THE ACTION OF PARATHYROID HORMONE AND Ca^{45} ON RAT BONE TISSUE

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In experiments on albino rats quantitative analysis of roentgenograms showed that the combined action of exogenous parathyroid hormone and Ca^{45} leads to complex changes in bone structure: thinning of the cortical layers of the long bones and an increase in the degree of mineralization of the bone tissue.

The most important role in the stimulation of bone reconstruction and the regulation of calcium metabolism is played by the hormone of the parathyroid glands – parathormone [2, 5, 11]. If exogenous parathormone is injected into animals [1, 2] changes in the mineral component of the bone tissue can be studied in the early and late stages of the bone lesion. The most suitable methods for this purpose are intravital observations: the radioisotope method using osteotropic elements (Sr^{85} and Ca^{45}) [7, 8], and the roentgenographic method [4]. With the latter method it is possible to estimate the development of the bone pathology resulting from exposure to radiation of the osteotropic substances administered.

Disturbances of mineralization of the bone tissue of rats in the late periods of action of parathormone and Ca^{45} were studied.

EXPERIMENTAL METHOD

Experiments were carried out on 135 noninbred male albino rats weighing 180 g; 88 of the animals received intramuscular injections of Soviet parathormone in various doses (from 1 to 3 ml daily for 22 days) for different periods (from 5 to 40 days, 2 ml daily). The activity of the parathormone used was 20 activity units/ml fluid. The same rats recieved radioactive Ca^{45} by mouth in a dose of 11 μCi daily for 40 days. The remaining animals either were left intact or received parathormone only or Ca^{45} only.

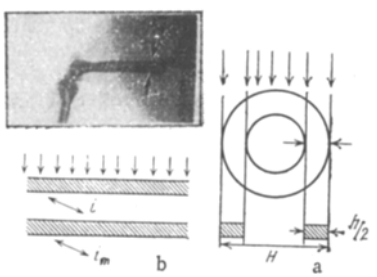

Fig. 1. Scheme of measurements of linear dimensions of bone on roentgenograms (a) and optical density of blackening of x-ray film (b). Explanation in text.

Roentgenography of the bone tissue was carried out on the 180th-200th day after the experiment began. Processing of the RM-1 film, operation of the URdD-2 apparatus, and the positioning of the animals were absolutely identical in all cases. The severity of the bone changes on the roentgenograms was determined by roentgenogramometry: the linear dimensions of the bones and the ratios between them were anlyzed [6] and the density of the bone was determined from the intensity of the x-ray image measured with a densitometer [10]. The zone of the meta-diaphysis from the proximal part of the femur immediately below the lesser trochanter was chosen for study. The value of the index R was

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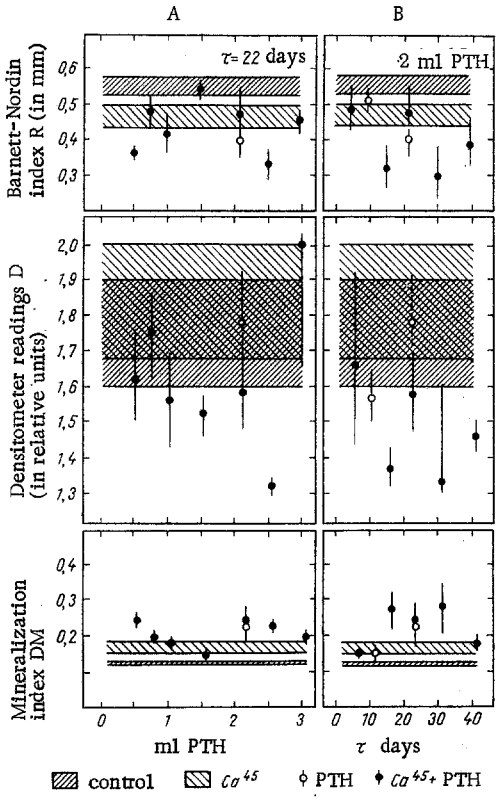

Fig. 2. Action of parathormone (PTH), irradiation (Ca^{45}), and a combination of both on roentgenologic characteristics of bone tissue in relation to dose (A) and duration of administration (B) of the hormone.

found from the measurements of the roentgenograms (Fig. 1a) as the ratio between the sums (h) of the cortical layers of the anterior and posterior surfaces of the diaphysis and the width (H) of the dialysis: R = h/H. The roentgenograms were measured with a type MF-4 densitometer under identical conditions with the optical density scale set at zero before each measurement. In the region between the cortical layers (Fig. 1b) the mean density of blackening of the x-ray film (i) was recorded from 5 or 6 readings of the microphotometer, and the shadow created by the soft tissues near the edges of the bone also was measured photometrically (i_m). The index $\phi = i_m/i$ was then calculated. To analyze the data the standard error was calculated for the results relating to each animal separately and for the groups. Using the equation DM = $(\ln \phi)/h$, deduced as a result of the analysis of data obtained by the use of the two methods, an effective value (DM) describing the degree of mineralization both of the cortical layers and of the inner portion of the long bone, was determined.

EXPERIMENTAL RESULTS

One of the main features of the disturbance of bone metabolism detectable by the method of quantitative roentgenography in the present experiments was the degree of osteoporosis. To determine this it is necessary to allow for differences in the intensity of bone destruction and bone formation [9].

The values of all indices used (R, D, M) demonstrate changes in bone formation in all the experimental groups compared with the control (Fig. 2). Prolonged administration of the hormone led to osteoporosis, chiefly through thinning of the cortical layer of the bone (R). In animals receiving Ca^{45} only, moderate osteoporosis also was observed, not only with a decrease in the linear dimensions of the bone but also with some increase in its density. Consequently, Ca^{45} (dose of irradiation to the skeleton 2.5-3 krad) not only causes bone destruction, but also produces some intensification of pathological bone formation.

The most intensive and complex reconstruction of bone tissue took place in response to the combined action of parathormone and Ca^{45}. The similar direction of their action evidently led to considerable thinning of the cortical layers in the late stages with an increase in the degree of mineralization of the bone (DM). The severity of these changes increased with an increase in the dose and duration of administration of the parathormone, but only up to a certain limit. The impression was obtained that parathormone catalyzers changes in the structure of the skeleton produced by the action of Ca^{45}.

These results confirm earlier information [1-3] according to which parathormone and Ca^{45} both induce osteoporosis. The methods used to process the roentgenograms in the present experiments reveal fundamentally important changes indicating a disturbance of the mineral component of the bone. In the late stages of combined action of parathormone and Ca^{45} complex structural changes in the bone tissue of the "hypertrophic osteoporosis" type are observed: compensatory or pathological condensation of the mineral component takes place in the depth of the atrophied or destroyed bone.

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