g of food consumed for the first 20 days were essentially the same, 11.8 and 11.0, respectively. Although the diet was maintained over a period of 17 weeks, no symptoms of lathyrism were observed. Since we were using a new lot of *L. odoratus* peas, we felt it necessary to confirm previous observations of the toxicity of this species for rats. Accordingly, we repeated our previous experiments[1] with the new shipment of sweet pea seed. All the rats developed characteristic experimental lathyrism in from 3 to 6 weeks. In view of the failure of young white mice to exhibit any symptoms of lathyrism on diets containing *odoratus*, it is notable that the mice ate from 71 to 86 g (average 77 g) of diet per 100 g of body weight over a typical 4-day period (17th to the 20th day of the experiment). This consumption was twice that of the young white rats under similar conditions (37.5 g), rats which without exception showed signs of acute lathyrism.

Since white mice fed *odoratus* showed no evidence of toxicity, it was of interest to study the effects of diets containing the 2 species of *Lathyrus*, which had proven to be most injurious to rats, *i.e.*, *Lathyrus sylvestris Wagneri* and *Lathyrus latifolius*. Three mice received diets containing 50% *latifolius*. None showed the marked irritability, convulsions or paralysis seen in rats fed this diet, but all lost weight rapidly, decreased the food consumption and died in 5, 10 and 12 days, respectively. Two mice, fed diets containing *latifolius* extracted with 30% ethanol as previously described[1] maintained their weight, ate the diet well and survived with no signs of toxicity for 18 days, at which time lack of available legume resulted in the termination of the experiment.

Three mice fed diets containing 50% of *L. sylvestris Wagneri* seed lost weight rapidly and died in 4, 6, and 7 days, respectively. Increased irritability and convulsions were observed, but these symptoms were, perhaps, slightly less acute than in young white rats.

It is of some interest to note that Schuchardt[2] in his classical paper on lathyrism states that *Lathyrus sylvestris* and *Lathyrus latifolius* afford "essbare Samen!"

Summary. 1. Young white mice of 12 to 15 g body weight fed diets containing 50% *Lathyrus odoratus* meal grew well and showed no development of experimental lathyrism in 17 weeks, although young white rats which received a similar diet developed experimental lathyrism in from 3 to 6 weeks. 2. Diets containing *Lathyrus latifolius* meal (50%) were toxic for both rats and mice, death occurring in from 3 to 8 days (rats) and 5 to 12 days (mice). The extraction of seed of *Lathyrus latifolius* meal with 30% ethanol removed the toxic principle. Mice fed the extracted meal survived and appeared normal over a period of 18 days. 3. Mice fed *Lathyrus sylvestris* seed died with symptoms of acute toxicity in 4 to 7 days.

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17217. Glycogen in Rachitic Cartilage and Its Relation to Healing.*

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The presence of glycogen in cartilage was described almost 100 years ago by Charles Rouget.[1] During the intervening years the feeling has grown that glycogen might have some relation to the calcification process. Marchand[2] noted the high glycogen content of hypertrophic cartilage cells in the region of lime salt deposition. Hoffmann *et al.*[3] observed that "a striking relationship exists between the disappearance of glycogen in car-

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1 Rouget, C., *J. de la Physiol.*, 1859, **2**, 308.

2 Marchand, F., *Virch. Arch.*, 1885, **100**, 42.

3 Hoffmann, A., Lehmann, G., and Wertheimer, E., *Pfluger's Archiv.*, 1928, **220**, 183.

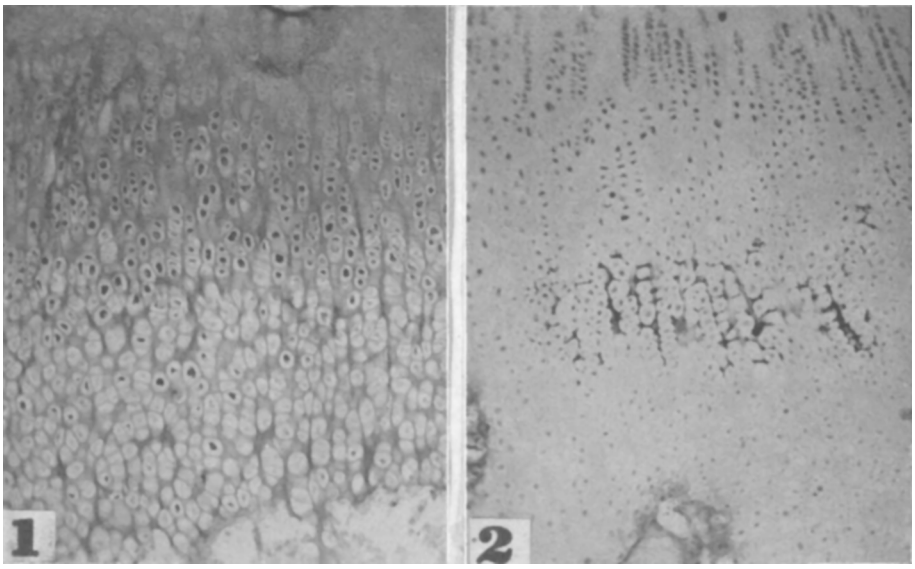

FIG. 1.
Epiphyseal cartilage of rachitic rat. Note widened zone of hypertrophic cells, the uppermost ones of which contain dark accumulations of glycogen. The cell nuclei stain poorly and should not be confused with the glycogen. Periodic acid-leucofuchsin technic.

FIG. 2.
Epiphyseal cartilage of rachitic rat (same magnification as Fig. 1) which had been given phosphate intraperitoneally 24 hours before. Note initial deposition of inorganic material in upper portion of hypertrophic cartilage corresponding to zone in which glycogen is found. Von Kossa technic.

tilage and its ossification." Harris,[4] shortly thereafter, suggested that glycogen might have a bearing on the process of calcification, possibly being related to Robison's[5] phosphatase mechanism. More recently, the presence of glycogen in hypertrophic cartilage cells has assumed further importance as a result of Gutman's[6] demonstration of phosphorylase activity in epiphyseal cartilage.

The following observations, which are part of a general histochemical survey of normal and diseased cartilage and bone,[7] are briefly reported because of the further evidence they bring to bear on the relationship of glycogen to the calcification mechanism. Weanling rats were placed on the Steenbock rachitogenic diet (No. 2965) supplemented with crystalline vitamins. After one to 5 weeks on this regimen some of the rats were injected intraperitoneally with 2.5 cc per 100 g of animal of a mixture of 1 part M/10 NaH_2PO_4 and 4 parts M/10 Na_2HPO_4 to produce healing as recommended by Urist and McLean.[8] Such animals were killed from 12 to 24 hours afterward; uninjected rachitic controls were likewise sacrificed. The upper end of the tibia was fixed in neutral formol-alcohol and, after sectioning without decalcification, stained for glycogen by the Bauer or McManus technics and for inorganic materials by the von Kossa procedure.

Glycogen is not present in the widened zone of hypertrophic cells, so characteristic of rickets. Glycogen is present in the usual increasing amounts in the cells which are undergoing the normal maturation cycle at the upper margin of the widened zone of hypertrophic cells. In other words, glycogen

[4] Harris, H. A., *Nature*, 1932, **130**, 996.

[5] Robison, R., *Biochem. J.*, 1923, **17**, 286.

[6] Gutman, A. B., and Gutman, E. B., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 687.

[7] Follis, R. H., Jr., and Berthrong, M., *Am. J. Path.*, 1948, **24**, 685.

[8] Urist, M. R., and McLean, F. C., *J. Bone and Joint Surg.*, 1941, **23**, 283.

appears in normal fashion as the cartilage cell reaches its full stage of differentiation; as the cell persists, however, for reasons which are not clear at this time, the glycogen disappears. In the rachitic animals in which healing had not been induced, no deposition of inorganic material is present in the vicinity of the hypertrophic glycogen containing cells, or those from which glycogen has disappeared. When healing was instituted, it took place, as has often been noted both *in vivo*[9] and *in vitro*,[10] in the matrix adjacent to those cartilage cells which have most recently matured, that is, in the immediate vicinity of the cells which contain abundant glycogen and, in the early period of observation, not down farther in the matrix adjacent to the hypertrophic cells devoid of glycogen. There is thus a regional relationship between the presence of glycogen and deposition of inorganic elements as demonstrated by the von Kossa technic. It is, of course, impossible to determine any precise reciprocal relationship between the disappearance of glycogen and the appearance of inorganic materials since to follow the disappearance of one and the appearance of the other is not possible. It is hoped that quantitative methods[11] now available, using larger animals, can be applied to study this particular problem.

The glycogen content of rachitic cartilage has received little attention. Some years ago Suppes[12] reported observations on postmortem human material and concluded that rachitic cartilage did not contain glycogen. No mention was made of the presence of glycogen in the uppermost hypertrophic cells so that one suspects autolytic changes may have been a complicating factor.

The localization of glycogen in rachitic cartilage in the region where calcification first appears during healing is, of course, important in any theory of calcification which has the glycogenolytic cycle as its basis.[13] More precise localization of phosphorylase activity[6] as well as that of other enzymes which participate in the cycle will have to be carried out before such an hypothesis can be fully accepted.

Summary. Glycogen is present in rachitic cartilage only in the most recently matured hypertrophic cells. The broad zone of hypertrophic cells beneath is devoid of glycogen. This localization coincides with the area where inorganic elements deposit during the initial stages of healing and furnishes further evidence for the relationship of glycogen, and possibly the glycogenolytic cycle, to the calcification mechanism.

[9] McCollum, E. V., Simmonds, N., Shipley, P. G., and Park, E. A., *J. Biol. Chem.*, 1922, **51**, 41.

[10] Shipley, P. G., Kramer, B., and Howland, J., *Biochem. J.*, 1926, **20**, 379.

[11] Follis, R. H., Jr., *Fed. Proc.*, 1949, **8**, 480.

[12] Suppes. J., *Frank. Z. Path.*, 1922, **26**, 268.

[13] Gutman, A. B., Trans. Conf. on Metabolic Aspects of Convalescence, Josiah Macy, Jr. Foundation, 1946, **14**, 20.

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17218. Simultaneous Administration of Adrenal Cortical Extract and Desoxycorticosterone; Effects on Blood Pressure of Hypertensive Patients.*

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Previous studies[1] have indicated that the continued administration of an adrenal cortical extract may be associated with a decrease in the "resting" blood pressure of patients with

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[1] Pines, K. L., Perera, G. A., Vislocky, K., and Barrows, A. D., PROC. SOC. EXP. BIOL. AND MED., 1948, **68**, 286.