CHANGES IN DISAPPEARANCE OF INTRAVENOUSLY ADMINISTERED $^{47}$Ca AT THE ONSET OF ALIMENTARY ABSORPTION OF UNLABELLED CALCIUM

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SUMMARY

1. Administration of a large amount of unlabelled calcium orally 60 min after intravenous injection of $^{47}$Ca leads to a temporary rise of serum specific radioactivity in healthy volunteers.

2. This short-term rise is followed by a more rapid decline and in some instances by oscillations of specific radioactivity.

3. Both these effects could be caused by secretion of thyrocalcitonin resulting from a rise of serum calcium concentration during calcium absorption from the gastrointestinal tract.

Key words: calcium kinetics, calcium absorption, $^{47}$Ca isotope, thyrocalcitonin.

During an investigation of the kinetics of the disappearance of intravenously administered $^{47}$Ca unusual results were observed if there was simultaneous alimentary absorption of a considerable amount of unlabelled calcium.

Administration of $^{47}$Ca alone in tracer amounts does not interfere with the dynamic equilibrium of calcium in the organism and the disappearance curves of activity from serum can be expressed as the sum of two or three exponentials. The oral administration of inactive calcium affects calcium homeostasis and stimulates regulatory mechanisms which oppose the change in serum calcium. The rise of serum calcium concentration due to absorption should result in secretion of calcitonin, which enhances the disappearance of calcium from the rapidly exchangeable pool (Munson & Hirsch, 1967). Such an effect should be revealed by a more rapid decline in serum radioactivity. We found, however, that in all subjects a temporary short-term rise of serum specific radioactivity occurred closely after the increase in total serum calcium. This observation is compared with the findings of other authors, who produced a similar effect in animals and human subjects by infusion of calcitonin (Caniggia, Gennari, Bencini, Palazzuoli, Borello & Cesari, 1968; Caniggia, Gennari, Piantelli & Vattimo, 1972; Milhaud, Moukhatar, Cherian & Perault, 1966).

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MATERIAL AND METHODS

Eight healthy male students, aged 20–22 years, with normal body weight ± 10% of the ideal weight, were studied. All agreed to the experimental procedure. Before the investigation the experimental subjects were on a normal diet and their calcium intake was about 800 mg daily, and phosphorus intake exceeded 1000 mg daily.

Experiment A. In the morning at 08.00 hours 10 μCi of $^{47}$Ca was injected intravenously in the form of $^{47}$CaCl$_2$ (calcium chloride) in 1 ml of saline. Blood specimens for the assessment of radioactivity were collected at time 0 and subsequently at 15, 30, 45, 60, 75, 90, 120, 180 and 300 min after administration of the radioisotope.

Experiment B. This trial was made 2 months after trial A. In the morning 10 μCi of $^{47}$Ca was injected intravenously as $^{47}$CaCl$_2$ in 1 ml of saline to fasting subjects. After 1 h 0·25 mmol of calcium per kg body weight, in the form of CaCl$_2$ dissolved in 100 ml of distilled water (i.e. 0·49 mmol of CaCl$_2$ per kg body weight), was administered orally. Blood was collected after the same intervals as in trial A for the estimation of serum calcium concentration and specific radioactivity of the isotope.

![Graph](image)

**Fig. 1.** Curves of $^{47}$Ca specific radioactivity in serum of individual subjects nos. 1–8 after intravenous injection of 10 μCi of $^{47}$Ca alone (broken lines) and after intravenous injection of 10 μCi of $^{47}$Ca with subsequent oral administration of CaCl$_2$ (at arrow) 60 min later (continuous lines). The specific radioactivities are expressed as % of the specific radioactivity assessed at 15 min after administration of the isotope.
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The serum calcium concentration was assessed by atomic absorption spectrophotometry (Kocián & Rubeška, 1968). The serum radioactivity was estimated by a scintillation well detector, with the volume of the estimated specimen 3 ml. The impulses were recorded in the area of the photopeak of $^{47}$Ca (1.31 MeV) by means of a one-channel analyser (scintillation gamma spectrometer Tesla NZG 319) discriminating from $^{47}$Sc.

RESULTS

Fig. 1 records the serum specific radioactivity curves of the experimental subjects (nos. 1–8) in experiment A (broken lines) and in experiment B (continuous lines). The specific radioactivities are expressed as % of the specific radioactivity 15 min after administration of the isotope, by which time a uniform distribution is achieved in the serum compartment. We deliberately omitted extrapolation to zero time. When this method is used, all curves start at the same value, which greatly facilitates their comparison. In Fig. 2 the same curves are expressed as a zone±SEM. Fig. 3 records the complete results of experiment B. The continuous line indicates the average serum specific radioactivity±SEM in % of the administered radioactivity and the broken line expresses the increment of serum calcium concentration as compared with the basal level in an analogous way, i.e. in % of the administered amount per litre of serum. The mean initial serum calcium concentration was $2.4±SD 0.19$ mmol/l (SD = 0.76)

![Graph](https://example.com/graph.png)

**Fig. 2.** Mean curve of specific radioactivity after injection of $^{47}$Ca alone (broken line) and after injection of $^{47}$Ca and subsequent oral administration (at arrow) of unlabelled calcium (continuous line). The curves are expressed as a zone±1 SEM.
and the values at different times after oral calcium were: in the fifteenth minute, 2.53 ± 0.225 mmol/l; in the thirtieth minute, 2.55 ± 0.288 mmol/l; in the sixtieth minute, 2.68 ± 0.225 mmol/l; at 120 min, 2.65 ± 0.075 mmol/l; at 180 min, 2.55 ± 0.1 mmol/l. The maximum serum calcium concentration was sometimes reached in 45 min but usually only 60 min after administration of calcium. The mean maximum increase of serum calcium concentration was 114 ± 9.5% of the initial value. In the individual subjects in Fig. 1, as well as in the mean curves presented in Figs. 2 and 3, a temporary increase of serum specific radioactivity which follows shortly after the oral administration of inactive calcium can be seen. Subsequently the majority of individual curves and the mean values display a more rapid decrease in specific radioactivity with an irregularity sometimes suggestive of periodic oscillations. In two subjects (no. 7 and no. 8 in Fig. 1) during the subsequent absorption of inactive calcium the disappearance of $^{47}$Ca is slower. In a minority of subjects there was a temporary rise of $^{47}$Ca radioactivity in experiment B; the reason for this is not clear.

DISCUSSION

The majority of authors agree that calcitonin inhibits the release of calcium from bone (Copp, 1970; Munson & Hirsch, 1967) and thus prevents the influx of this element into the 'rapidly exchangeable pool' and plasma. Moreover, calcitonin inhibits reabsorption of calcium in the distal tubule (Cochran, Peacock, Sachs & Nordin, 1970) and thus increases urinary excretion of calcium. Both mechanisms reduce the serum calcium concentration. It is known that the hypocalcaemic effect of calcitonin begins after 30–60 min (Copp, 1970); less is known about the mode of its initial action. Milhaud, Moukhtar, Cherian & Perault (1966) observed in rats that
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after injection of calcitonin the decline of specific radioactivity after previous injection of $^{47}$Ca is temporarily arrested; a similar effect is described also by O'Riordan & Aurbach (1968). Caniggia et al. (1968) found in the disappearance curve of $^{47}$Ca administered intravenously a temporary increase of specific radioactivity after calcitonin infusion, and explained this phenomenon by reduced dilution of the isotope by stable calcium released from bone, i.e. by interference with bone absorption and consequent calcium release. This explanation was elaborated in a later paper by Caniggia et al. (1972), who demonstrated that the temporary increase of the specific radioactivity and plasma total radioactivity after a thyrocalcitonin infusion 60–240 min after intravenous injection of $^{47}$Ca is most probably due to a release of $^{47}$Ca from bone cells, as these authors demonstrated a simultaneous decline of the surface radioactivity of bone during the same period. They therefore suggested that at the beginning of the action of calcitonin cellular calcium first declines, only to increase during its later action. This may be compared with the similar though opposite effects of parathormone: after its administration intravenously the serum calcium concentration first declines temporarily and only rises later (Parsons, Neer & Potts, 1971).

Our findings are in keeping with the theory of Caniggia et al. (1972). Moreover the findings suggest a very sensitive and rapid regulation of calcium metabolism, the first small increase of serum calcium concentration due to alimentary absorption of calcium stimulating calcitonin secretion. According to Munson (1971) calcitonin secretion may be stimulated also by liberation of some gastrointestinal hormones (gastrin, cholecystokinin or glucagon) at the onset of calcium absorption. Later in our experiments the already recognized effects of calcitonin are manifested, i.e. a more rapid disappearance of $^{47}$Ca from plasma, which corresponds to findings of impaired bone absorption (Copp, 1970; Munson & Hirsch, 1967) and to the enhanced urinary calcium excretion (Cochran et al., 1970) shown previously in the same experimental subjects (Kocián, Brodan, Bakos & Kuhn, 1971). The oscillatory course of the specific radioactivity curves in experiment B may indicate feedback action of factors regulating serum calcium concentration.

This paper provides evidence that the oral administration of a large amount of calcium rapidly affects the homeostatic mechanisms. The curves have a shape identical with those of Caniggia et al. (1968, 1972), suggesting that the temporary rise of $^{47}$Ca serum specific radioactivity after oral administration of unlabelled calcium is due to calcitonin release, which according to those authors temporarily releases labelled calcium from bone cells before its other actions are manifest.

REFERENCES


