Calcium, phosphorus and magnesium requirement

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The nutrient requirement of an adult can be defined in various ways, some of which are unfortunately not amenable to direct measurement. Thus if we define requirement as the amount required to preserve normal health we come up against the impossible task of measuring normal health. Similarly, if we define it as the amount required to preserve normal weight, we encounter the difficulty of defining normal weight. These difficulties can be avoided with mineral nutrients, which pass through the body unchanged, by defining the requirement as the amount needed to preserve mineral balance. It can hardly be disputed that prolonged negative mineral balance (be it of sodium, potassium, magnesium, phosphorus or calcium) must ultimately deplete the body stores and be detrimental to health.

This definition is adequate as far as it goes but is probably not quite sufficient. Adaptation to low intakes of Mg and P is achieved by lowering the plasma concentration and so lowering the urinary excretion. It would clearly be misleading to define requirement purely on the preservation of balance if this preservation of balance involved such a lowering of the plasma concentration of the nutrient concerned that it significantly impaired normal health. Thus there is abundant experimental evidence on animals and confirmatory data in man that hypophosphataemia can lead to osteomalacia (Lotz, Zisman & Bartter, 1968). Our definition of mineral requirement, therefore, has to take into account the preservation of a normal, or at least a safe, plasma concentration of the nutrient concerned.

The purpose of the present communication is to look briefly at the Mg and P requirements of adults, which appear to be relatively low, and contrast them with the requirement for Ca, which is relatively high. We suggest that there are at least three reasons for this difference between Mg and P on the one hand and Ca on the other. First, there are differences in the absorptive mechanisms for the three elements. Secondly, there are differences in the plasma homoeostatic mechanisms. And thirdly, there are differences in the regulation of urinary excretion. In addition, there seem to be age and sex effects on Ca requirement but no comparable age and sex effects on Mg requirement.

Methodology

Our balances were performed by the standard procedure previously described (Bullamore, Nordin, Wilkinson & Marshall, 1971; Gallagher & Wilkinson, 1973).

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We administer a constant diet and a non-absorbable marker (polyethylene glycol) for 2 weeks and collect faeces and urine daily from days 8 to 14. The final balance is the mean of the daily balances in the second week.

Magnesium requirement

The (US) National Research Council (1974) recommends a Mg allowance of 300–500 mg/d for adults. Using the data from 941 Mg balance experiments collected from the literature, Seelig (1964) claimed that after allowing for sweat losses the minimum Mg requirement was 6 mg/kg body-weight per d or about 400 mg/d, which would make the allowance even higher. In our opinion, both these estimates are too high.

Magnesium balances. We have performed 208 Mg balances in miscellaneous subjects and found a simple linear relation between Mg intake and output with a slope of 0·83 and an intercept at theoretical zero intake of 37 mg (Fig. 1).

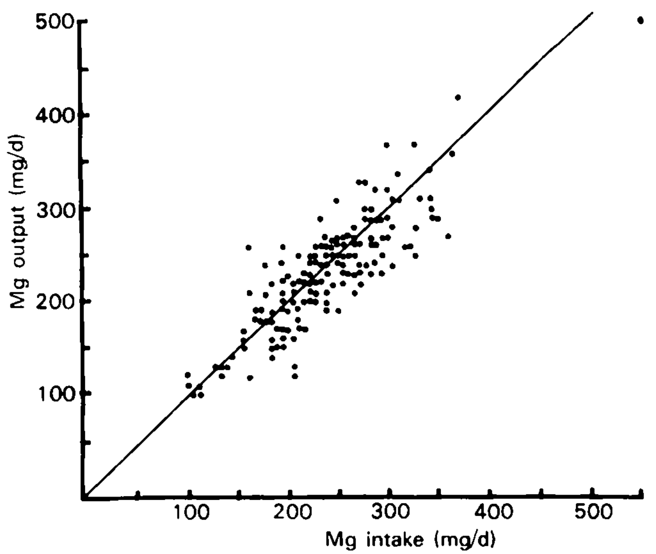

Fig. 1. The relationship between magnesium output and Mg intake in 208 balances on miscellaneous subjects. The line of equality is indicated.

Regression of output *v.* intake yields a mean equilibrium value of 223 mg, which might be regarded as the mean requirement and is compatible with the recommended USA allowance of 300–350 mg/d. However, inspection of the data shows that this calculation depends entirely on the preponderance of positive balances at high intakes; there is no corresponding preponderance of negative balances at low intakes, which would be expected if there were a genuine mean requirement of 223 mg/d. In fact, the data suggest that negative Mg balance can be prevented at least down to intakes of 100 mg/d, and that the Mg requirement must be below this value but cannot be defined from our data. This is entirely compatible with the findings of experiments which have had to use dietary Mg

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levels of 10–20 mg daily to produce Mg depletion (Fourman, 1961; Shils, 1969). We therefore turn to the consideration of plasma Mg homoeostasis in an attempt to define Mg requirement in terms of maintenance of plasma Mg.

Plasma magnesium. The normal range of plasma Mg in adults is 0·70–0·95 mmol/l. The Mg throughput required to maintain the lower limit of this normal range can be estimated from the relation between plasma and urinary Mg in normal subjects (Nordin, 1976). This shows that when the plasma Mg is at the lower normal limit, the mean Mg excretion is about 8 µmol/l glomerular filtrate, or approximately 30 mg/d in a subject with a glomerular filtration rate of 100 ml/min. This therefore represents an estimate of the absorbed Mg required to maintain a normal plasma level. Since the Mg absorption is about 35% of intake this points to a daily Mg intake of about 100 mg. The allowance should be somewhat higher.

Conclusion. It is therefore safe to say that normal subjects, eating normal diets containing 300–400 mg Mg/d, run no risk of Mg deficiency whether we define such deficiency as a negative Mg balance or a low plasma Mg concentration. This accords with clinical experience inasmuch as Mg deficiency states are never encountered in the absence of gastrointestinal or renal disease, or some highly artificial situation such as post-operative intravenous feeding.

Phosphorus requirement

The (US) National Research Council (1974) recommends a P allowance of 800 mg/d for adults.

Our data suggest that the position with regard to P balance is rather similar to that of Mg. In our 646 P balances on miscellaneous subjects, output is very closely related to intake, certainly down to a P intake of 400 mg/d (Fig. 2). It is true that most of the balances are positive at high intakes, but there is no suggestion of the

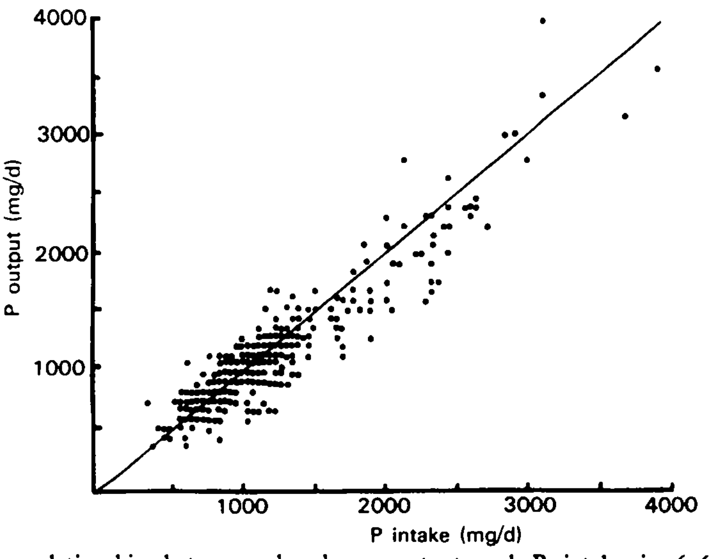

Fig. 2. The relationship between phosphorus output and P intake in 646 balances on miscellaneous subjects. The line of equality is indicated.

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population moving into negative balance at the lower intakes. It does not therefore seem possible to define a P requirement on these data. More balances at low intakes will be needed to define this value, but it would appear to be less than 400 mg/d. We shall therefore consider whether P requirement can be defined in terms of plasma phosphate homoeostasis.

Plasma phosphate. The rate of phosphate flow through the plasma required to maintain a normal plasma phosphate concentration can be estimated from the normal relation between plasma and urinary phosphate (Robertson, 1976). This relationship is such that the lower normal limit of plasma phosphate concentration (0·775 mmol/l) is associated with a mean urine phosphate flow of about 0·058 mmol/l glomerular filtrate, corresponding to about 8·4 mmol/24 h when the glomerular filtration rate is 100 ml/min. The dietary P required to produce this flow rate is about 400 mg/d, since net absorption is 60% of intake. This value is also so far below the mean normal value for absorbed phosphate that there can be no danger of significant hypophosphataemia within the normal dietary range. Thus both on balance and plasma level criteria, the P requirement seems to be not more than 400 mg/d. The allowance should presumably be higher, but whether it needs to be as high as 800 mg/d seems unlikely.

Calcium requirement

The situation with regard to Ca is rather different. We have collected and analysed 212 Ca balances on eighty-four normal subjects published in the literature (see Appendix for references) and found that although Ca output is a function of Ca intake, the relationship between them differs from the corresponding Mg and P relationship (Fig. 3). Simple inspection shows that most

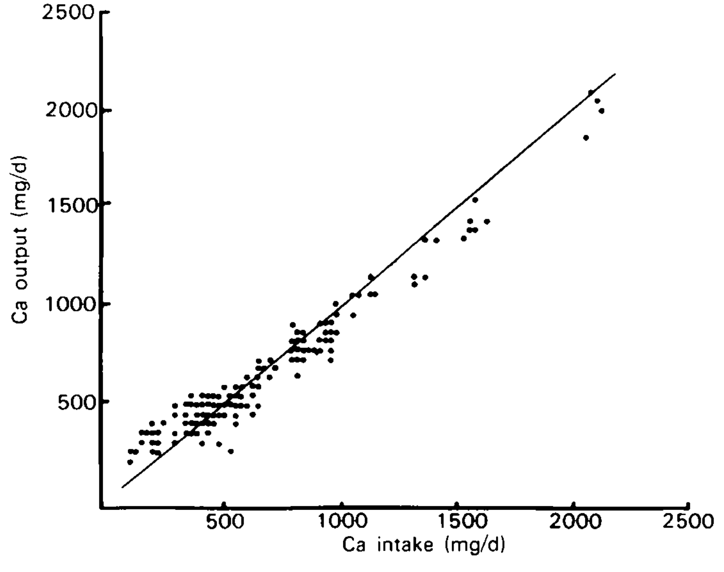

Fig. 3. The relationship between calcium output and Ca intake in 212 Ca balances on eighty-four normal subjects published in the literature. The line of equality is indicated.

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balances are negative at intakes below 600 mg/d and positive at intakes above this level. This is a relatively high equilibrium value, or mean requirement, for which there are several explanations.

First, although net absorbed Ca is a function of dietary Ca, it is negative at intakes below 190 mg/d, due to a relatively high loss of Ca into the gastrointestinal tract via the digestive juices, only some of which is reabsorbed (Fig. 4). Thus there is a mean Ca requirement of 190 mg/d simply to avoid a net loss of Ca through the gastrointestinal tract.

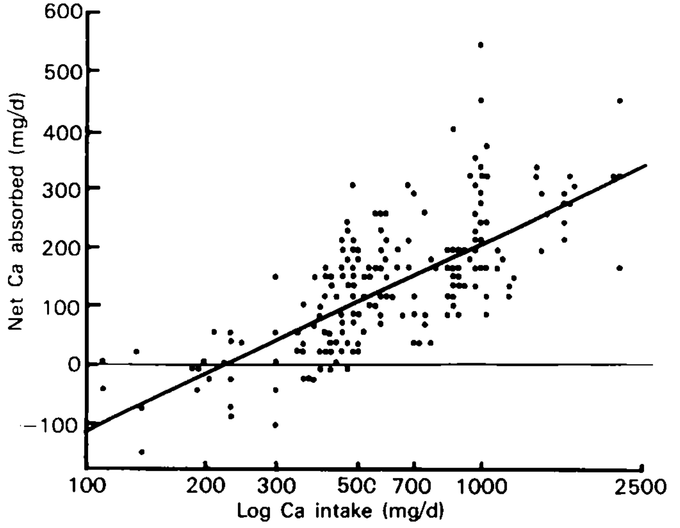

Fig. 4. The relationship between calcium absorbed and log Ca intake in the Ca balances depicted in Fig. 3. The calculated regression line is indicated (r 0·724; $P<0·001$).

Secondly, after the Ca has been absorbed, its excretion differs from that of Mg and P with the result that an additional requirement arises from a relatively large obligatory loss of Ca in the urine. Whereas with Mg and P, excretion is a linear function of dietary intake which passes virtually through the origin, i.e. urinary P and Mg approach zero values in severe dietary deficiency, urinary Ca is not a simple linear function of dietary Ca and certainly does not approach zero at low Ca intakes (Fig. 5). The mean urinary Ca at theoretical zero Ca intake in normal subjects is 110 mg/d, but the absorbed Ca does not reach the Ca excretion (so establishing Ca balance) until it amounts to about 160 mg/d (Fig. 6). This amount is absorbed when the diet contains about 600 mg Ca/d, which is therefore one estimate of the mean Ca requirement.

The reason for this apparently inappropriate relation between absorbed and excreted Ca at low Ca intakes probably lies in the physiological system which governs plasma Ca homoeostasis. Unlike plasma Mg and phosphate, which are labile values and vary with response to dietary intake, the plasma Ca never falls below 2·25 mmol/l in normal subjects, even on very low-Ca diets, because of the

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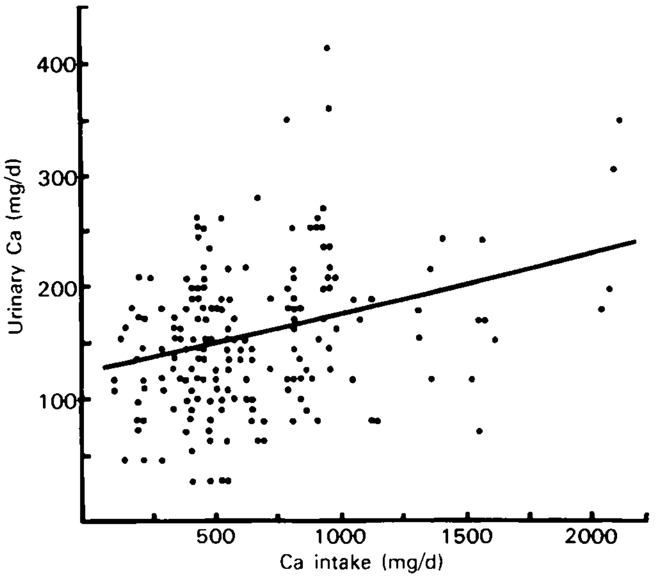

Fig. 5. The relationship beteen urinary calcium and Ca intake in the Ca balances depicted in Fig. 3. The calculated regression line is indicated (r 0·310; P<0·001).

intervention of the parathyroid gland feedback mechanism. The secretion of parathyroid hormone maintains the plasma Ca at this minimum value by, in the first instance, increasing Ca absorption and tubular reabsorption of Ca, and, if these mechanisms are insufficient, by increasing bone resorption (Peacock & Nordin, 1973). In the final analysis, the organism will sacrifice the skeleton to maintain the plasma Ca concentration rather than preserve the skeleton intact and allow the plasma Ca concentration to fall.

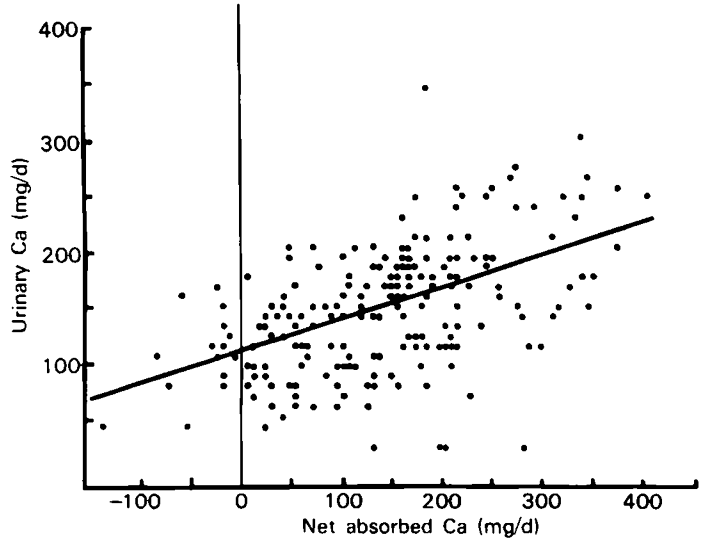

Fig. 6. The relationship between absorbed calcium and urinary Ca excretion in the Ca balances depicted in Fig. 3. The calculated regression line is indicated (r 0·515; P<0·001).

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The mean urinary Ca when the plasma Ca is at the lower normal limit of 2·25 mmol/l is about 0·025 mmol/l glomerular filtrate or about 150 mg daily, as calculated from the simultaneous observation of plasma and urinary Ca before and during Ca infusion (Marshall, 1976). This value is eventually the same as the 160 mg absorbed Ca estimated to be required from the balance data.

Thus by both methods, the mean Ca requirement seems to be about 600 mg/d, which is extremely close to the value of 9·3 mg/kg body-weight per d calculated by Mitchell & Curzon (1939) from 139 Ca balances which had appeared in the literature up to that date. However, the median requirement, which is similar to the mean value, would by definition protect only 50% of the population. The recommended allowance should perhaps be the intake which protects 95% of the population.

To calculate this from the 212 Ca balances, we have assumed an error on each balance of up to 30 mg/d or 5% (whichever was the greater) and have assumed the individual to be in balance unless the stated negative Ca balance exceeded this amount. (The effect of this is of course to reduce the calculated requirement and recommended allowance.) We have then calculated the proportion of the 212 balances which are negative at different intake levels and plotted this against the log of the intake (Fig. 7). It will be seen that after our correction for possible error, 50% of the balances are negative at an intake of 500 mg/d, which is the corrected mean requirement. To establish the amount required to preserve balance in 95% of the population, we have transformed the percentage in negative balance onto a logit scale, which then produces a linear relation between percentage in balance and log Ca intake (Fig. 8). This shows that the intake required to protect 95% of the population is about 900 mg/d. Moreover, the upper limit of Ca excretion at a

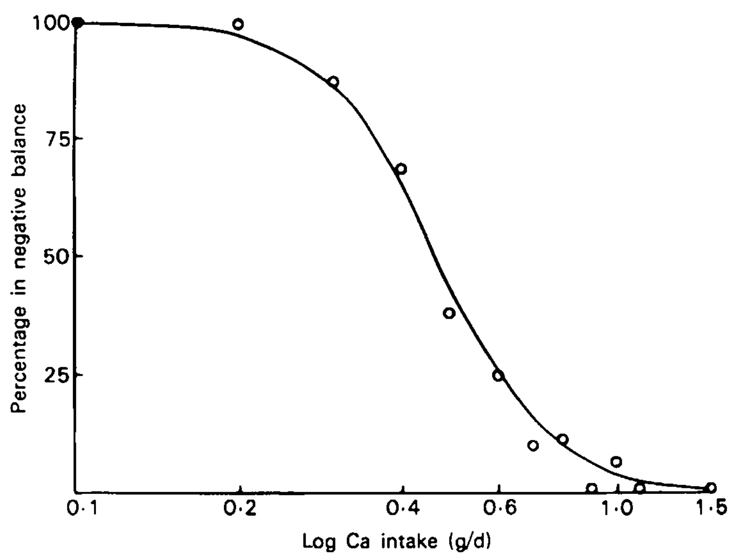

Fig. 7. The percentage of 212 normal calcium balances which are negative at different intake levels *v.* log Ca intake. (The balances have been corrected for an error of 30 mg/d or 5%, as indicated above).

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plasma Ca level of 2·25 mmol/l is in fact about 0·038 mmol/l glomerular filtrate (Marshall, 1976), which represents 216 mg Ca absorbed/d, or an intake of about 900 mg/d.

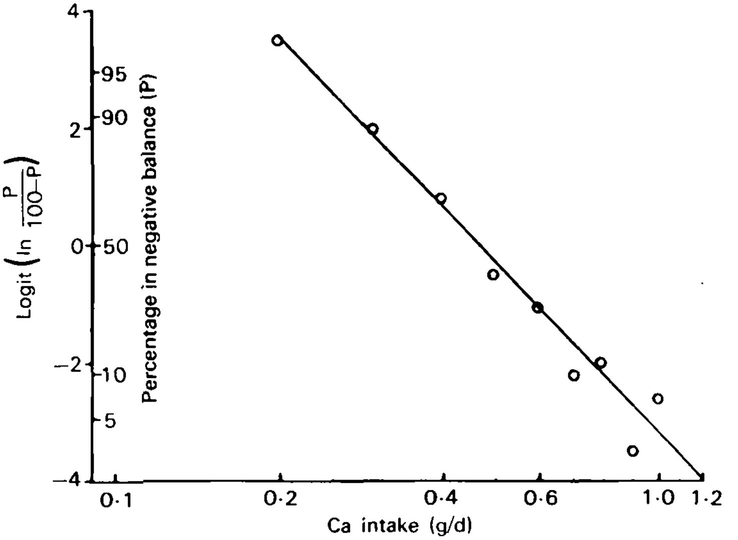

Fig. 8 The percentage of 212 normal calcium balances that are negative (P) shown on a logit scale (ln $\frac{P}{100-P}$) and related to log Ca intake.

These considerations suggest that the recommended Ca allowance should be approximately 900 mg/d and not the 500 mg recommended by the FAO/WHO expert group in 1962 (FAO/WHO, 1962) and subsequently accepted by the Department of Health and Social Security (1969). If these earlier recommendations had any scientific basis whatever (which seems rather doubtful) it was perhaps the mean Ca requirement, which is not of course the same as the recommended allowance.

The effects of age and sex

Males

The best available data on the Ca requirement of men are still to be found in the work of Malm (1958) who, by means of prolonged Ca balances at various Ca intakes in twenty-six men, concluded that their mean requirement was 465 mg/d (CV 23·1). These men were aged 20–69 years and although the mean requirement was slightly higher in the older than the younger men (485 *v.* 440 mg/d) this difference was not significant. Thus the Ca requirement of 95% of fully adapted men would appear to fall within the range 210–720 mg/d, and the allowance for such men should be 700–800 mg/d.

Females

Young women. The best available set of data in young women are still the 275 Ca balances collected by Knapp (1943). When output is related to intake in these balances, the crossover point is about 600 mg/d, i.e. most of the balances are negative below this value and positive above it. The data are in fact very similar to the 212 balances collected by us in normal subjects.

Post-menopausal women. We know of no substantial series of balance studies on post-menopausal women, the group which is of course of particular interest because of the bone loss which starts at this time of life (Nordin, 1971). We have, therefore, used our own balance data and have analysed all the post-menopausal balances available to date. This series comprises sixty-one post-menopausal women with varying degrees of 'spinal osteoporosis'. There is no obvious difference between those with and those without vertebral fractures and the data have therefore been pooled.

The relationship between Ca output and intake in these sixty-one balances is shown in Fig. 9. It will be seen that most of these subjects are in negative Ca balance at all Ca intakes. In other words, their Ca requirement appears to be increased, though it is impossible to define it from these data because there is no crossover point.

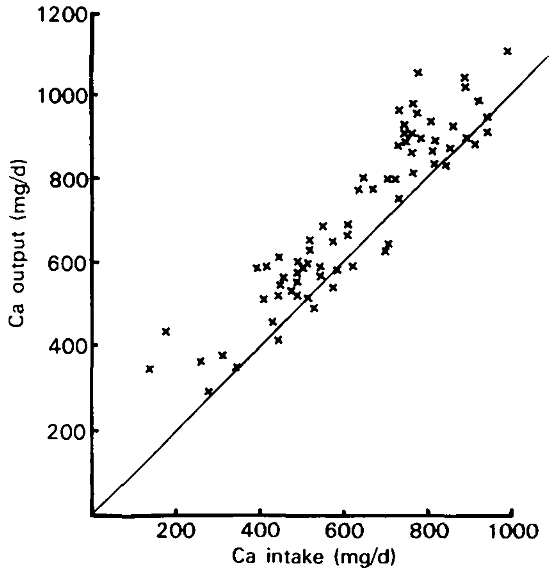

Fig. 9. The relationship between calcium output and Ca intake in sixty-one Ca balances on post-menopausal women. The line of equality is indicated.

It is difficult to escape the conclusion that the negative Ca balance of about 50–70 mg/d in our post-menopausal women reflects the loss of bone which is occurring at this time of life at a rate of about 1% per annum, representing a Ca loss of about 30–35 mg/d. Closer agreement than this between these two values could hardly be expected with existing techniques.

The reason for this increased Ca requirement, if such it may be called, is a reduced Ca absorption, sometimes an impaired renal conservation of Ca and sometimes both, the ultimate cause probably being oestrogen deficiency. As we have reported elsewhere (Horsman & Nordin, 1976) Ca balance tends to be more negative in post-menopausal women with severe oestrogen deficiency than in those who are moderately well oestrogenized, and we have also noted that women with severe oestrogen deficiency tend to lose bone faster than other post-menopausal women. Moreover, the negative Ca balance can always be corrected with oestrogen therapy (Gallagher & Nordin, 1975).

Conclusions and summary

Our data suggest that there is a fundamental difference between Ca as a nutrient on the one hand and Mg and P on the other. Owing to the nature of the Ca absorptive mechanism, the mechanism of plasma Ca homoeostasis and the control of Ca excretion, Ca requirement is perceptibly higher than that of other comparable nutrients. The recommended dietary allowance of Ca must rest on this fundamental concept. Approximately 800 mg Ca/d is needed to meet the Ca requirement even of men and young women. The Ca requirement of post-menopausal women is probably substantially higher, but the correct approach to this group is likely to be oestrogen-replacement therapy rather than Ca supplementation. However, oestrogen-replacement therapy is contraindicated in a significant number of women owing to ischaemic heart disease, a past history of thromboembolism and possibly hypertension. There are also some women who do not wish to take hormones after the menopause. It is possible therefore that ultimately a higher Ca allowance should be recommended for this age-group, but present knowledge does not enable one to define it with any degree of certainty.

APPENDIX

The 212 normal Ca balances used in this paper have been compiled from the following references. Consecutive balance periods at the same intake have been combined to produce single balance values.

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