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Chemical Composition of Transverse Metaphyseal Bands Produced in Growing Bones by Phosphorus Ingestion.

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Transverse bands of increased density in the metaphyseal region of growing long bones, caused by the ingestion of elemental phosphorus, were first described by Wegner.[1] The exact chemical nature of these bands has not been known.

An increase in the absolute and relative amount of inorganic phosphorus in the metaphyseal regions has been suggested. Parks, Goodwin, and Kajdi[2] have shown that lead lines, seen in the X-rays of growing long bones in children suffering from lead poisoning, are produced by the actual deposition of lead in the newly formed bones. Bone growth is most active in the metaphyseal region and the lead deposited there may be demonstrated roentgenologically as a transverse band of increased density. Caffey[3] found that these zones of increased density contained 0.7 g of lead in each gram of bone analyzed. There was only 0.19 g of lead in each gram of bone taken from the shaft of the same bones. In a previous report I have shown that phosphorus causes increased density only in the metaphyses and not in callus of healing fractures.[4]

Harris[5] and others have contended that the phosphorus lines represent zones of arrested longitudinal growth. In a previous report,[4] I postulated the theory that the toxicity of ingested phosphorus causes retardation of the reproduction of new cartilage cells in the epiphyseal plate, while mineral salts continue to be deposited at approximately the normal rate.

The theory that ingested elemental phosphorus causes a marked stimulation of osteoblastic activity in the metaphyseal regions has also been suggested.[2]

If the phosphorus bands were produced by an increase in the percentage or the ratio of phosphorus in this dense bone, a marked

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1 Wegner, G., *Virchows Arch. f. path. Anat.*, 1872, **55**, 11.

2 Parks, E. A., Jackson, D., Goodwin, T. C., and Kajdi, L., *J. Ped.*, 1933, **3**, 265.

3 Caffey, John, *Radiol.*, 1931, **17**, 957.

4 Adams, C. O., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 449.

5 Harris, H. A., *Brit. J. Radiol.*, 1931, **4**, 561, 622.

change from the normal chemical content should be detected by quantitative analyses of the calcium and phosphorus elements.

Twenty-nine young rabbits from 5 litters were used. To each of half of the animals of each litter was given, in addition to the stock diet, a pill of 0.6 mg of yellow phosphorus each day. Phosphorus lines were demonstrated roentgenologically during the second week. Three of the animals which showed wide, dense zones of transverse density in the metaphyseal regions and 3 normal litter mates were selected for this study (Fig. 1).

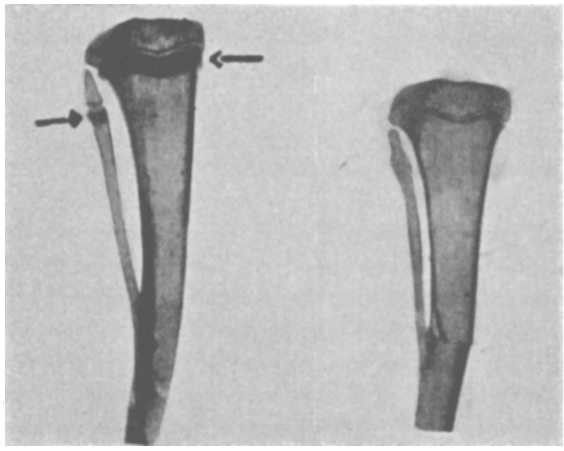

FIG. 1. FIG. 2.

FIG. 1.

Roentgenogram of the tibia and fibula of a young rabbit which was sacrificed after being fed 0.6 mg of elemental phosphorus each day for 9 days. The transverse bands of increased density are distinctly defined.

FIG. 2.

Litter mate control. The diet was identical, but no phosphorus was added.

The right tibiæ were split longitudinally and the metaphyseal region dissected out. In the specimens from the animals which had been receiving phosphorus, the transverse zone of increased density in the metaphysis was grossly visible, and readily excised. The corresponding region of the bone was dissected from the control animals. A portion of the cortex from the shaft of these bones was taken as a further control.

The 12 samples were dried at 80°C and extracted with ether in a Soxhlet apparatus. The fat-free bone was then weighed, ashed in a muffle furnace at 500°C and reweighed. The ash was dissolved in dilute HCl and made up to 25 cc total volume with distilled water.

TABLE I.
Results of Chemical Analysis of the Dry Fat-Free Bones.

Day of Experiment	Calcium				Phosphate				Ratio Ca/P			
	Cortex		Metaphyseal Region		Cortex		Metaphyseal Region		Cortex		Metaphyseal Region	
	No P %	With P %	No P %	With P %	No P %	With P %	No P %	With P %	No P	With P	No P	With P
9	25.6	23.2	21.7	22.2	13.3	12.5	10.5	11.3	1.93	1.86	2.07	1.96
21	25.1	22.3	18.6	21.2	12.3	12.0	9.1	10.3	2.04	1.86	2.04	2.06
26	24.8	24.3	18.1	23.5	12.6	11.7	9.0	11.5	1.97	2.08	2.01	2.04

Determinations of the calcium and phosphorus of these samples were made in duplicate.[6, 7]

The percentage of calcium and the percentage of phosphorus were essentially the same in all specimens. The ratio of the phosphorus and calcium was even more constant. Any variation shown in these ratios is entirely within the range of analytical error (Table I).

These results indicate that the phosphate-calcium ratio in the bones is not changed by the ingestion of phosphorus.

Conclusions. 1. The bone in the phosphorus bands produced in the metaphyses of growing long bones by the ingestion of phosphorus is of normal chemical composition. 2. The increased density represents deposition of radio-opaque salts in greater amount per unit of tissue calcified, since calcification and ossification have continued unchecked while the cartilaginous growth was inhibited. 3. This observation constitutes additional evidence that the zones of increased density in metaphyses of growing bones, produced by ingested phosphorus, are in fact "growth arrest lines."

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Heptaldehyde as a Tumor Inhibitor.*

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In connection with studies on tumor-inhibition by oil of wintergreen, Strong identified heptaldehyde in the active fraction of the oil.[1, 2, 3] He then fed a diet containing commercial heptaldehyde to mice with spontaneous tumors, and observed liquefaction in most of the tumors followed in many cases by regression. More recently, Strong and Whitney reported a similar response in dogs with spon-

6 Fiske, C. H., and Logan, M. A., *J. Biol. Chem.*, 1931, **93**, 211.

7 Fiske, C. H., and Subbarow, Y., *J. Biol. Chem.*, 1925, **46**, 285.

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1 Strong, L. C., *Am. J. Ca.*, 1936, **28**, 550.

2 Strong, L. C., *Am. J. Ca.*, 1938, **32**, 227.

3 Strong, L. C., *Science*, 1938, **87**, 144.