5537

Rate of Decalcification and the Sites of Bone Lesions in Experimental Hyperparathyroidism.*

HENRY L. JAFFE, AARON BODANSKY AND JOHN E. BLAIR.

From the Laboratory Division, Hospital for Joint Diseases, New York City.

A relatively rapid rate of mineral metabolism is associated with rapid bone growth in young animals. Our studies in acute and chronic experimental hyperthyroidism have shown a greater susceptibility to parathormone and a more rapid excretion of calcium in the young than in the adult.[1, 2]

Bauer, Aub and Albright[3] stated that in bone resorption the calcium of the trabeculae is "labile" and is drawn upon in the first instance, while the calcium of the compact bone ("the structural part of the bone") becomes available only "in the case of unusual body demands." Our studies suggest another conception: If we are to speak of labile calcium, it is the calcium in the regions of most active growth; if we are to speak of less readily available calcium, it is the calcium in the regions of less active growth.

We have examined the skeletons of about 150 young guinea pigs, 50 old guinea pigs, 25 young dogs, and 10 rats. The so-called characteristic lesions were severest and most easily produced in young animals suffering from acute and chronic hyperparathyroidism. The bones and portions of bones most affected were the metaphyses of the long tubular bones, and the cortex of the shaft, particularly near the epiphyseal cartilage plates; the costochondral junctions, and the cortex of the ribs used most in the respiratory act; the bones of the skull and of the lower jaw. The metaphyses of the slower growing short tubular bones showed relatively few lesions; the cortex of the shafts of these bones showed practically none. In the guinea pig, most epiphyses are already formed and the centers of ossification for the tarsal and carpal bones are present at birth. No specific lesions were found in these bones, at most a simple atrophy of their trabeculae was observed.

In adult animals, lesions were produced with greater difficulty. When definite, they followed doses so great that the lesions appeared

* Aided by a grant from the Herbert L. Celler Research Fund.

1 Bodansky, A., Blair, J. E., Jaffe, H. L., *J. Biol. Chem.*, 1930, **88**, 629.

2 Jaffe, H. L., Bodansky, A., Blair, J. E., PROC. SOC. EXP. BIOL. AND MED., 1930, **28**, 174.

3 Bauer, W., Aub, J. C., Albright, F., *J. Exp. Med.*, 1929, **49**, 145.

in sites which escaped the effects of the smaller doses administered to the young (epiphyseal ends of the long tubular bones).

Thus, the typical lesions of experimental hyperparathyroidism which are merely secondary to the primary process of decalcification, occur especially in the regions of rapid growth. A higher rate of mineral metabolism in particular bones may also be associated with active use of these bones. However, a generalized thinning of the bones, without evidence of active resorption, is observed in the less susceptible bones.

The following formulation of the mechanism that determines the availability of calcium is suggested: Bone resorption and bone deposition are processes that go on in *all* bone constantly. When the rate of these processes is increased, it is increased in *all* bone. Both processes are more rapid in the regions of active growth, irrespective of anatomical structure. A mechanism is therefore indicated for rapid decalcification in those regions when a condition is present favoring an excess of resorption over deposition. In regions of less active bone growth, resorption and decalcification proceed more slowly under normal conditions, and a great stimulus is required to produce a considerable degree of resorption.

This conception makes intelligible the pronounced resorption of the trabeculae of the metaphyses, especially of the rapidly growing bones and the localization of the lesions in these regions; the trabeculae of all epiphyses under the same conditions are subject only to general thinning. It also explains not only the generally greater susceptibility of the bony skeletons of actively growing animals to parathormone, but also the quantitative difference in response of different bones, and of different portions of given bones, which is observed strikingly in young animals, but also to a certain degree in older animals.

It is suggested that the same principle applies in experimental rickets and scurvy, which show the localization of the so-called characteristic lesions in the regions of active growth; and in a number of clinical conditions (the so-called osteochondritides), which show localization of lesions in bones (and in regions of bones) of slow metabolic exchange and therefore of slow reparative capacity. Schmorl[4] in 1909 stated, in a discussion of clinical rickets, that the lesions appear earliest and are most severe in the regions of rapid growth.

[4] Schmorl, G., *Gesell. f. Natur. u. Heilk. in Dresden, Jahresbericht,* 1908-1909, 90, 18th sitzung.