Comparison of Mineralization of the Tibial Epiphyseal Plate in Immature Rats Following Treatment with Cortisone, Propylthiouracil or after Fasting

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Comparison of mineralization in the hypertrophic zone of the tibial epiphyseal plate in immature rats was carried out after treatment with cortisone, propylthiouracil, or after fasting. Under normal conditions, in the extracellular matrix at the calcification front, calcium and phosphate increased, sulfated mucopolysaccharides decreased, and matrix vesicles, which serve as the locus for the formation of hydroxyapatite crystals, increased.

In propylthiouracil-treated rats, hydroxyapatite crystals were prominent, related to an increase in calcium deposition, a decrease of mitochondrial granules (thought to contain calcium and phosphate), an increase in the number of matrix vesicles, and to a marked decrease in the amount of sulfated mucopolysaccharide. In cortisone-treated rats, hydroxyapatite crystals were present but they were not as numerous as in the propylthiouracil-treated rats. Correspondingly, calcium deposition was slightly reduced, mitochondrial granules were more numerous than in the previous groups of rats, matrix vesicles were less numerous, and sulfated mucopolysaccharide were more prominent than in the propylthiouracil-treated rats. In fasted rats, hydroxyapatite crystals were markedly reduced or absent, and related to a decrease in calcium deposition, an increase in the number of mitochondrial granules (suggesting a delay in transport to the extracellular matrix). Matrix vesicles were markedly reduced in number, and sulfated mucopolysaccharide much more prominent than in either the cortisone or the propylthiouracil-treated rats.

Key words: Cartilage — Mineralization — Histochemistry — Matrix vesicles.

Les expériences portent sur la minéralisation de la plaque épiphysaire tibiale du rat de souche Long-Evans, étudiée après traitement à la cortisone, propylthiouracile ou après jeûn prolongé.

Dans des conditions normales, le calcium et le phosphate augmentent au niveau de la matrice extracellulaire, alors que les mucopolysaccharides sulfonés diminuent. Par contre, les vésicules de la matrice au niveau desquels se forment les cristaux d’hydroxyapatite, augmentent.


Dans les rats traités à la cortisone, les cristaux d’hydroxyapatite sont présents, mais dans une quantité moindre que dans les rats ayant subi l’effet du propylthiouracile. Le dépôt en calcium est légèrement réduit; les granules des mitochondries sont plus nombreuses que dans les groupes précédents, le nombre des vésicules de la matrice est plus faible, et les mucopolysaccharides sulfonés sont plus apparents que dans les rats traités à la propylthiouracile.

Dans les rats ayant subi l’effet du jeûn, les cristaux d’hydroxyapatite sont fortement réduits ou entièrement absents. Ceci est du à une réduction de dépôt du calcium, une augmen-

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Introduction

Mineralization of epiphyseal cartilage commences in the hypertrophic zone and depends upon a sufficient concentration of calcium and phosphate for their precipitation (Alcock, 1972), modification of the extracellular matrix to favor mineralization, and the presence of "calcifying globules" in the matrix which seem to be the initial sites of calcification (Bonucci, 1971).

In the normal process of calcification, calcium and phosphate increase toward the zone of calcification (Wuthier, 1969; Matthews et al., 1970); sulfated mucopolysaccharides (Schubert and Pras, 1968; Campo, 1970; Smith, 1970) and collagen (Wuthier, 1969) decrease; "calcifying globules" (Bonucci, 1967, 1969) or "matrix vesicles" (Anderson, 1968, 1969) increase, and hydroxyapatite crystals appear within or in close association with these structures. Intracellular glycogen deposition increases (Wuthier, 1969), chondrocytes hypertrophy and subsequently degenerate as mineralization of the extracellular matrix intensifies.

Under experimental conditions, wherein tibial growth is retarded following treatment with cortisone (Dearden and Mosier, 1972), propylthiouracil (PTU; Dearden, in press), or after fasting (Dearden and Mosier, in preparation), the normal conditions of calcification are differentially altered. These findings suggest the possibility that different growth inhibitors may differentially effect the mineralization process. To determine the effects of treatment with cortisone, PTU, and fasting, on mineralization of the tibial epiphyseal plate in immature