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SHADOWS PRODUCED BY LEAD IN THE X-RAY PICTURES OF THE GROWING SKELETON*

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Fifty-six years ago (1874) Wegner¹ showed that inorganic phosphorus administered in small doses, as was formerly the practice in the treatment for rickets, causes the freshly forming trabeculae at the ends of the shafts of the long bones to multiply and become closely packed together. To this dense, thicket-like formation of trabeculae at the end of the shaft induced by phosphorus Wegner gave the name "osteosclerosis." Years later (1918) Phemister² discovered that dense shadows appear in the x-ray photographs of the long bones of children after the administration of minute doses of elementary phosphorus for five weeks or more. These shadows appeared in the parts of the shaft that were in process of growth during the administration of phosphorus and continued to form, so Phemister thought, for a time after the phosphorus had been stopped. Since the long bones grow in length at their ends because of the growth activity in the proliferative zone of the epiphyseal cartilage, the dense shadows made their appearance at the ends of the shafts immediately under the cartilage. Old bone remained unaffected, and new bone, formed some time after the administration of

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* The fact that lead produces these shadows in the x-ray pictures of long growing bones was observed at the same time by Dr. John Caffey of the Department of Pediatrics, Columbia University (personal communication). A report of this phenomenon induced by lead was made by one of us (E. A. P.) in the discussion of a paper by Stafford McLean, "The Bone Lesions of Congenital Syphilis: The Correlation of the Roentgen and Pathologic Observations," and delivered before the Pediatric Section of the New York Academy of Medicine on Nov. 14, 1929. The discussion was published in the *AMERICAN JOURNAL OF THE DISEASES OF CHILDREN* 30:899 (April) 1930; the article will be published in full in a later issue.

1. Wegner, G.: Ueber das normale und pathologische Wachstum der Röhrenknochen, *Virchows Arch. f. path. Anat.* 61:44, 1874; Der Einfluss des Phosphors auf den Organismus, *Ibid.* 65:11, 1872.

2. Phemister, D. B.: The Effect of Phosphorus on Growing, Normal and Diseased Bones, *J. A. M. A.* 70:1737 (June 8) 1918.

phosphorus had been stopped, seemed normal in structure. If the administration of the phosphorus had been stopped long enough, the shadow took the form of a band which in the x-ray picture had the appearance of having sunk back toward the middle of the shaft. In reality, of course, it remained where it had developed, but new normal bone had formed beyond it. Phemister attributed these dense shadows, which he noted in the x-ray photographs of the long bones after the phosphorus administration, to the osteosclerotic formations of Wegner.



Fig. 1.—X-ray photographs of the knees of a white boy, aged $6\frac{1}{2}$ years, who had been receiving cod liver oil and elementary phosphorus for nineteen months. The action of elementary phosphorus in the production of such shadows in bones was first described by Phemister. Not only the ends of the shafts which grew rapidly but also the nuclei of ossification show the effect of phosphorus. The photograph is exhibited for purposes of comparison with the somewhat similar though less dense shadows produced by lead.

In the course of study of the x-ray pictures of many bones removed after death from the bodies of children, we observed that the ingestion of lead may cause shadows to appear at the growing ends of the long

*I am permitted to include this X-ray photograph through the courtesy of Dr. Helen J. Zillmer of Milwaukee. (See *Am. J. Dis. Child.* **38**:1344 [Dec.] 1929.)

bones similar to those seen after continued administration of phosphorus, though the bands induced by lead in our four cases were not so broad or so striking as those obtained by means of phosphorus. Altogether, we have now seen the phenomenon well developed in three cases of chronic lead poisoning and moderately developed in one. In two of the cases we had the opportunity to study the condition at autopsy.

REPORT OF CASES

CASE 1.—History.—T. L., a boy, aged 13 months, was admitted to the Harriet Lane Home on March 14, 1929, with the complaint of convulsions. For three weeks before admission the patient had had a cold, and eight days before admission a treatment of three injections daily of "cold vaccine" was started. Five days before admission, on the third day of treatment, two generalized convulsions occurred, each of which lasted for several minutes. The temperature rose to 39 C. (102.2 F.), and all night the baby remained in a convulsive state. On the following day, he seemed dull, had a stiff neck and the arms kept twitching, and again a severe generalized convulsion developed. During the three days before admission, the child had no fever, but seemed more and more sick, and on the day before admission he ceased taking fluids. On the day of admission he was regarded as dying, but his condition improved slightly after a lumbar puncture which was said to have yielded a normal fluid. Throughout the illness the patient was constipated.

"A feature of the child's story," the history relates, "is that he has been in the habit of gnawing paint from his pen, from his crib and from his walker. This has been going on for about four months and was such an obstinate habit that his mother had recently taped these objects so that he could not satisfy himself."

A blood smear examined on the day before admission by Dr. Margaret Handy of Wilmington, Del., showed stippling of the red blood cells.

Examination.—On admission we found a well nourished and developed pale baby, apparently conscious but unresponsive even when painful stimuli were applied, flaccid between convulsions and sweating profusely. The fontanelle was depressed. The musculature was hypotonic, but there was no paralysis. The neck was not stiff. The tendon and abdominal reflexes were considered normal. The Babinski sign was negative. The examination of the heart, lungs and abdomen yielded negative results. The spleen was not felt. There was no lead line on the gums. The temperature was 36.6 C. (97.3 F.). The urine was normal. The cerebrospinal fluid was clear, under normal pressure, with 6 cells per cubic millimeter, and there was no globulin. Examination of the blood showed: hemoglobin, 50 per cent; red cells, 4,000,000; white cells, 10,000; polymorphonuclears, 64 per cent; lymphocytes, 26 per cent, and monocytes, 7 per cent. The red cells varied in size, shape and staining properties, but exhibited no stippling.

Course.—The patient remained in the hospital for eighteen days. On the second day of his stay, the left arm and leg were found partially paralyzed, a condition that continued until death. At first the left arm lay limp at the side, but later it was held rigidly flexed at the elbow; the left leg was similarly held in extension. The right arm and leg, on the other hand, were cast about continually in purposeless movements. A slight improvement in the general condition seemed to take place until the sixth day after admission. Then the temperature rose without discoverable cause from its slightly subnormal level to 40.4 C.

(104.7 F.) and from that time remained continuously elevated. The baby lay with eyes open and seemed conscious, but responded poorly to stimuli and took food poorly. The eyegrounds were found normal on two examinations. Another spinal puncture yielded normal fluid (2 cells and no globulin). Though stippled red blood cells were seen before admission, as already mentioned, they could not be found on the five days succeeding admission, but on the sixth day (the day of the commencement of fever) stippled cells suddenly appeared in numbers amounting to from 2 to 3 per high power field. On the ninth day they were absent, but on the eleventh and eighteenth days they were again noted "in some fields but not in all." The blood calcium was 10 mg., and the phosphorus, 4 mg. The urine remained normal. The Wassermann test of the blood and the spinal fluid gave negative results. An intradermal tuberculin test gave a negative reaction. No attempts were made to identify lead in the urine or stools.

The baby was treated, according to the suggestions of Aub,³ with a milk diet and calcium lactate in large doses and also irradiated ergosterol, with the idea, which was probably erroneous, that the latter might favor the deposition of lead in the bones. On discharge the child was improved to the extent that death no longer appeared imminent, but he remained critically sick.

After five days at home the baby was again admitted, because generalized convulsions had once more set in, and he now seemed in an almost hopeless condition. The entire body was spastic, except for the right arm, which, as before, was in ceaseless motion. Similarly, the head was rolled continually from side to side and the mouth continuously performed a chewing movement. On admission the temperature was 38.2 C. (100.8 F.), but it rose in the next thirty-six hours to 42 C. (107.6 F.). Still no lead line was demonstrated, and the eyegrounds were normal. The spinal fluid contained 10 cells, and the Pandy test now gave positive results. The red blood cells on this admission showed no stippling. Death occurred.

Autopsy.—At autopsy nothing of great importance came to light, except that on chemical analysis lead was found in the brain. Dr. W. G. MacCallum's note states: "There are defects in the convolutions on both sides of the median fissure just above the occipital lobe. On one section with the knife through this part there is no gross abnormality to be seen. The microscopic sections of the brain are said to show distinct degenerative changes in the ganglion cells with reduction in their number. There is no inflammatory reaction. There is a definite thrombus in the superior sagittal sinus; it is quite fresh." No edema of the brain was thought to be present. Slight pneumonia was found. The organs otherwise appeared normal.

In regard to the ribs, which were the only parts of the skeleton examined, the examiner's note states: "The line of ossification in the ribs is not irregular but it forms a broad band sharply outlined against the rest of the bone, evidently containing laminae of the bone, and this band is marked out by its paler color and by an especially pale line along its border toward the bone. The other border, toward the cartilage, is also pale yellowish but not jagged."

The x-ray photographs (fig. 2) of the anterior ends of three of the middle ribs obtained at autopsy revealed narrow bands of intense shadow extending transversely across the terminal 3 mm. There were three of these bands; the one lying farthest back from the cartilage junction, a ribbon-like stripe of dense shadow

3. Aub, J. C.; Fairhall, L. T.; Minot, A. S., and Reznikoff, P.: Lead Poisoning, *Medicine* 4:1, 1925.

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about 1.5 mm. wide, crossed the shaft 1.5 mm. from the end; the second, a mere line of intense shadow at the extreme end of the bone, corresponded to the zone of provisional calcification of the cartilage and subjacent trabeculae, and the third was situated between the other two, appearing as a line of shadow of much less intensity and clearly visible only in the middle one of the three ribs. The ribbon-like stripe first mentioned is the unusual one, and is thought to have been formed under the influence of the lead. The two lines of shadow may or may not have been produced by the lead. They resemble the growth lines in bones described by one of us⁴ as the result of a variety of factors which suddenly alter the growth of the cartilage.

Microscopic examination of the ends of the ribs showed that the trabeculae at the ends were normally formed but unusually numerous and thickly placed, and seemed thickest at the levels at which the transverse stripe and lines lay in the x-ray photographs. The examination indicated that the cause for the shadows in the x-ray photographs was the abnormally dense formation of trabeculae which

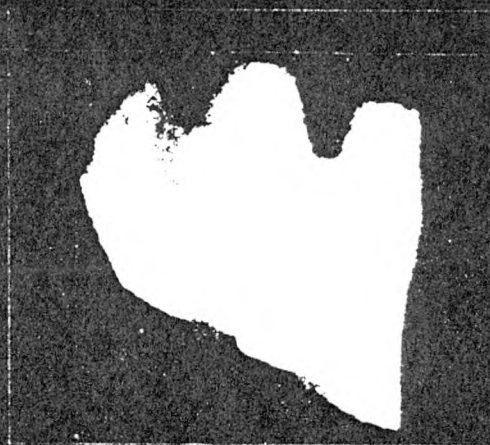


Fig. 2 (case 1).—X-ray photograph of three of the middle ribs of T. L., taken after their removal at autopsy. The ends of the ribs are marked by a band about 1.5 mm. wide and two lines. The band is thought to have been produced under the influence of the lead. The most distal line, i. e., the one at the extreme end of the rib, marks the provisional zone of calcification of the cartilage and adjacent trabeculae. The other line, lying between the band and the line just mentioned, is not distinct and can be clearly seen only in the middle one of the three ribs. The two lines may or may not have been produced by the lead.

must have obstructed the x-rays by superimposition. Of course the trabeculae may have contained lead, and the lead may have been a factor in the production of the dense shadows.

CASE 2.—History.—H. R., a boy, aged 22 months, was the youngest of three children. The parents described a decrease in activity and drowsiness beginning three weeks before admission, then constipation, projectile vomiting, occurring in attacks, and, finally, a generalized convulsion. The convulsion was the immediate cause of entry into the hospital.

4. Eliot, M. M.; Souther, S. P., and Park, E. A.: Transverse Lines in X-Ray Plates of the Long Bones of Children, *Bull. Johns Hopkins Hosp.* 41:364, 1927.

At 16 months the baby had begun to walk, and since then, that is, for six months, had gnawed paint off the furniture and porch railing.

Examination.—On admission examination showed a well nourished, pale child, thought to have slight rickets, in a state of recurring convulsions, each limited to the right side, including the face, and lasting for about ten minutes. Between the convulsions the body was completely flaccid, with tendon reflexes absent. The fontanelle, which was small, bulged a little. The eyes were staring and crossed; the dilated pupils reacted sluggishly to light. Both disks were choked, but there were no hemorrhages in the fundi. No lead line was demonstrated in the gums. Examination of the heart, lungs and abdomen gave negative results. The spleen was not felt.

The temperature was 37 C. (99.2 F.). The spinal fluid showed greatly increased pressure, 9 cells per cubic millimeter; the results of the Pandy test were positive. Examination of the blood revealed: white cells, 16,000; polymorphonuclear neutro-



Fig. 3 (case 2).—X-ray photographs of two of the middle tier of ribs of H. R., removed after death. The terminal 2.5 mm. of the ribs are covered by a dense shadow, which can be explained by unusually great density of the trabecular formation in the corresponding part of the bone, as revealed by microscopic study (see figures 4 and 5).

phils, 58 per cent; lymphocytes, 40 per cent, and monocytes, 2 per cent. The hemoglobin was not determined. The red blood cells showed coarse and fine stippling, from 3 to 5 stippled cells per oil immersion field. Many ring forms were seen. The results of the Wassermann test of the blood were negative.

Treatment.—The patient was treated, according to the method recommended by Aub,³ with intravenous injection of calcium chloride, but without demonstrable favorable effect. The convulsions continued, moderate fever appeared, and death took place about forty-eight hours after admission.

Autopsy.—At autopsy the brain was found to be edematous. "The convolutions were so swollen that the sulci were not visible." On examination with the microscope no changes in the nerve cells or evidences of inflammation were found. In other respects the autopsy showed little that was abnormal. In the bone-marrow many stippled red cells were found and in the bone-marrow of vertebrae

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On gross examination of the ribs and femur, nothing definitely abnormal was noted. The cut surface of the upper end of the femur was described as entirely normal, and that of the rib as suggestive of "a late stage of healing rickets," without reason being given. The "line of ossification" was described as being "slightly irregular." Doubtless the gross appearance at the costochondral junction was abnormal, owing to the zone of thickly placed interlacing trabeculae so clearly seen on examination with the microscope, but its nature was not recognized.

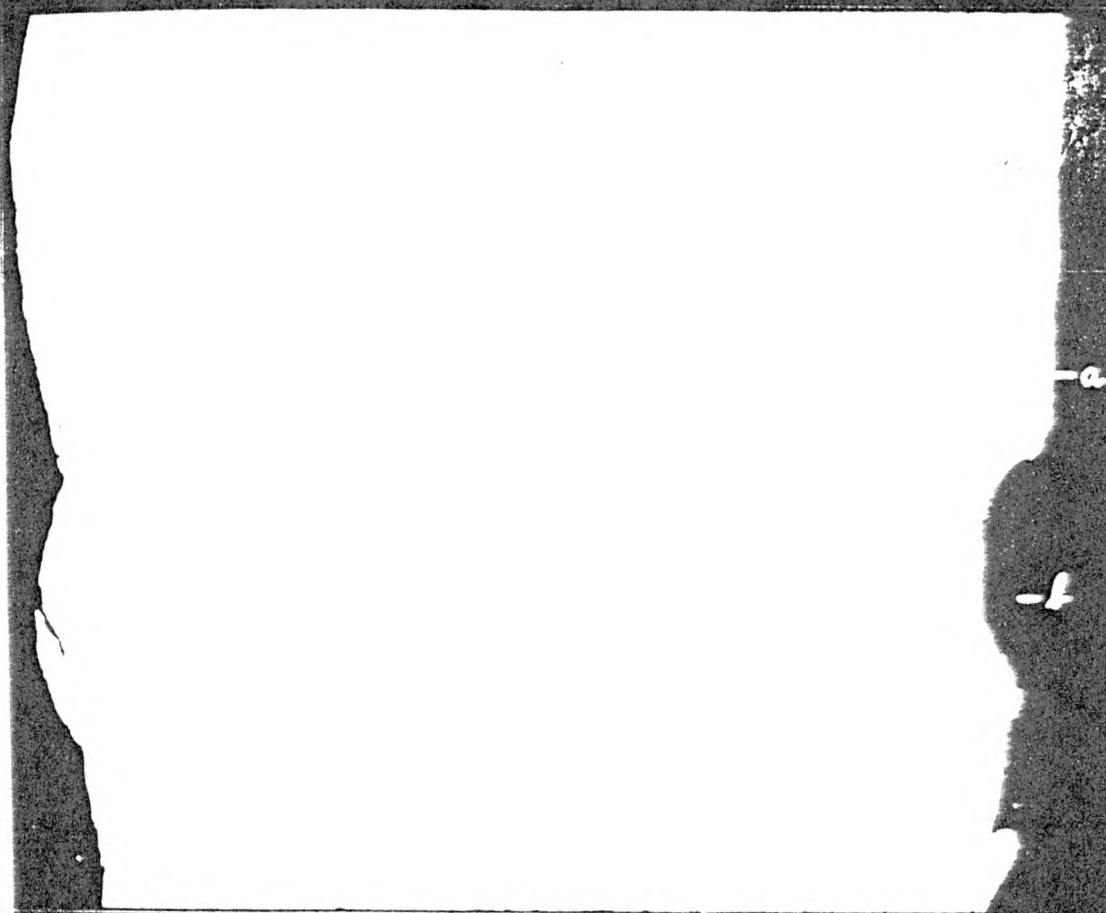


Fig. 4 (case 2).—The cartilage shaft junction of one of the ribs of H. R., shown in figure 3. Decalcification in formic acid staining with hematoxylin. The dense formation of trabeculae in the terminal part of the bone (a-b) is clearly shown. The somewhat similar condition sometimes seen in congenital syphilis teaches that these thickly studded trabeculae may be the cause of dense homogeneous shadows at the ends of bones in x ray photographs. Magnification, $\times 10$

The x-ray pictures (fig. 3) of the anterior portions of two of the middle tier of ribs, taken after autopsy, showed a dense homogeneous shadow which covered the terminal 2.5 mm. of the bones and completely hid their inner structure.

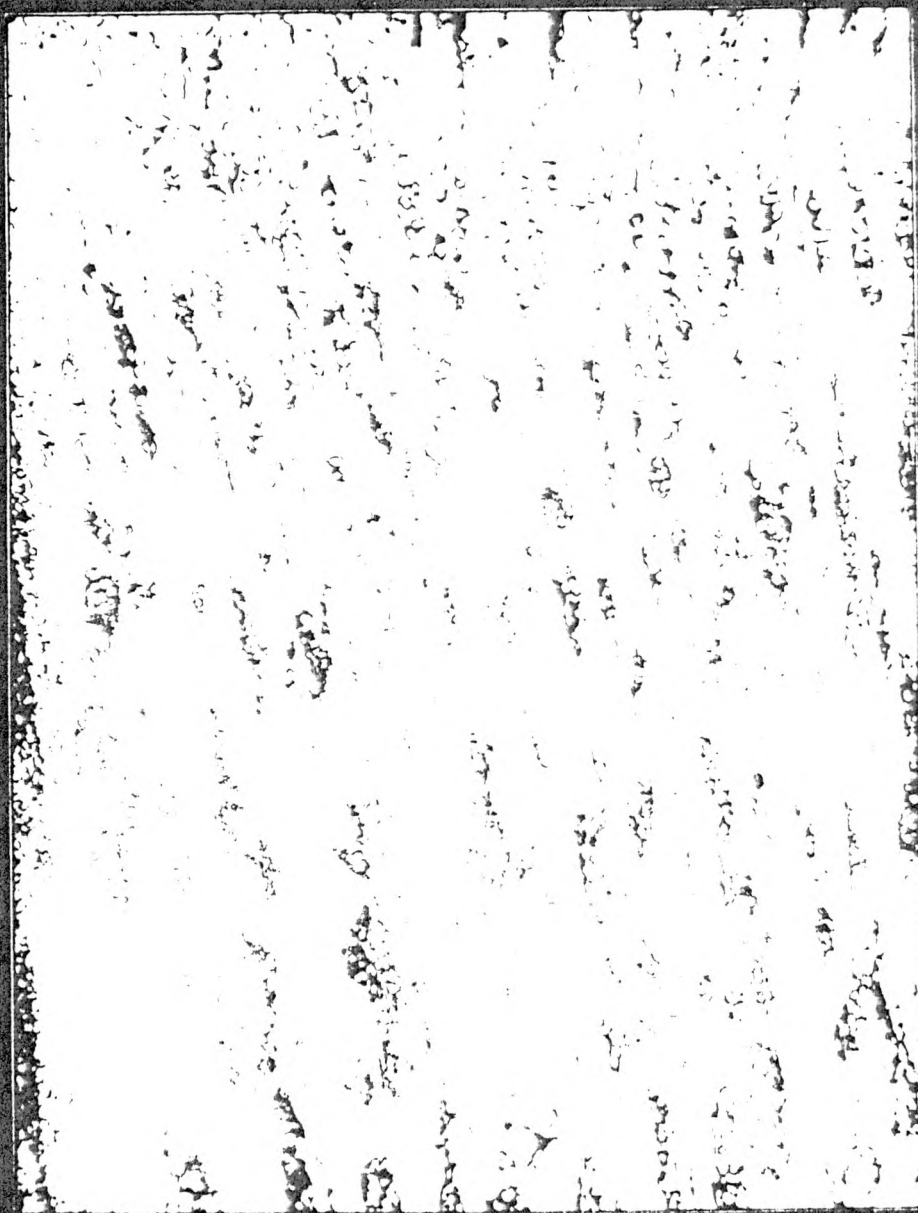


Fig. 5 (case 2).—A high power view of a part of figure 4, showing especially well the dense formation of trabeculae. The cartilage is just visible above the trabeculae which appear black. Magnification, $\times 90$.

When the ends of the two ribs were examined under the microscope (figs. 4 and 5), in order to learn the cause of the dense shadows, it was found that the trabeculae for a depth of several millimeters from the extreme ends were unusually numerous. They did not seem abnormal individually, but were packed close together. In the aggregate they must have formed a much denser mass than exists ordinarily at the end of the bone.

A cause sufficient to explain the dense shadows at the ends of the ribs in this case would seem to be the unusually thick mass of parallel branching trabeculae, though a factor which cannot be excluded is the lead itself. The lead may have been deposited in these trabeculae and may have contributed to the density of the shadows.

CASE 3.—History.—F. S., a Negress, aged 7½ years, was first admitted to the hospital in June, 1929, in what appeared at the time to be an attack of catarrhal jaundice, but afterward was regarded as the beginning of the lead poisoning.

Examination.—In addition to the jaundice, the child showed a moderate anemia, with a hemoglobin of 60 per cent. The gums were not examined for a lead line. The patient recovered from this illness without event.

Second Admission.—The patient was admitted to the hospital a second time, in August, because of convulsions. On this occasion a definite lead line was found, and the spinal fluid contained 14 cells per cubic millimeter and gave a positive Pandy reaction.

Course.—The patient was treated with sedative, the convulsions stopped within twelve hours, and complete recovery seemed to take place.

Third Admission.—On September 22, the patient was admitted for the third time. In the interval she was well, except for attacks of abdominal pain and occasional vomiting. She now had generalized convulsions. There was a marked lead line in the gums. The spinal fluid gave an unusually marked Pandy reaction with 9 cells per cubic millimeter. There was a moderate anemia—hemoglobin of 60 per cent—with marked stippling of the red blood cells. The convulsions kept on recurring, largely in the form of twitchings, for more than one month. When the convulsions ceased, the child entered into a state of motionless coma which lasted one week. Then voluntary movements returned. Later, she began to take notice of her surroundings, but at first could recognize only large objects very close to her. Finally, she sat up and mumbled words. At present, almost a year after the first admission, the child is healthy, but has almost no intelligence. The intradermal tuberculin and Wassermann tests of the blood were both negative.

The treatment during the last admission consisted of magnesium sulphate given intravenously when convulsions developed.

No satisfactory history of the ingestion of lead was ever obtained, but the greatest shiftlessness and ignorance in the household (Negro) made the search unsatisfactory.

X-Ray Examination.—On examination of the x-ray pictures of the extremities characteristic shadows were seen at the upper and lower ends of the tibia and fibula (fig. 6), the lower end of the radius, ulna and femur and the upper end of the humerus. The shadows could not be picked out at the slow-growing ends of these bones or in the compact bones of the tarsus or carpus, in the metacarpal or metatarsal bones or phalanges, in the cortices of the long bones or their centers of ossification in the epiphyses. The breadth of the shadows varied. At the lower ends of the tibiae and fibulae the shadow was approximately 1 cm. broad, but at the upper ends it was about 1.5 cm. broad. It was about 1.1 cm. broad at

the lower end of the radius and ulna. The shadow was not clearly defined at its upper border in the x-ray picture of the lower end of the femur, but seemed to measure 2.5 cm. The upper end of the humerus was not shown clearly in the x-ray pictures. These measurements are interesting, because they indicate the relative rates of growth at the various ends of the different bones mentioned.

When the x-ray pictures were held far away from the eye, the impression was gained that the affected ends of the bones mentioned were clouded. When they were held close, it became apparent that the clouding effect depended on an intensification of the shadows cast by the trabeculae in the parts affected. The individual trabeculae stood out more plainly in the affected than in the nonaffected parts. The trabeculae in the parts that cast the dense shadows seemed more numerous,

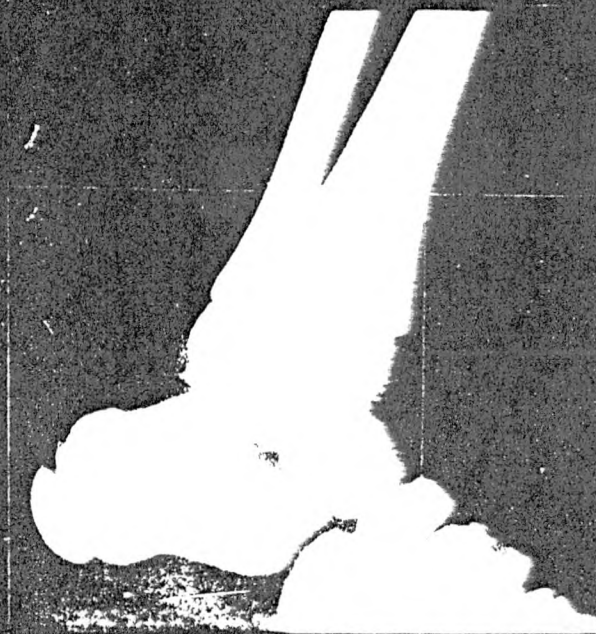


Fig. 6 (case 3).—X-ray photograph of the ankle of F. S., aged 7½, showing a shadow 1 cm. broad marking the lower ends of the tibia and fibula. The shadow is obviously formed by a summation of the shadows of the trabeculae which are thought to be more numerous and perhaps larger in the affected than in the adjacent normal parts. The width of the shadow in a child, aged 7, indicates that the factor responsible for the shadow, lead, has been in operation a long time.

and perhaps individual trabeculae seemed thicker. But in regard to these last two points it is most difficult to be certain. The line of demarcation between affected and unaffected bone was sharp, except in the lower end of the femur and the upper end of the humerus. But the x-ray photographs of the humerus and the femur were poor. The shadow at the lower end of the femur was the most dense and homogeneous—in the x-ray picture it had a snowy appearance—probably because of the greater thickness of the bone. X-ray pictures taken a year later showed the shadows as distinctly as before. Very little growth in the

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length of the bones had occurred in that time, not more than from 1 to 2 mm., for example, at the lower end of the radius or the upper end of the fibula, and no normal bone had made its appearance immediately adjacent to the epiphyseal cartilage; so the shadows still seemed to reach to the extreme ends of the shafts.

CASE 4.—History.—B. C., a white girl, aged 2¼ years, was known to have eaten paint for one and a quarter years. For the six months prior to admission frequent vomiting and obstinate constipation had been present. During pertussis, six months before admission, nine long, severe, generalized convulsions had taken place. Since then there had been gradual mental deterioration.

Examination.—On examination the defective mental development was obvious. A state of anemia was found, with a hemoglobin of 50 per cent; the red blood cells showed marked stippling, from 3 to 4 cells per high power field. Three weeks later the stippling could not be found. No lead line was demonstrated. The spinal fluid was normal, except for a positive Pandy reaction. The eye-grounds were not examined.

Course.—A rapid improvement in the constipation and eating habits took place in the hospital, and the child was discharged.

A year after discharge the following special note was made by Dr. T. Campbell Goodwin: "Patient began ingesting lead when she was from 11 to 12 months old. This continued steadily for six months, when she became too weak to walk. But from the mother's story her restricted environment did not decrease the amount of paint chewed, so even up to the time of admission to the hospital at 27 months she was steadily eating paint, plaster, chewing on toys, etc.

"When seen today, she was physically perfectly normal, reflexes all right, no lead line, not anemic, weight and height average for her age. Her mental retardation was not as marked as it was when she was in the hospital. She is beginning to talk, using short sentences. She recognizes all of her family, calls them by name and can play fairly well for a child of 3¼ years."

X-Ray Examination.—The x-ray pictures of the extremities showed shadows at all of the rapidly growing ends of the long bones. The shadows at the upper and lower ends of the tibia and fibula, the upper end of the humerus and the lower ends of the radius and ulna were about 1 cm. broad, that at the lower end of the femur was wider, measuring about 1.5 cm. The shadows were light, giving the impression, when the x-ray picture was held at a distance, of a faint clouding. The shadows were not dense enough to hide the finer structure on close examination. Indeed, on close inspection of the x-ray photographs, the finer structure could be seen in both its longitudinal and transverse arrangements more clearly than in the unaffected parts of the bones, and one gained the impression that it was the increased density of the finer structure that gave rise to the clouded appearance. Extending transversely through the affected ends of the shafts were many transversely disposed lines of growth. It was difficult to say whether or not the slowly growing ends of the long bones, namely, the lower end of the humerus and the upper and lower ends of the radius and ulna were affected. No definite evidence could be found of involvement of the centers of ossification of the epiphyses or of the small bones of the hands and feet or of the cortices.

COMMENT

When taken for a sufficiently long period in sufficient dosage, lead, apparently, can produce changes in the bone in process of formation

which are reflected in the x-ray photographs as shadows of increased density. Like elementary phosphorus and perhaps some other heavy metals, e. g., arsenic,⁵ lead can cloud bones in x-ray photographs. The clouding is most conspicuous where growth is occurring most rapidly, namely, at the anterior ends of the middle six ribs, the lower ends of the femora, the upper end of the humerus, the lower ends of the radius and ulna and at both ends of the fibula and tibia.

In our two cases in which the banding was most marked, cases 1 and 2, only the ribs were studied with the x-ray, but in cases 3 and 4, in which banding was well marked in the fast growing parts of the skeleton, it was not noted in the slow-growing parts. That only those parts of the skeleton in process of growth at the time of ingestion of lead are affected is proved by the entirely normal structure of the old bone proximal to the lesions, the sharp limitation of the lesions to the growing parts and a degree of involvement at any point exactly proportional to the rate of growth at that point. Obviously growth in any bone takes place in many places, but only where growth occurs rapidly do the changes readily reach such magnitude as to show in x-ray photographs.

The fact that only the bone in process of growth is affected must mean that the lead either enters into the chemical composition of the bone or influences cellular activity in such a way that the character of the bone formed becomes altered. The work of Hunter and Aub⁶ indicated that lead is actually deposited in the bones, and this study, in conjunction with that of Bauer, Aub and Albright,⁷ brings forward strong indirect evidence that the place of deposit is the trabeculae lying in close proximity to the cartilage. The evidence just cited, that lead actually does enter the skeleton, and the fact supplied by our own x-ray photographs, that only the growing ends of the shafts showed the lesion, led us to expect that the dense shadows cast by the ends of the shafts were actually due to the presence of lead in them and to anticipate that the appearance under the microscope would be normal. When we made sections of the bones through the zones of clouding in cases 1 and 2 (figs. 2 and 3), which were the only cases available for microscopic study, we found that a pathologic condition existed in the part of the bone corresponding to the clouding in the x-ray plate, which could

5. Gies, T.: Experimentelle Untersuchungen über den Einfluss des Arsens auf den Organismus, *Arch. f. exper. Path. u. Pharmacol.* 8:175, 1877.

6. Hunter, D., and Aub, J. C.: Lead Studies: XV. The Effect of the Parathyroid Hormone on the Excretion of Lead and of Calcium in Patients Suffering from Lead Poisoning, *Quart. J. Med.* 20:123, 1926.

7. Bauer, W.; Aub, J. C., and Albright, F.: Studies of Calcium and Phosphorus Metabolism: V. A Study of the Bone Trabeculae as a Readily Available Reserve Supply of Calcium, *J. Exper. Med.* 40:145, 1929.

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account for the latter (figs. 4 and 5). The trabeculae were far more numerous than normal and in consequence more closely packed together. In the aggregate these trabeculae, so greatly increased in number, must have been capable of obstructing the passage of the x-rays and of producing the shadows. So far as it is possible to be influenced toward any conclusion from our two cases, we should suppose that the lead modified endochondral ossification in such a way that the trabeculae formed under the cartilage a much more dense thicket than normally, and that these formations of densely packed trabeculae were the cause of the bandlike shadows. On the other hand, we admit the probability that lead itself was in the trabeculae, and that it may have been partly responsible for the shadows. In any event, an anatomic explanation for the shadows was present in the only two cases which permitted of histologic study. In some cases of congenital syphilis the columns of calcified intercellular substance of the cartilage accumulate in a thick, interlacing network almost undisturbed in the shaft. These columns of calcified intercellular substance are capable of casting dense homogeneous shadows in x-ray pictures, and the dense homogeneous shadows which become visible after the prolonged ingestion of elementary phosphorus depend on an "osteosclerotic" condition in the bone which, as described by Wegner and also by Hess,⁸ seems to consist merely in dense formations of trabeculae similar to those which we have described as resulting from lead.

In the first two cases (fig. 2 and 3), the shadows were narrow and intense, the children were young, and death occurred. From the facts that death took place and that the shadow in the bone was intense, one might think that the amount of lead eaten was large, and from the fact that the band was narrow one might infer that the period of poisoning was of short duration. In case 1 the eating of lead was pronounced and had been in progress four months. In case 2 the amount of lead continually eaten must have been large, and the duration of the habit was six weeks. The failure of the shadow in case 1 to involve homogeneously the entire end of the bone must mean that the ingestion of lead was irregular or intermittent. But there are no statements in the history in case 1 to indicate this. Unfortunately, in case 3 we could get no history of lead poisoning, although the evidence of the presence of the condition in the child was entirely satisfactory. In this case (fig. 6), however, the breadth of the shadow in the rapidly growing

8. Hess, A. F., and Weinstock, Mildred: The Value of Elementary Phosphorus in Rickets: An Experimental Study. *Am. J. Dis. Child.* 32: 485 (Oct) 1926.

end of the bone (from 1 to 1.5 cm.) of a child,⁹ aged 7½ years, indicates that the habit must have been in progress for two years or more, and the position of the shadow immediately under the cartilage, i. e., the involvement of the most recently formed trabeculae, makes one think that the poisoning lasted to the time of the patient's admission to the

9. Dr. Martha M. Eliot and Dr. Susan P. Souther furnished us with the data at their disposal resulting from the study of rickets in New Haven, Conn., by the United States Children's Bureau, concerning the rate of growth of the radius and ulna in young children. Dr. Souther writes: "I collected as many cases as I could in which the ages lay between eighteen and twenty-four months, between twenty-four and twenty-seven months, and also between twenty-four and thirty months, in order to see what variations there were in rate between those periods. The measurements have not been worked out statistically in relation to age periods, and there are not many cases falling in the different periods, but they do show at about what rate the bones of the average child of two years are growing. These measurements are for total growth and not for the lower ends of the bones. The few measurements we had in which we could measure from a definite line indicated that about three fourths of the total growth occurred at the lower ends.

18-24 months (39 children)

Range in growth of radius between 1.05 cm. and 0.45 cm.

Average for group, 0.73 cm. in 6 months period

24-27 months (13 children)

Range in growth of radius between 0.58 cm. and 0.2 cm.

Average for group, 0.33 cm. in 3 months period

24-30 months (14 children)

Range in growth of radius between .9 cm. and .5 cm.

Average for group, .64 cm. in 6 months period

"I collected the figures for the ulna at the same time, and it is interesting that there is a variation between the two bones in the eighteenth to twenty-fourth month period.

18-24 months (12 children)

Range, 1.2 cm. to 0.6 cm. Average, 0.79 cm.

24-27 months (16 children)

Range, 0.55 cm. to 0.17 cm. Average, 0.334 cm.

24-30 months (21 children)

Range, 0.85 cm. to 0.4 cm. Average, 0.63 cm.

"Because of the small number of cases I do not know how much value can be placed on this variation. I thought, however, that you might be interested in the figures."

The lower end of the radius in a child aged from 18 to 30 months, therefore, grows about at the rate of 0.5 cm. in six months or 1 cm. in a year. Unfortunately, in the case of the older child, the child aged 7½ (case 3), Drs. Eliot and Souther could furnish no data. But the child of 7 averages a growth in total body length of 6 cm. between the seventh and eighth years, whereas the child of 2 averages a growth in total body length of 11 cm. between the second and third years. In other words, the child of 7 grows in length only 55 per cent as rapidly as the child of 2 years. Hence the lower end of the radius in the child of 7 should grow about 0.25 cm. in six months or 0.5 cm. in one year. The rate of growth at the lower ends of the fibula and tibia approximates that at the lower end of the radius.

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hospital. In the last case, the history indicates that the eating of lead was marked for one year before the child came under observation and was continued up to the time when she was admitted to the hospital and the x-ray pictures were taken. We know that the child was young, $2\frac{1}{4}$ years, and that the poisoning was sufficient to injure the mentality, but was never of such intensity as to cause death. The shadows in the bones in this instance were not as heavy as the history might lead one to expect, but their breadth (from 1 to 1.5 cm.)⁹ was in keeping with the long duration of the poisoning (1 year), and their position just under the cartilage corroborated the statement that the habit of eating lead continued to the time when the pictures were taken.

There are pertinent questions that we cannot answer. Since the phenomenon seems to be dependent on growth, one would expect it to occur less and less frequently with increase in age, and never to occur in the fully grown person. Wegner stated that phosphorus produced its effect only in the growing organism. We feel certain from theoretical considerations that lead can affect the skeleton in the way described only in the case of children, and we believe that the phenomenon will be the more strikingly developed, the younger the subject. We are influenced in so thinking by the confinement of the lesion to the growing parts of the skeleton, and, in a given case, by the correspondence between the degree of involvement of the ends of the long bones and the growth at those ends. Another question is the constancy of the phenomenon in cases of lead poisoning in children. In the four cases of lead poisoning in which x-ray pictures were available, the shadows in the long bones were present. We do not believe, however, that the shadows will be found in all cases, though we guess that they will be found in most cases of severe poisoning in young children. At any rate, the clouding of the rapidly growing ends of the long bones as seen in x-ray photographs ought to be a useful, corroborating, or perhaps suggestive, sign of lead poisoning in children.¹⁰

The action of lead on the growth of bone is now being made the object of special study.

10. A word of caution is necessary. In the very young infant the outline of the rapidly growing end of the shaft of a long bone is not marked by a dense shadow unless it is the seat of congenital syphilis or rickets in a state of active lime salt deposition (healing). But in the normal child of 1 or 2 years or older, the outlines of the fast growing ends of the long bones are marked by dense shadows, so dense that if they were seen in the young baby they would at once suggest previous rickets or congenital syphilis. These normal shadows at the ends of the tibia and fibula or the lower ends of the femur or radius and ulna in older children must not be mistaken for the phenomenon described as produced by lead.