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PROGRESSIVE DECREASE OF TRUE INTESTINAL CALCIUM ABSORPTION WITH AGE IN NORMAL MAN

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The true intestinal absorption coefficient of calcium (a-value) was determined in 26 men and 26 women, normal in respect to calcium metabolism and intestinal function, by a double-isotope ratio technique. The age of the patients ranged from 12 to 81 years, and the a-values were between 20 and 75% of oral dose with a geometric mean of 34%. A highly significant negative linear correlation was present between the logarithm of a-value and age ($r = -0.526$, $p < 0.001$). No differences were found between the men and women either in respect to regression coefficients or to position of regression lines.

Although the eventual role of decreased calcium intake and/or absorption in the pathogenesis of senile osteoporosis has been repeatedly discussed (*1,2*), the question of influence of age on calcium intestinal absorption in normal man is still controversial. Thus, Avioli, et al (*3*), using early plasma radioactivity measurements after administration of ^{47}Ca by mouth as an index of absorption, reported a progressive decrease of intestinal absorption in normal women between the ages of 12 and 85 years. Bullamore, et al (*2*), using a similar method, modified somewhat by applying kinetic analysis on the plasma radioactivity values, found a decrease of calcium absorption only in their older patients, i.e. after the age of about 55 years in women and 65 years in men. However, the methods used in these studies have been repeatedly criticized (*4–6*) as giving values that could be influenced by a considerable number of factors other than true intestinal calcium absorption.

We therefore considered it worthwhile to reexamine this question using a double calcium tracer technique, a method less open to criticism for measuring calcium intestinal absorption.

MATERIALS AND METHODS

This study was carried out on 52 patients (26 men and 26 women) between the ages of 12 and 81 years who were hospitalized for minor ailments and who were free of skeletal disorder or conditions known to affect calcium metabolism. The true calcium intestinal absorption coefficient of these patients was determined according to the method described by De Grazia, et al, in 1965 (*7*). All the patients were on free hospital diet when studied.

In the morning of the first day, with the patient fasting since the previous night, an oral tracer dose of approximately 25 μCi ^{47}Ca was given in 160 mg of carrier calcium (as the chloride) together with a strictly standardized breakfast containing 80 mg of calcium. Apart from breakfast, the patient remained fasting for at least 4 hr. Exactly 2 hr after the oral tracer, a second tracer dose containing about 7 μCi of ^{45}C was administered intravenously. For younger patients the dose was reduced according to age. The concentrations of the two radiotracers in percent of respective doses per liter plasma were determined in blood samples obtained exactly 24 hr after administration of the second tracer. Calcium radioactivity was determined by a well scintillation counter for ^{47}Ca with the discriminator set to exclude all radiation from the daughter ^{47}Sc. Calcium-45 radioactivity was measured at least 1 month later so that most of the ^{47}Ca and ^{47}Sc radioactivity had already decayed. The samples were prepared according to the method of Lutwak (*8*) and measured in a liquid scintillation spectrometer. Appropriate corrections were applied for any interference from remaining ^{47}Ca or ^{47}Sc radioactivity and also for ^{45}Ca present as a contaminant (5%) in the tracer ^{47}Ca

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solution (*7*). The calcium absorption coefficient, a, in percent of oral dose was calculated according to the formula

$$a = \frac{^{47}Ca\ \%\ \text{oral dose/liter plasma}}{^{45}Ca\ \%\ \text{intravenous dose/liter plasma}} \times 100.$$

Statistical analysis was carried out according to standard techniques (*9,10*).

RESULTS

The values of true intestinal absorption coefficient, a, ranged from 20 to 75% of oral dose and approximated very well a log normal distribution. The mean of $\log_{10}a \pm$ s.d. was equal to 1.529 ± 0.146, corresponding to a geometric mean of 33.9% for the population studied. Statistical analysis revealed a negative linear correlation between $\log_{10}a$ and age both in men and women, the corresponding regression equations being

$$\log_{10}a = 1.768 - 0.0047x \quad (r = -0.531, p < 0.01) \text{ for men}$$

and

$$\log_{10}a = 1.7175 - 0.0041x \quad (r = -0.523, p < 0.01) \text{ for women}$$

where x is age in years. Since covariance analysis revealed no difference between men and women in either regression coefficients or position of regression lines, all data were pooled and the common regression line shown in Fig. 1 was drawn according to the equation

$$\log_{10}a = 1.7317 - 0.0042x \quad (r = -0.526, p < 0.001). \quad (1)$$

Using the neperian instead of decimal logarithm and rearranging Eq. 1, we obtain

$$a = 53.7\, e^{-0.0969x} \quad (2)$$

which shows that the intestinal absorption coefficient, a, can be described as a negative exponential function of age.

DISCUSSION

Although a decrease of calcium intestinal absorption with age is well documented in animals (*11,12*), data concerning normal man are few and conflicting (*2,3,13*). Part of the problem was, no doubt, the fact that no simple method that was unanimously accepted as accurate was available for measuring true intestinal absorption of calcium in man. In the last few years, however, since the two radioisotopes ^{45}Ca and ^{47}Ca became widely available, the problem seems to be adequately met by using double labeling of dietary and body calcium by two different radioisotopes of calcium, the one being given by mouth and

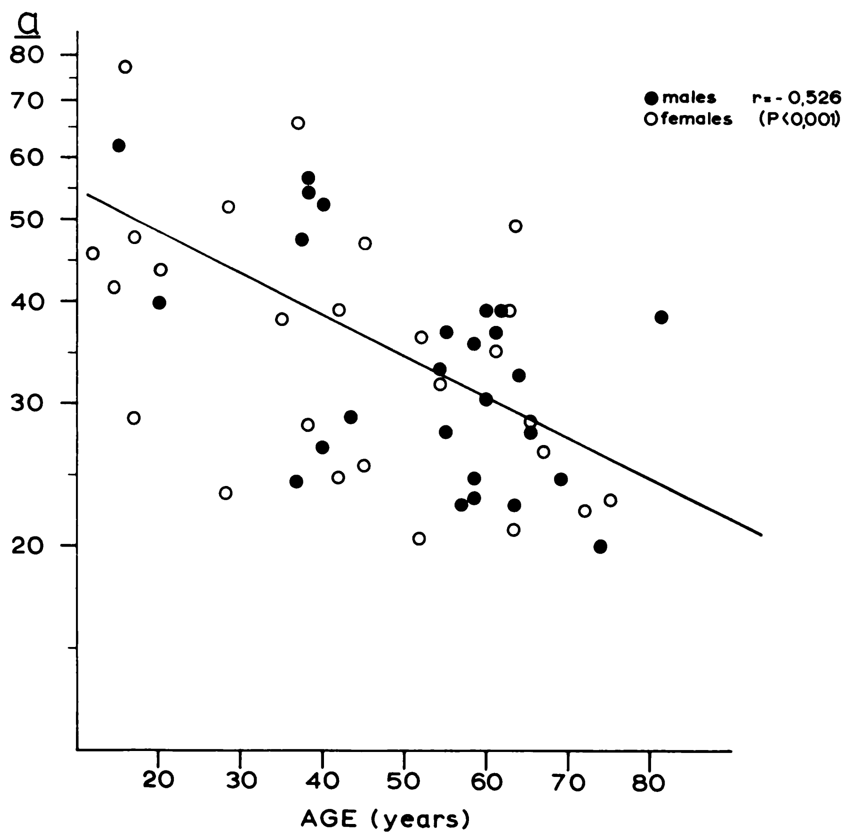

FIG. 1. Relationship between coefficient of intestinal absorption of calcium (a) and age in normal male and female subjects. Regression line is also presented.

the second intravenously (*4–7*). It has been shown that if the intravenous tracer is given at about 2 hr after the oral tracer and a relatively long time interval is allowed before measuring the two isotopes' equilibration ratio, the two tracers can be considered for all practical purposes as given simultaneously (*5,6*). Thus, the influence of any disturbing factor, apart from calcium absorption, can be allowed for in the calculation of the true intestinal absorption coefficient since it will affect in an exactly similar way the concentration of the intravenously administered tracer.

The mean value of about 34% found in the present study for the intestinal absorption coefficient of calcium (a) is in good agreement with similar reports (*4,7*) using comparable methods.

The finding that the intestinal absorption coefficient of calcium could be fitted with a negative exponential function of age between ages 12 and 81 years, suggests that the decline in intestinal calcium absorption is a continuous process rather than an abrupt phenomenon of old age as suggested by Bullamore, et al (*2*) and Sack (*13*). The reason for the difference between the present findings and those of the two aforementioned studies is not clear.

Methodology differences may account for the different results found by Bullamore, et al (*2*), since these workers used a kinetic analysis technique and very low carrier calcium levels. On the other hand, Sack (*13*) used a technique similar to ours, but the study was carried out in a population of patients suffering from cancer, a fact making comparison of the results obtained in that study with the findings in an essentially normal population like ours difficult. On the other hand, our results are in general agreement with findings made by Avioli, et al (*3*), using a totally different method to that used in our study.

Any explanation as to the mechanism involved in the phenomenon of the progressive decrease of intestinal calcium absorption is, based on the present evidence, purely speculative. Vitamin D deficiency has been suggested (*2*), but, in view of the early onset of the decline in calcium absorption, this seems rather unlikely. As has been pointed out by Avioli, et al (*3*), decrease in intestinal absorption with age occurs in a considerable number of other substances, such as D xylose, carotene, and vitamin B_{12}. Therefore, the decline in calcium absorption coefficient may be only a manifestation of a general decrease of intestinal function with advancing age.

From a practical viewpoint, the present findings suggest that age should be taken into account when studying calcium absorption in health or disease.

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