gee's disease). This disease occurs in both sexes, and the history nearly always goes back to early childhood. The following features may be present: fatty stools, dilatation of the colon, tetany, osteomalacia, anæmia, skin lesions, and infantilism. These manifestations develop in spite of an adequate diet. We must therefore suppose that there is some disturbance of gastro-intestinal function resulting in deficient production, absorption, or utilization, of one or more essential factors. In fifteen cases recently investigated[2] steatorrhœa and disturbances of calcium metabolism were alone common to the whole group. Changes in the skeleton were found in all cases investigated. Radiograms of the bones showed diminution in density, together with the deformities of osteomalacia. In three cases histological examination of portions of bone showed osteomalacia and osteoporosis. It would therefore appear that osteomalacia may occur not only in persons deprived of calcium salts and vitamin D, but also in others with a defective mechanism for absorption or utilization of these substances.

DR. V. KORENCHEVSKY said Professor Maxwell's observations showed (1) that the causes of rickets and osteomalacia in China were chiefly deficiency in vitamin D and calcium; (2) that there was no essential difference between rickets and osteomalacia, the latter being the manifestation of rickets in adults: (3) that the blood of rachitic mothers was often poorer in calcium and phosphorus than that of children borne by these mothers.

[1] Hunter, D., and Turnbull, H. M., *Brit. Journ. Surg.*, 1931, xix, 277.
[2] Bennett, I., Hunter, D., and Vaughan, J. M., *Quart. Journ. Med.*, 1932, N.S. i, 603.

These clinical observations were in complete agreement with the following results of his (the speaker's) experiments on rats, published from 1922 to 1924 ("The Ætiology and Pathology of Rickets from an Experimental Point of View," *Med. Res. Counc. Spec. Rep. Ser.*, No. 71, 1922; *Biochem. Journ.*, xvii, 597; xviii, 1308): (1) Typical rickets was produced by a diet deficient in fat soluble vitamins and calcium in young rats and, using the same diet, a picture typical of osteomalacia was produced in adult rats.

(2) At the day of birth the water, calcium phosphorus and nitrogen content in the young was nearly the same, irrespective of the deficiency or abundance of fat-soluble vitamins in the diet of the mother during pregnancy. However, deficient diet of the mother during pregnancy influenced the young in other respects. The young from deficient mothers developed more severe rickets than those from normal rats. The litters were smaller in number, and the number of young born dead or weaker and eaten by the mothers was greater (*Biochem. Journ.*, xvii, 597). At the same time the skeleton of these mother rats was found to be poorer in calcium (see *Med. Res. Counc. Spec. Rep.* 110) than that of normal rats of the same age and showed osteomalacia or osteoporosis.

The normal chemical composition shown to exist at birth in fœtuses born of mothers kept on a diet deficient in fat-soluble vitamins was explained by the fact that the maternal organism would, as far as possible, yield all the necessary substances to the offspring by the sacrifice of its own tissues. Another case of maternal sacrifice caused by general fasting of the mother during pregnancy was clearly shown by Rudolsky in 1893 (Dissertation: Petrograd; ref. Korenchevsky and Carr, *Biochem. Journ.*, 1924, xviii, 1313).

DR. H. B. FELL: Is there any histological difference between the osteoid tissue in fœtal rickets and the osteoid tissue of the normal fœtus? I ask this question because Miss C. F. Fischmann, one of my colleagues at the Strangeways Laboratory, finds that there is a marked difference between osteoid tissue formed *in vitro* by osteogenic tissue grown in vitamin D-deficient medium and the osteoid tissue formed by similar cultures grown in normal medium.

Miss L. WILLS said that in connexion with the question of osteomalacia being low-calcium rickets in the adult, it was interesting to note that in Bombay tetany was a rare complication of osteomalacia and that blood analyses showed that the majority of the cases had very low inorganic-phosphate figures, the serum calcium being only slightly reduced. Osteomalacia in Bombay, therefore, more closely resembled infantile rickets as commonly seen in this country than did Professor Maxwell's low-calcium osteomalacia cases.

Mr. V. B. GREEN-ARMYTAGE said that the whole tropical world owed a debt of gratitude to Professor Maxwell and his collaborators for their biochemical research on osteomalacia which only those who had an intimate knowledge of the difficulties besetting such work in the tropics could fully appreciate. The clinical aspect of this disease was not perhaps so easily recognized as would appear from the photographs shown this evening since he (the speaker) considered that there were five common clinical types which might or might not dovetail into one another. In the first the symptoms were almost entirely gastro-intestinal; in the second they were those of severe anæmia and tetany only; in the third the symptoms were mainly those of rheumatism and of joint pain or stiffness. In the fourth the lower motor neuron and sympathetic system was mostly involved, whereas in the fifth, and most easily diagnosed, the lesions were obviously osseous.

In his experience as to the acuteness of symptoms and the combination of these clinical types, much depended upon the presence of added oral or intestinal sepsis.

He had seen great numbers of cases of neonatal rickets and a smaller number of prenatal rickets, but his impression was that these features in the infant very much depended upon whether the disease in the mother was acute or chronic. In his experience pre- and neo-natal rickets were only met with if the maternal osteomalacic symptoms were acute.

He had observed that these infants were wizened and thin and very liable to suffer from hæmorrhage from the rectum or subcutaneously and that at the time of Cæsarean section the omentum of the mother was so shrivelled (due to absorption of fat) that it could not be found or brought down. Another feature of the operation was that, despite the lack of calcium, there was never any post-partum bleeding or difficulty in controlling the uterus at laparotomy. Owing to the gross deformity of the lower limbs so often met with, he considered that the ideal Cæsarean incision was the fundal one described by McCann. With this incision there was little hæmorrhage and far greater ease of approach.

He was particularly interested in Professor Maxwell's remarks on the funnel pelvis, because for years he had been teaching that, just as in this country some pregnant patients complained of vitamin A and D deficiency symptoms—such as insomnia, tetany, joint pains, cramps, rashes and pains referred to the "gliding" symphysis—so in others at or about the time of puberty, there were signs if looked for, of alteration of the outlet of the pelvis with the typical funnel deformity, which was perhaps more likely to be seen now than hitherto, in the northern depressed areas of Great Britain. In a consecutive series of 3,000 labour cases in European and Anglo-Indian communities he had found a pelvis with an outlet less than $3\frac{3}{4}$ in. in 67, the other measurements being normal. There was just one question of some interest he would like to ask Professor Maxwell, and that was, whether he had observed a greater tendency to eclampsia in his acute or chronic osteomalacics, as compared with the ordinary toxæmic patients met with during pregnancy in China. The reason he requested this information was that out of hundreds of cases of osteomalacia, many of them with gross albuminuria and anæmia, he had no memory of one in which eclampsia had developed. The question was one of some importance, because there were many who considered that the preventive treatment of eclampsia and toxæmia was mainly that of the diet and the exhibition of calcium in large doses. If that was so, it seemed strange that in a condition like osteomalacia in which there was invariably an obvious large defect in the calcium and phosphorus content of the blood-serum, eclampsia should be practically unknown. It would be illuminating to hear Professor Maxwell's experience.

Dr. G. W. THEOBALD said that the two points in the paper which struck him most were: (1) The percentage of serum calcium in patients suffering from osteomalacia varied within wide limits, and women with osteomalacia sometimes had a higher percentage of serum calcium than others without symptoms of the disease. (2) The fœtal blood contained a higher percentage of calcium than the maternal. The first point indicated that calcium was present in the blood in various forms and that estimations of the percentage of total calcium in the blood was of relatively little value in calcium-deficiency diseases. The second showed that the fœtus was a true parasite and robbed the mother of substances she could ill-afford.

Dr. MAXWELL (in reply) said that with regard to several of the points raised in discussion, such as the question of osteoid tissue and the rarity of the coexistence of œsteomalacia and eclampsia, he was unable to give definite answers. It was his impression that osteomalacia and eclampsia were rarely found together, but on his return to China he would pay special attention to this point. The whole subject contained many unsolved questions and he hoped to deal specially with some of these in the future.