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POST-FRACTURE BONE SALT RESORPTION STUDIED IN RATS

By

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INTRODUCTION

In radio-isotope experiments on bone salt metabolism, the isotope is usually administered *after* the factor to be studied. This method permits an accurate determination of the accretion rate of the bone salt (*Bauer, Carlsson,* and *Lindquist* 1955), and, though less conveniently, of the resorption rate.

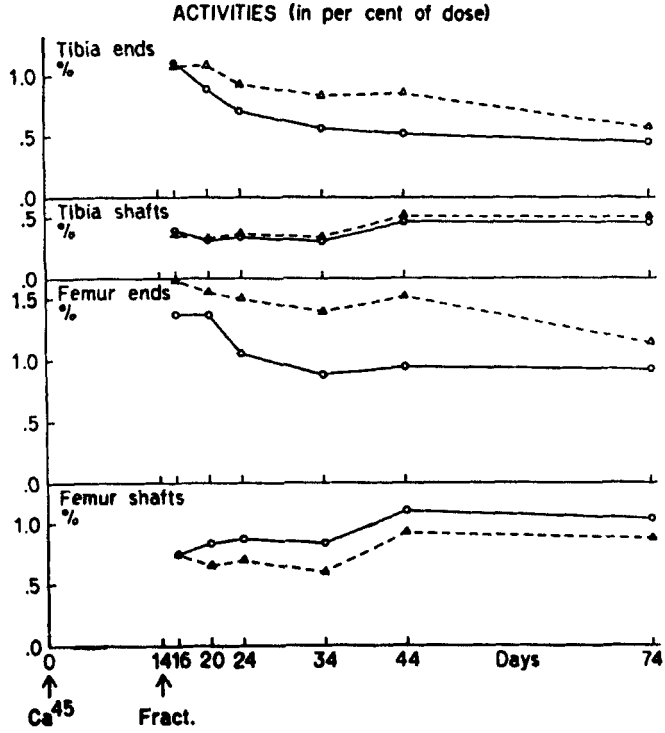
However, if isotope is administered a suitable length of time *before* the factor to be studied is allowed to set in, *even a small change in resorption rate may influence the bone salt activity more than would a marked change in accretion rate.*

In the present paper this method has been used to study the effect on bone salt metabolism caused by an experimental fracture in adult rats.

EXPERIMENTAL

Twenty-four male, adult rats of an inbred strain received each a subcutaneous injection of 4.5 ml calcium gluconate solution containing 1 mg low specific activity Ca^{40} + Ca^{45} per ml. Fourteen days after the isotope injection, one femur in each animal was fractured manually under ether anesthesia. The rats were killed with ether in groups of four, two to sixty days after the fracture.

In each animal the right and left femurs and tibias, and the incisor teeth were removed and dissected free from adhering soft tissues. The bones from one animal in each group were used for an autoradiographic investigation. The bones from three animals in each group were divided in ends and shafts, the incisor teeth from all animals of the last three groups of the experiment and the bone samples were ashed in an electrically heated muffle. The ash of each sample was



Graph. 1.
Activity Values of the Tibias and Femurs Following Fracture of One Femur Shaft in Adult Rats.

○———○ Fracture side.
△- - - - -△ Uninjured side.

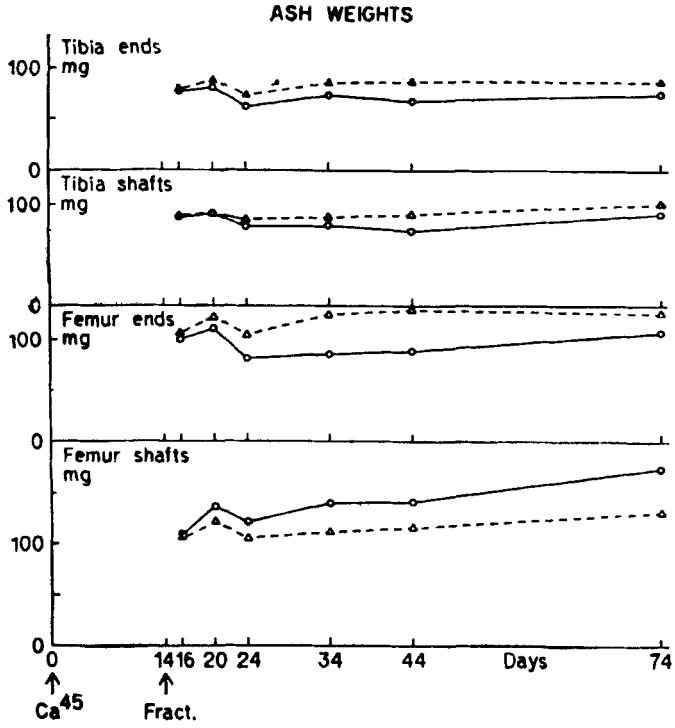
Ca^{45} was given as a subcutaneous injection fourteen days prior to fracture. Three animals in each group. For all kinds of bone samples the ratio uninjured/fracture side differed significantly from 1.00 (Tibia ends and femur ends and shaft: $P < 0.001$; tibia shaft: $P < 0.01$). The calculations are based on the pooled ratios of all animals of the experiment.

weighed (accuracy ± 0.1 mg) and the activity was determined on nitric acid solutions of the ash (accuracy better than ± 3 per cent of values). See *Carlsson*, 1951, and *Bauer*, 1954, for a detailed description of the procedure followed during treatment of the samples.

Throughout this paper the activities of the samples have been expressed in per cent of dose.

RESULTS AND DISCUSSION

From graphs 1 and 2 it is seen that the femur shaft fracture caused a loss both in ash weight and in activity in the metaphyseal ends of



Graph. 2.
Ash Weights of the Tibias and Femurs Following Fracture of One Femur Shaft in Adult Rats.

○———○ Fracture side.
△- - - - -△ Uninjured side.

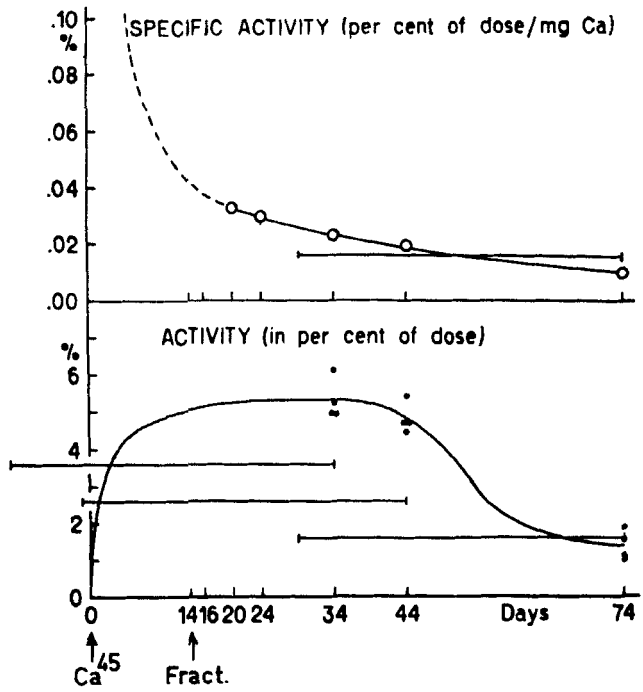
Three animals in each group. For all kinds of bone samples the ratio uninjured/fracture side differed significantly from 1.00 ($P < 0.001$). The calculations are based on the pooled ratios of all animals of the experiment.

the fractured femur and in those of the tibia of the fracture side. This effect can be due to one or both of the following factors (so long after the administration of the isotope, exchange reactions can be disregarded, *Bauer, Carlsson,* and *Lindquist,* 1955):

a) a decrease in the rate of bone salt accretion;

b) an increase in the rate of bone salt resorption.

At the time of fracturing, the specific activity of the serum Ca was low. The eight-fold increase in the rate of bone salt accretion (*cf. Bauer,* 1954) thus caused but a 25 per cent increase in activity in the fractured femur shaft (graph 1). Hence, the 30 per cent loss in activity in the femur ends can hardly be explained by a decrease in the rate of bone



Graph. 3.
Activity Values of the Incisor Teeth Following Administration of Ca^{45} to Adult Rats.

Lower curve: In the graph are indicated the incisor teeth activity values of each animal of the 34-, 44-, and 74-Day groups. The curve has been drawn after *Bauer*, 1954, table 1, p. 172. The horizontal lines indicate the 45-Day life span of the incisor teeth of the three groups.

Upper curve: The horizontal line which indicates the 45-Day life span of the 74-Day incisors has been drawn at the level of their specific activity.

The curve has been drawn through the specific activity values of the fracture callus of the femur shaft. For each animal the specific activity of the fracture callus has been calculated from the activity and ash weight differences between fractured and uninjured femur shaft. The mean value for each group (3 animals) has been indicated in the graph.

salt accretion, and it must, then, be due mainly to an enhanced rate of bone salt resorption. The same is true for the tibia ends of the fracture side.

In earlier investigations (*Bauer* 1954; *Bauer* and *Carlsson* 1955) it was found that the bone salt of the one- to two-week-old fracture callus is reached by resorption already within four to five days following its formation. If this is so even in an older callus, the *specific activity*

(per cent of dose per mg Ca) of the fracture callus should be practically equal to that of the serum Ca when the decline in the latter is no longer rapid. From the incisors' activity (graph 3, lower curve) the average specific activity of the serum Ca during a 45-day period can be computed. It will be seen in graph 3, upper curve, that the average specific activity of the serum Ca during the last 45 days of the experiment was in close agreement with that of the fracture callus. The calculation of the specific activity of the fracture callus is liable to obvious errors. It is tempting to suggest, however, that even the old fracture callus is rapidly rebuilt.

(Provided the life span of the incisors is known, this method of estimating the specific activity of the serum Ca, even months after the administration of the radiocalcium, is easy to perform and gives a reliable value).

SUMMARY

Fourteen days after Ca^{45} had been administered to adult rats, one femur shaft was fractured manually in each rat. Owing to the rapid decline in blood activity, a change in the resorption rate of the labelled bone salt influenced the activity values more than did a change in the accretion rate of the bone salt. A marked enhancement in the resorption rate of the bone salt was found in the metaphyseal ends of the long bones of the injured leg.

RESUME

Quinze jours après que l'on ait administré du Ca^{45} à des rats adultes, un fémur a été fracturé manuellement chez chaque rat. En raison du déclin rapide de l'activité du sang, un changement du taux de résorption du sel osseux de l'os en question a influencé l'activité plus qu'un changement dans le taux d'accrétion du sel osseux. Une augmentation marquée du taux de résorption du sel osseux a été constatée dans les extrémités métaphysaires des longs os de la jambe fracturée.

ZUSAMMENFASSUNG

Vierzehn Tage nachdem erwachsene Ratten Ca^{45} erhalten hatten, wurde ein Femurschaft mit der Hand gebrochen. Infolge des raschen Niederganges der Blutaktivitet beeinflusste eine Veränderung in der Resorptionsgeschwindigkeit des gemerkten Knochensalzes die Aktivitetswerte mehr als dies der Fall bei einer Veränderung der Zunahme-

geschwindigkeit der Knochensalze war. Eine deutliche Erhöhung der Resorptionsgeschwindigkeit des Knochensalzes wurde in den Enden der Metaphyse der langen Knochen des geschädigten Beines gefunden.

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