

Calcium in health and disease

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Calcium is an essential but controversial nutrient: there is no consensus on the level of human calcium requirement or the significance of calcium deficiency. The explanation for this must be sought in the history of calcium research since Pommer (1885) first established the difference between osteoporosis and osteomalacia. Pommer showed that rickets and osteomalacia represented a failure to mineralize new bone as it was being formed, leading ultimately to a calcium deficit in the bony tissue itself, whereas osteoporosis was a deficit of whole bone tissue without change in its mineral content. Not long afterwards, Miwa and Stoeltzner (1898) demonstrated that calcium deficiency caused osteoporosis, not osteomalacia, in experimental adult animals. It was Mellanby (1918) who finally identified vitamin D as the factor that prevented and cured rickets. Soon after that, Telfer (1926) showed that vitamin D deficiency led to malabsorption of calcium. From this it was assumed that vitamin D deficiency and calcium deficiency must have the same metabolic consequences. Accepting the concept that both calcium and vitamin D deficiencies led to rickets or osteomalacia, Albright *et al.* (1938) invoked a new pathogenetic mechanism – failure of new bone formation because of sex hormone deficiency and/or negative nitrogen balance – to explain postmenopausal and other forms of osteoporosis.

This paradigm prevailed for a generation until a seminal paper from Sweden (Carlsson and Lindquist, 1955) showed that vitamin D not only regulated calcium absorption but also independently regulated plasma calcium homeostasis. This made it possible to distinguish vitamin D deficiency from calcium deficiency (Nordin, 1960) and allowed the re-emergence of the concept (Hess, 1929) that calcium deficiency led to osteoporosis and vitamin D deficiency to osteomalacia. Although this concept is increasingly accepted in theory, there is in practice no consensus about the contribution of calcium deficiency to clinical osteoporosis or about the reality of a calcium requirement in humans (Kanis and Passmore, 1989). Clearly the menopause is associated with a rise in bone breakdown rather than a fall in bone formation (Young and Nordin, 1967; Gallagher, Young and Nordin, 1972; Stepan *et al.*, 1987; Nordin and Polley, 1987; Prince *et al.*, 1995). The

current issue is whether oestrogens inhibit bone resorption directly or whether they operate through the calcium economy; it is no longer maintained that they promote bone formation. In the meantime, Albright and colleagues' original ideas about osteoporosis survive in relation to corticosteroid-induced osteoporosis and perhaps as part of the explanation for age-related osteoporosis, particularly in men.

PHYSIOLOGY

Calcium is an essential nutrient accounting for about 2 percent of body weight, ranking fifth after oxygen, carbon, hydrogen and nitrogen. Nearly 99 percent of the body's calcium (1 200 g or 30 mol) is stored in the skeleton; the remainder is in the teeth and soft tissues (each containing 7 g or 175 mmol) and the extracellular fluid (ECF) (1 g or 25 mmol) (Nordin, 1976). Calcium comprises 25 percent of the dry weight of the skeleton and circulates in the ECF at a concentration of 6 to 7 mg per 100 ml (1.5 to 1.75 mmol per litre). The total calcium concentration within cells is comparable to that in the extracellular water, but the free calcium concentration is about 10^4 times lower (Robertson, 1988).

The most obvious function of calcium is to provide rigidity to the skeleton by virtue of the insoluble salts it forms with phosphoric acid. Primitive exoskeletons (such as shells) are composed of calcium carbonate formed in seawater, which is high in calcium but low in phosphorus. Fish endoskeletons may be composed of cartilage or bone. All mammalian skeletons are composed of true bone in which rigidity is provided by a particularly insoluble calcium salt analogous to the mineral hydroxyapatite $[\text{Ca}_{10}(\text{OH})_2(\text{PO}_4)_6]$ but containing also a small component of calcium carbonate (Terminé and Posner, 1967).

The calcium salts do more than provide rigidity to the skeleton; they also constitute a very large reservoir of calcium for the maintenance of the (ionized) calcium concentration in the extracellular water at or very close to 4.8 mg per 100 ml (1.2 mmol per litre). The protection of this critical concentration by parathyroid hormone and vitamin D reflects the vital role that calcium plays in the neuromuscular system, in regulation of the heart, in

enzyme-mediated reactions and in many other metabolic processes. Since only about 1 g (25 mmol) of calcium normally circulates in the ECF, the skeleton can maintain the extracellular ionized calcium against external calcium deprivation for years before it suffers significant damage. It is important to recall that as calcium is removed from bone, the matrix is also resorbed; this is why the result is osteoporosis rather than osteomalacia.

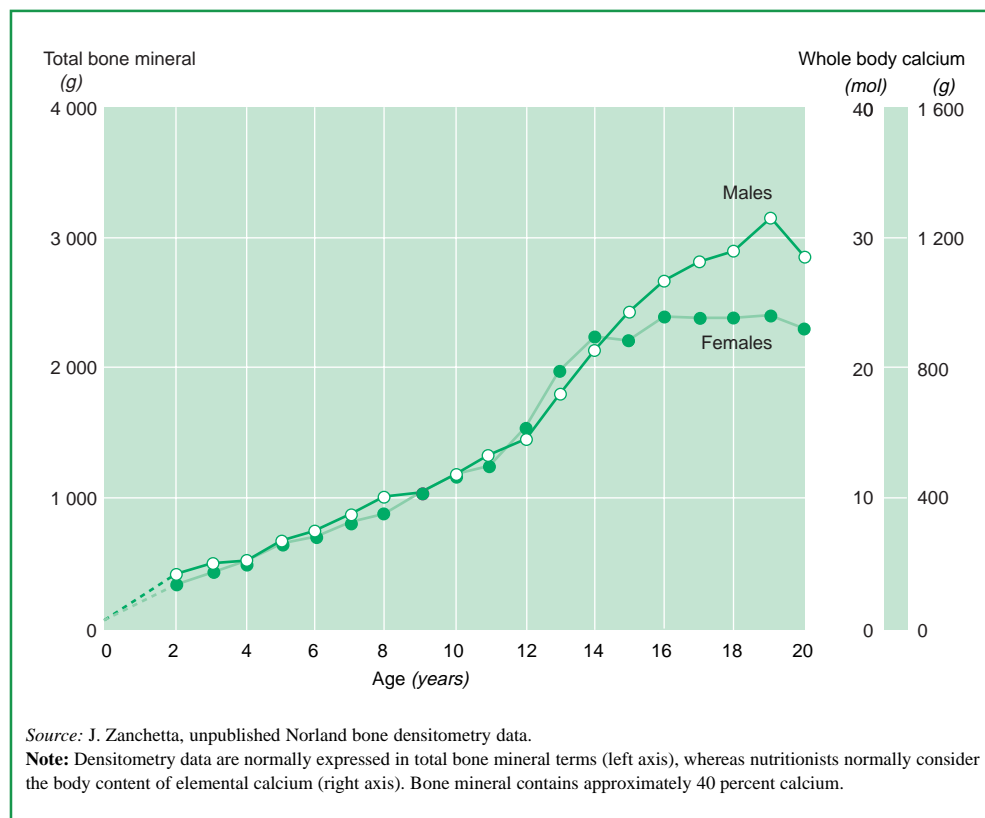
BONE GROWTH AND DECAY

Calcium enters the body through the gastro-intestinal tract, is absorbed mainly in the upper small intestine and is excreted via the bowel, kidneys and skin. During skeletal growth and maturation, i.e. until the age of the early twenties in humans, calcium accumulates in the skeleton at an average rate of 150 mg a day (Figure 1). During maturity, the body – and therefore the skeleton – is more or less in calcium equilibrium. From the age of about 50 in men and from the menopause in women, bone balance becomes negative and bone is lost from all skeletal sites (Figure 2). This bone loss is associated with a marked rise in fracture rates, starting with non-hip fractures in women after the menopause but leading to rising hip fracture rates in both sexes (Figures 3 and 4). The cause of the bone loss associated with menopause and ageing is uncertain. This paper looks at this question, particularly in relation to the body's calcium economy.

THE CALCIUM ECONOMY

Regulation of the calcium economy is somewhat more complex than that of other minerals such as sodium, potassium, phosphorus and magnesium (Marshall, Nordin and Speed, 1976). These other minerals are primarily regulated by a relatively simple homeostatic system in which variations in input modify the concentration in the ECF, which in turn modifies the urinary loss; as input rises or falls, the ECF concentration follows suit, and so does urinary excretion, until a new equilibrium is established at which input and output are equal. This account is of course an oversimplification, but it represents the essential feature of these systems.

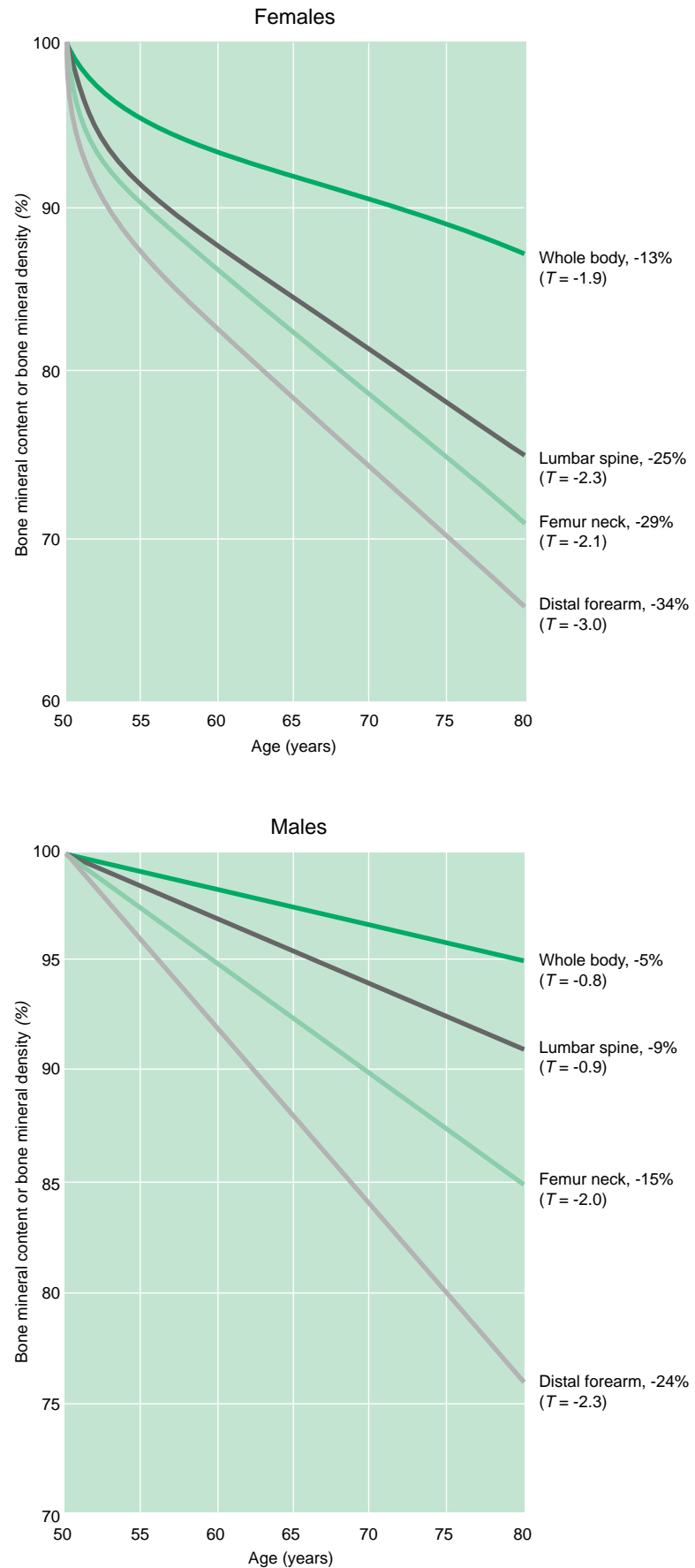
The calcium system contains a similar component but differs from the others in that the concentration of (ionized) calcium in the ECF is more vigorously defended, presumably because it is critical to so many physiological functions. Although it is true that raising calcium input raises ECF and urine calcium and therefore tends to equilibrium, the converse process (lowering of ECF and urine calcium when input falls) is limited by the intervention of parathyroid hormone secretion when the ionized calcium approaches the lower limit of the normal range. The result is the maintenance of the ECF ionized calcium and thus of calcium excretion via the kidneys and the bowel. The immediate effect of this parathyroid response is to increase renal tubular resorption of calcium



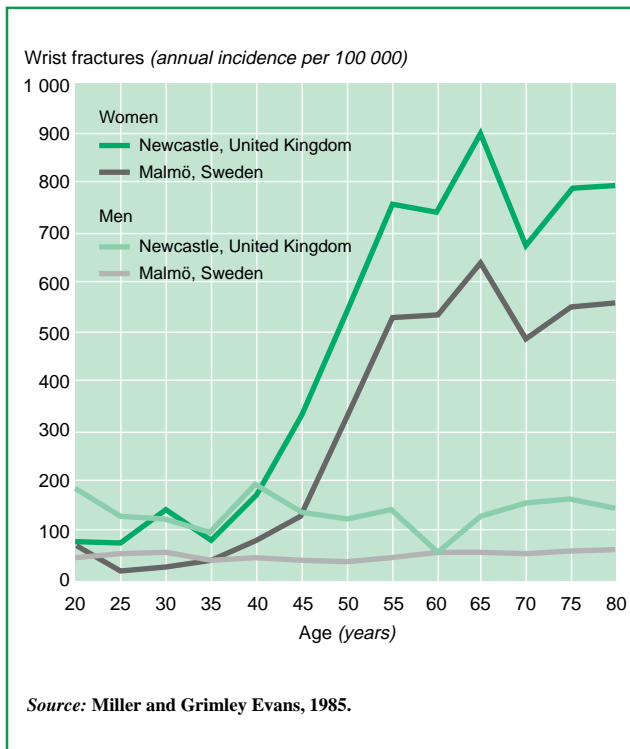
1
Accumulation of total bone mineral and whole body calcium in boys and girls as a function of age

2

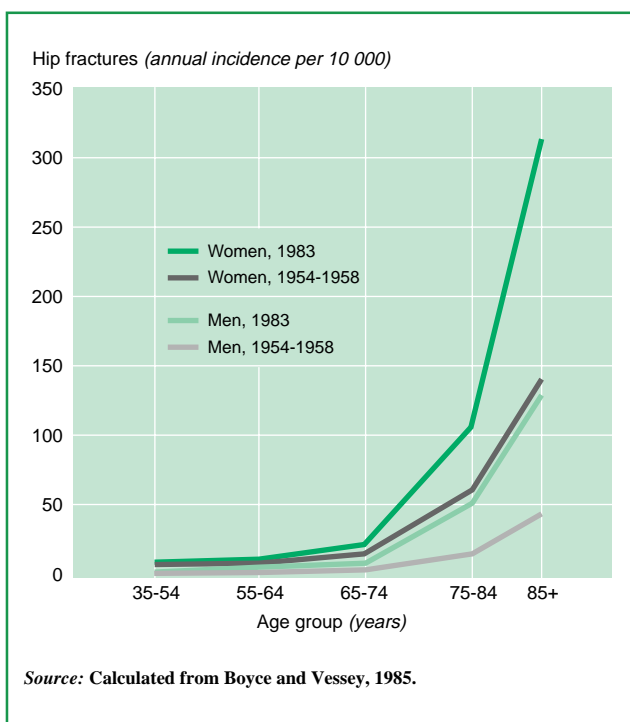
Percentage loss of bone at four different sites as a function of age in men and women



Source: Calculated from Wahner and Fogelman, 1994.



3
Wrist fracture rates as a function of age in men and women in two European cities



4
Hip fracture rates as a function of age in men and women in Oxford, United Kingdom, 1954 to 1958 and 1983 (note the apparent increase in hip fracture rates between the 1950s and 1983)

(and so to conserve calcium) and to stimulate the synthesis of calcitriol [$1,25(\text{OH})_2\text{D}_3$] in the kidneys to promote calcium absorption. If these mechanisms are insufficient to maintain the concentration of ionized calcium, parathyroid hormone secretion rises and increases bone resorption. This is the response of the organism to calcium deprivation, and it leads sooner or later to osteoporosis in experimental animals (Nordin, 1960). Osteoporosis can also be produced experimentally by oophorectomy, but the magnitude of the effect depends on the calcium intake (Hodgkinson *et al.*, 1978; Shen *et al.*, 1995) and can be amplified by sodium feeding, which increases the obligatory calcium loss (Goulding and Campbell, 1983). Since oestrogen insufficiency is regarded as the most important single risk factor for osteoporosis – at least in women – it is important to establish whether the negative calcium balance that follows the menopause is the cause or the result of the bone loss. This question requires consideration of the calcium requirement and therefore of the relationship among calcium intake, absorption and excretion.

Intake

Calcium consumption varies greatly worldwide, ranging from 800 mg per day or more in industrialized countries to 200 to 300 mg in some developing countries (FAO, 1991) (Table 1). The differences are mainly due to variation in the intake of dairy products, which are the richest sources of calcium. In countries where milk is scarce, calcium may be obtained from certain cereals, notably millets. Despite this large variation in calcium consumption, there is no evidence that osteoporosis is more common in developing than in industrialized countries – rather the reverse. In fact, the prevalence of hip fracture, as measured by mortality from fractures in the elderly (Eddy, 1972), is positively rather than negatively related to calcium intake (Figure 5). This paradox, and evidence of adaptation to low calcium intakes in Norwegian male prisoners (Malm, 1958), led a 1960 FAO/WHO Expert Committee to recommend a calcium allowance of only 500 mg (FAO, 1962). This recommendation is now being seriously questioned if not abandoned as the influence of other dietary constituents becomes increasingly apparent (Nordin *et al.*, 1996).

Absorption

Calcium is absorbed from the small intestine by a saturable active transport system with a diffusion component (Wilkinson, 1976; Marshall, 1976; Bronner, 1987; Heaney, Saville and Recker, 1975) (Figure 6). At low calcium intakes, most calcium travels by the active pathway, but as intake rises, the amount transported by diffusion (6 percent of

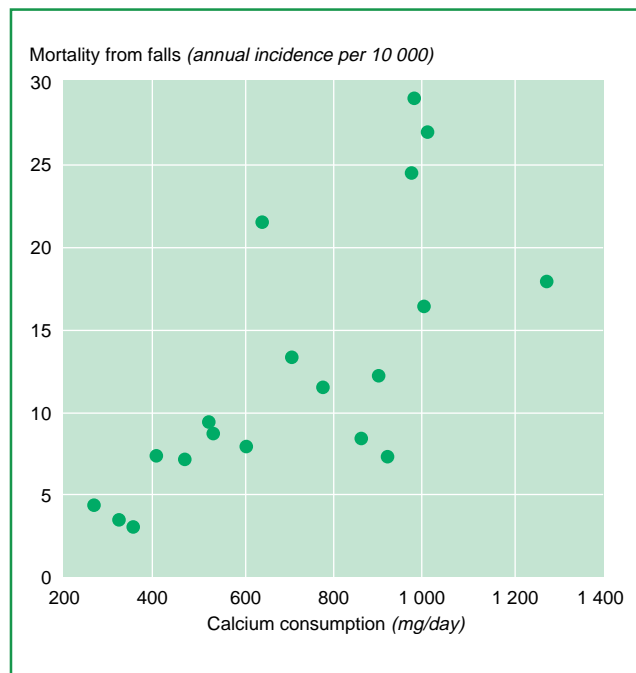
TABLE 1
Food consumption, latitude, hip fractures and standard of living in 19 countries

Country	Calcium consumption ^a (mg/day)	Animal protein ^a (g/day)	Latitude of capital city (degrees N or S)	Mortality from falls in women over age 75 ^b (per 10 000)	Gross domestic product (purchasing power) ^c (US\$ per caput)
Japan	354	52.2	19.2	2.9	21 140
Jamaica	319	27.5	17.6	3.4	3 400
Guatemala	262	7.6	14.5	4.3	3 440
Chile	466	27.1	33.0	7.2	8 890
Brazil	406	24.5	16.5	7.4	5 400
Australia	921	65.7	35.1	7.4	18 120
Argentina	603	63.6	34.4	7.9	8 720
United Kingdom	855	53.0	51.3	8.5	17 970
Ecuador	529	22.3	1.0	8.7	4 190
Colombia	519	25.6	4.4	9.3	5 330
New Zealand	771	70.2	41.2	11.6	15 870
Canada	898	62.7	45.3	12.4	19 960
Israel	704	55.1	32.1	13.4	15 300
Netherlands	997	64.7	52.2	16.6	18 750
Finland	1 267	61.6	60.1	18.0	16 150
Italy	637	57.3	41.5	21.6	18 460
France	969	76.1	48.5	24.6	19 670
Norway	1 002	64.7	59.6	27.0	20 210
Denmark	974	66.2	55.5	29.0	19 880

^aFAO, 1991.

^bWHO, 1990-1995.

^cWorld Bank, 1996.



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Mortality from falls in women over age 75 as a function of calcium consumption in the countries in Table 1

intake) gradually becomes dominant. In the calcium intake range of 500 to 1 000 mg (12.5 to 25 mmol), active transport is the main component, but at higher intakes (e.g. when calcium supplements are taken), the additional calcium is mainly absorbed by diffusion. It follows that true fractional calcium absorption is inversely related to calcium intake and falls from about 70 percent for very low intakes to

10 percent or less for high intakes (Nordin and Marshall, 1988). However, there is always loss of calcium in the faeces from the digestive juices (endogenous faecal calcium), and it follows that the net calcium absorbed (the difference between calcium intake and faecal calcium) is negative at zero intake, becomes zero when intake matches endogenous loss and then increases with intake, rapidly at first and then more slowly. This relationship [based on 212 calcium balances in 84 normal Western subjects (Marshall, Nordin and Speed, 1976)] is shown in Figure 6; the equation is: $y = [491x/(287 + x)] + 0.06x - 206$ mg, where y represents net absorbed calcium and x represents intake (Nordin and Marshall, 1988).

The principal regulator of calcium absorption is vitamin D [generally derived from the effect of sunlight on the skin (Holick, 1995)] in the form of its two active metabolites, 25-hydroxyvitamin D (calcidiol) and 1,25-dihydroxyvitamin D (calcitriol) (Holick, 1995), acting almost certainly on the active transport component. It would therefore be expected that the absorption line in Figure 6 would move up or down with vitamin D status (see below).

Excretion

Apart from the loss of calcium through the bowel, the principal routes of calcium excretion are via the kidneys and the skin. In normal individuals in zero calcium balance, calcium excreted via the skin and urine must equal net calcium absorbed. The slope of urinary calcium (y) to dietary calcium (x) in normal Western subjects is:

$y = 0.051x + 128$ mg per day (Nordin and Marshall, 1988). However, skin loss of some 40 mg (1 mmol) per day (Charles *et al.*, 1983) also needs to be taken into account. If this skin loss is assumed to be independent of intake, it can be added to the urine calcium component, and the equation of skin plus urine calcium to intake becomes $y = 0.051x + 168$ mg per day, as represented by the central excretion line in Figure 6. It must be emphasized that this relationship is based on Western data. Urine calcium is closely related to phosphate and sodium excretion, and variation from an average Western diet will move the urine calcium line up or down as indicated in Figure 6 and discussed below.

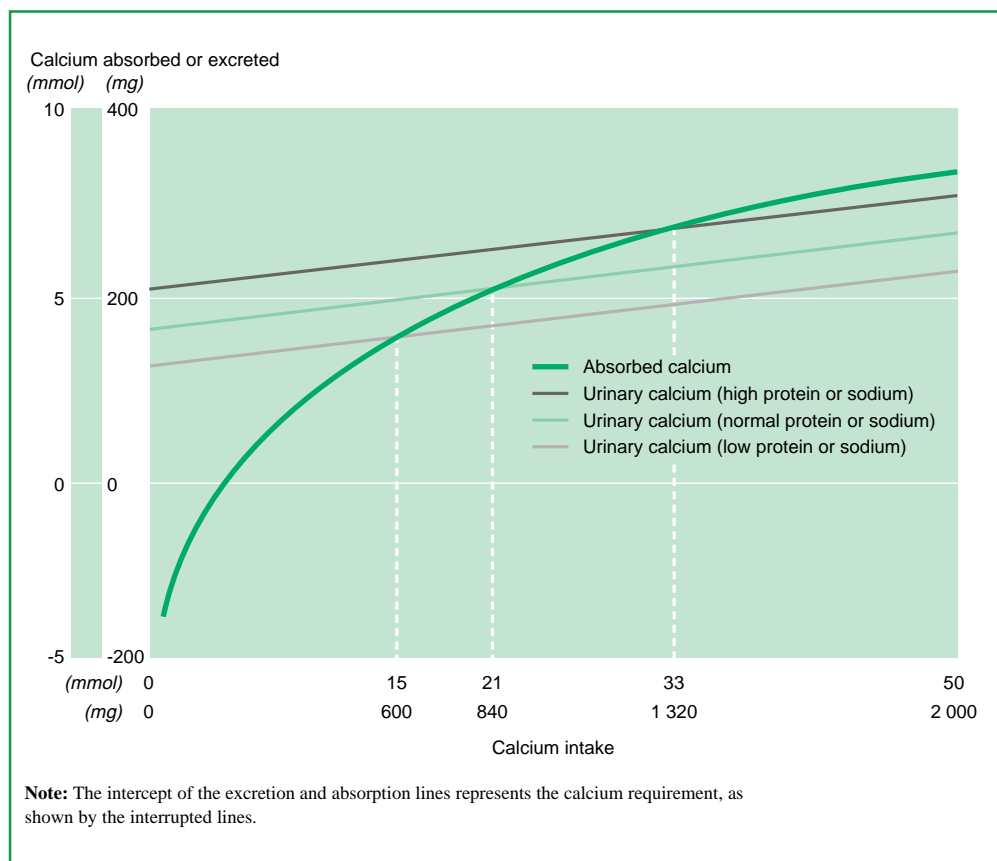
Calcium requirement

The mean calcium intake at which urine plus skin calcium equals net absorbed calcium can be taken as the calcium requirement of adults. As calculated by Nordin and Marshall (1988) from 212 Western calcium balances, this requirement amounts to about 840 mg (21 mmol) daily (Figure 6). It is clear that calcium consumption in most developing countries falls well short of this value (Table 1), which would lead to the conclusion either that the values derived from balance studies are misleading and do not take sufficient account of adaptation (which was the view of the FAO/WHO Expert Committee) or that there are special circumstances that reduce the calcium requirement of poorer nations. The

reduction could be related to reduced calcium excretion and/or increased calcium absorption.

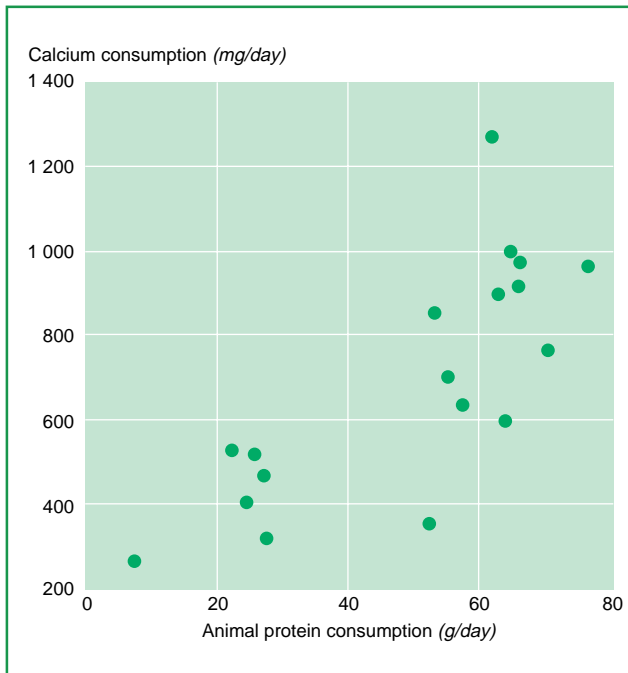
Reduced calcium excretion. At least two factors modify urine calcium at any given calcium intake: dietary protein and sodium. A positive relationship between urine calcium and protein (particularly animal protein) intake has been well documented (Linkswiler *et al.*, 1981; Margen *et al.*, 1974) and is probably due to the complexing of calcium by phosphate in the renal tubules. This explains the significant correlation between urine calcium and phosphate in normal subjects on free diets (Nordin and Polley, 1987), but the quantitative relation between protein intake and urine calcium has not been precisely defined. However, in one small study (Nordin *et al.*, 1996) in which calcium intake was held constant, raising the animal protein intake from 40 to 80 g increased the urine calcium by 40 mg (1 mmol) in six postmenopausal women. If this relationship operates at all calcium intakes (which is not certain), the addition of 40 g of animal protein to a basal intake of 60 g would double the calcium requirement. Conversely, reducing the animal protein intake from 60 to 20 g would be expected to reduce the calcium requirement from 840 to 480 mg per day (21 to 12 mmol) (Figure 6). Since animal protein and calcium intakes are strongly related (Table 1 and Figure 7), populations that have low calcium intakes may be at least

6
Calcium absorbed and excreted as a function of calcium intake in normal subjects



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Relation between calcium and protein consumption in the countries in Table 1



partially protected from negative calcium balance by their low protein consumption.

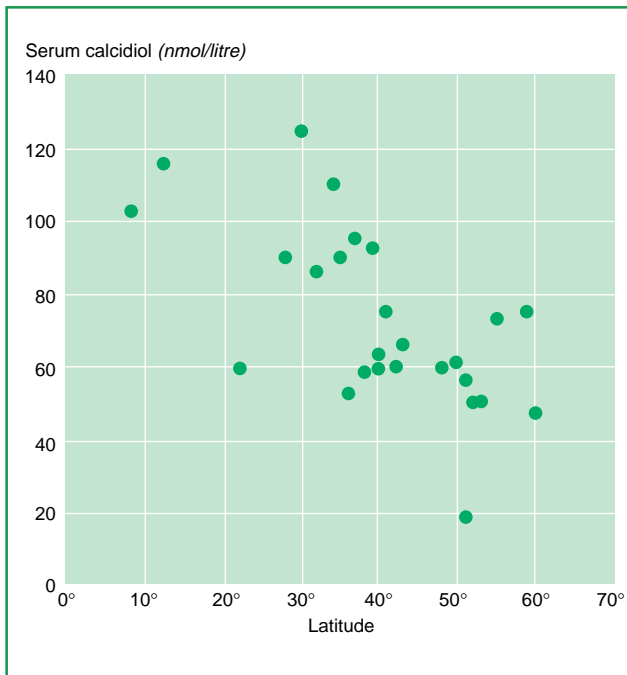
Urine calcium is also greatly influenced by sodium intake, because of competition between calcium and sodium ions for renal tubular resorption; 2.3 g of sodium

(100 mmol) results in excretion of 1 mmol of calcium (40 mg) in the urine (Nordin and Polley, 1987; Nordin *et al.*, 1996; Goulding, 1981; Nordin *et al.*, 1993; Nordin and Need, 1994). Varying the sodium intake by this amount therefore has the same effect on urine calcium as 40 g of animal protein (Figure 6). It is likely that these two effects are additive (since the mechanisms are different) and that populations on low sodium and low protein intakes would have even lower calcium requirements, but sodium data from poorer countries are scanty (Intersalt Cooperative Research Group, 1988). In hot climates, there may also be loss of sodium in sweat, which would tend to divert sodium from the urine and reduce renal calcium excretion and therefore the calcium requirement. However, this effect might be offset by greater losses of calcium in sweat (Klesges *et al.*, 1996), which would have the opposite effect. This is relatively unexplored territory.

Increased calcium absorption. Higher calcium absorption must also lower the calcium requirement. Since calcium absorption is a function of the serum calcitriol level (Morris *et al.*, 1991), and since the serum concentration of its precursor calcidiol is a function of latitude (because of the angle of incidence of the sun's rays) (Table 2 and Figure 8), it is very likely, although unproven, that calcium absorption also falls with latitude. However, serum calcidiol is also a function of racial factors (skin

TABLE 2
Latitude and vitamin D status in 27 cities

City	Latitude (degrees N or S)	Serum calcidiol (nmol/litre)	Reference
Recife, Brazil	8	103	Linhares <i>et al.</i> , 1984
Curaçao, Netherlands Antilles	12	116	Dubbelman <i>et al.</i> , 1993
Hong Kong SAR, China	22	60	Pun <i>et al.</i> , 1990
Brisbane, Australia	28	90	Personal communication
Houston, USA	30	125	Breslau <i>et al.</i> , 1982
Perth, Australia	32	86	Personal communication
Sydney, Australia	34	110	Personal communication
Adelaide, Australia	35	90	Personal communication
Buenos Aires, Argentina	36	53	Personal communication
Melbourne, Australia	37	95	Personal communication
Saint Louis, USA	38	58	Villareal <i>et al.</i> , 1991
Baltimore, USA	39	92	Sherman, Hollis & Tobin, 1990
Indianapolis, USA	40	60	Personal communication
Philadelphia, USA	40	63	Matsuoka <i>et al.</i> , 1995
Madrid, Spain	40	59	Moreiras <i>et al.</i> , 1992
Omaha, USA	41	75	Personal communication
New York, USA	42	60	Meier, 1991
Hobart, Australia	43	66	Personal communication
Paris, France	48	60	Chapuy, Durr & Chapuy, 1983
Brussels, Belgium	50	61	Bouillon <i>et al.</i> , 1987
Cardiff, UK	51	56	Compston <i>et al.</i> , 1981
London, UK	51	18	Corless <i>et al.</i> , 1985
Groningen, Netherlands	52	50	Dubbelman <i>et al.</i> , 1993
Leeds, UK	53	50	Personal communication
Copenhagen, Denmark	55	73	Hartwell, Riis & Christiansen, 1990
Oslo, Norway	59	75	Falch, Oftebro & Haug, 1987
Helsinki, Finland	60	47	Von Knorring <i>et al.</i> , 1982

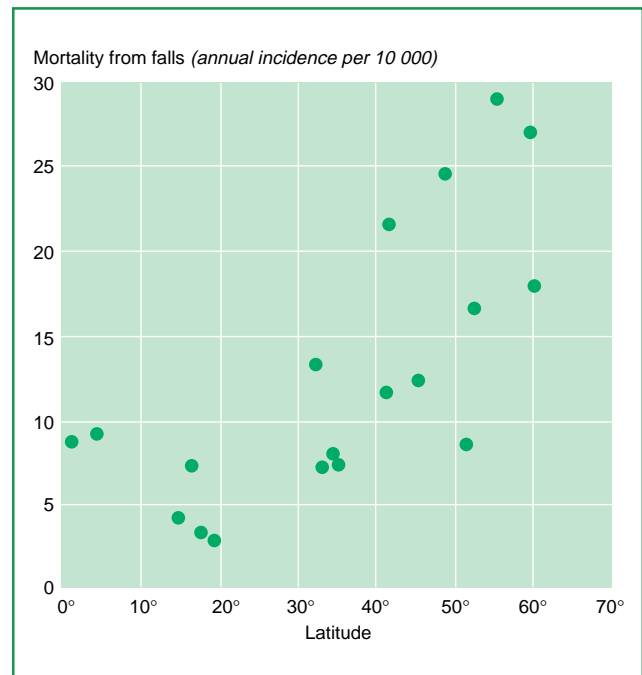


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Relation between serum calcidiol and latitude in the cities in Table 2

pigmentation) (Matsuoka *et al.*, 1995), social habits and climate (exposure to sunlight) (van der Wielen *et al.*, 1995), diet (McKenna, 1992) and age (Baker, Peacock and Nordin, 1980; MacLaughlin and Holick, 1985), all of which contribute to the scattered pattern in Figure 8. Hip fracture rates (inferred from mortality from falls in the elderly) are also a positive function of latitude (Figure 9) and are thus more closely related to vitamin D status than to wealth or animal protein intake (Table 1). Moreover, low vitamin D status is a well-documented feature of hip fracture cases in the West (Aaron *et al.*, 1974; Baker *et al.*, 1979; Lips *et al.*, 1982; Morris *et al.*, 1984), and the risk of hip fracture was significantly reduced by vitamin D with calcium in a controlled study in France (latitude 48°) (Chapuy *et al.*, 1992). Vitamin D supplementation was also shown to inhibit bone loss in a controlled study of elderly women in Leeds, United Kingdom (latitude 53°) (Nordin *et al.*, 1985).

MENOPAUSE

Although the above account may offer a possible explanation for the apparent differences in calcium requirement and hip fracture rates among nations, it leaves the important role of the menopause unexplained. The menopause is associated with a rise in obligatory calcium excretion (Young and Nordin, 1967; Gallagher, Young and Nordin, 1972; Stepan *et al.*, 1987; Nordin and Polley, 1987; Prince *et al.*, 1995) and a probable decrease in calcium absorption (Heaney *et al.*, 1989; Nordin, 1997) which are commonly attributed to a cytokine-induced increase in bone



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Mortality from falls in women over age 75 as a function of latitude in the countries in Table 1

resorption secondary to oestrogen deficiency (Manolagas *et al.*, 1993; Pacifici, 1996). This aspect tends to separate postmenopausal bone loss from the rest and to imply a need for hormones or other expensive treatment regimens. However, it can be argued that menopausal bone loss results from an increase in calcium requirement and can be managed accordingly. The increase in calcium loss at the menopause is some 20 to 40 mg (0.5 to 1.0 mmol) (Young and Nordin, 1967; Gallagher, Young and Nordin, 1972; Stepan *et al.*, 1987; Nordin and Polley, 1987; Prince *et al.*, 1995), which is comparable to the salt and protein effects described above and shown in Figure 6.

This argument, fully reviewed elsewhere (Nordin, 1997), relies on the experimental evidence that ovariectomy-induced osteoporosis in experimental animals is modified by calcium and sodium intake (Hodgkinson *et al.*, 1978; Shen *et al.*, 1995; Goulding and Campbell, 1983) and on physiological evidence that the increase in calcium excretion in women at the menopause is due to a renal calcium "leak" (Nordin *et al.*, 1991; Nordin *et al.*, 1994) rather than to an overflow of calcium lost from the skeleton by a primary process. This paradigm is supported by 20 prospective bone density trials in which mean bone loss was close to zero in 855 calcium-treated postmenopausal women and highly significant in 625 controls ($P < 0.001$) (Nordin, 1997). Although treatment with calcium is not quite as effective as treatment with oestrogen [which produces a small gain of bone (Prince *et al.*, 1991;

Christiansen and Riis, 1990), which was not seen in the calcium trials], this may be because oestrogens simultaneously lower urinary calcium (Gallagher and Nordin, 1973; Reginster *et al.*, 1993; Prince, 1994; Selby *et al.*, 1985) and improve calcium absorption (Civitelli *et al.*, 1988; Horowitz *et al.*, 1993), thus having a greater effect than simple calcium supplementation. This issue is not yet resolved, but the old paradigm is changing, and the concept that menopausal bone loss is (at least in part) secondary to an increase in calcium requirement is gaining support. Recent consensus conferences (United States National Institutes of Health, 1994; American Journal of Medicine, 1993) have recommended a calcium allowance of 1 500 mg for postmenopausal women, without however explicitly stating that postmenopausal osteoporosis is, or could be, caused by calcium deficiency.

CONCLUSIONS

It is remarkable that there should be so much controversy over the roles of calcium and vitamin D in human nutrition in general and in osteoporosis in particular, given that both are acknowledged to be essential nutrients. Classical work on rickets and osteomalacia casts a long shadow. No sooner have osteomalacia and osteoporosis been satisfactorily distinguished than evidence of their overlapping aetiologies becomes apparent. The theses put forward in this paper are that primary negative calcium balance is the major, but not the only, cause of osteoporosis; that such a negative balance may be the result of inadequate calcium intake, low calcium absorption or high calcium excretion; that low calcium absorption may be the result of moderate vitamin D insufficiency; and that high calcium excretion may be due to dietary factors (such as protein and sodium intakes) or to hormonal effects (such as oestrogen deficiency). Seen in this light, the worldwide pattern of osteoporosis becomes comprehensible, but carefully targeted fieldwork – exemplified by studies on the relationship between calcium intake and bone density in the Gambia (Prentice, 1994) – will be required to fill in the picture. ♦

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Calcium in health and disease

There is a remarkable amount of controversy about the roles of calcium and vitamin D in human nutrition in general and in osteoporosis in particular. This article reviews the functions of calcium in the body, highlights major findings about calcium during the past century and explains the current debates.

The calcium salts that provide rigidity to the skeleton also constitute a large reservoir for the maintenance of the calcium concentration in the body's extracellular water. The protection of this concentration by parathyroid hormone and vitamin D reflects the vital role of calcium in the neuromuscular system, in regulation of the heart, in enzyme-mediated reactions and in many other metabolic processes.

During the period of skeletal growth and maturation, i.e. until the age of the early twenties in humans, calcium accumulates in the skeleton. During maturity, the body is more or less in calcium equilibrium; from the age of about 50 years in men and from the menopause in women, bone balance becomes negative and bone is lost from all skeletal sites. This bone loss is associated with a marked rise in fracture rates. The cause of the bone loss associated with menopause and ageing is uncertain.

Calcium consumption varies greatly worldwide, ranging from 800 mg per day or more in industrialized countries to 200 to 300 mg per day in developing countries. Paradoxically, osteoporosis is more common in the industrialized countries.

The theses put forward in this paper are that primary negative calcium balance is the major, but not the only, cause of osteoporosis; that such a negative balance may be the result of inadequate calcium intake, low calcium absorption or high calcium excretion; that low calcium absorption may be the result of moderate vitamin D insufficiency; and that high calcium excretion may be correlated with dietary factors (such as protein and sodium intakes) or hormonal effects (such as oestrogen deficiency). Seen in this light, the worldwide pattern of osteoporosis becomes comprehensible, but carefully targeted field work will be required to fill in the picture.

Le rôle du calcium dans la santé et la maladie

Le rôle du calcium et de la vitamine D dans l'alimentation humaine en général, et dans l'ostéoporose en particulier, est très controversé. Le présent article examine les fonctions du calcium dans le corps, souligne les principales conclusions des recherches entreprises au cours du siècle dernier et explique les débats actuels.

Les sels de calcium, qui assurent la rigidité au squelette, constituent également un vaste réservoir destiné à maintenir la concentration du calcium dans le liquide extracellulaire (LEC) du corps. L'hormone parathyroïde et la vitamine D protègent cette concentration qui reflète le rôle vital joué par le calcium dans le système neuromusculaire, dans le fonctionnement cardiaque, dans les réactions dépendant d'une activité enzymatique et dans beaucoup d'autres processus métaboliques.

Pendant la période de croissance et de maturation du squelette (dans les 20 premières années environ), le calcium s'accumule dans le squelette. A maturité, le corps est plus ou moins en équilibre calcique; à partir de 50 ans chez l'homme, et à partir de la ménopause chez la femme, le bilan osseux devient négatif et on enregistre une perte de masse osseuse dans toutes les parties du squelette, qui se traduit par une augmentation sensible de la fréquence des fractures. Les raisons de la perte osseuse liée à la ménopause et au vieillissement ne sont pas encore bien connues.

La consommation de calcium varie considérablement dans le monde: elle se situe entre 800 mg par jour ou plus dans les pays industrialisés, et à 200-300 mg par jour dans les pays en développement. Paradoxalement, l'ostéoporose est plus fréquente dans les pays industrialisés.

Les thèses exposées dans le présent article sont les suivantes: *i)* un bilan calcique primaire négatif est la raison principale, mais non la seule, de l'ostéoporose; *ii)* ce bilan peut être dû à un apport insuffisant de calcium, à une faible absorption ou à une excrétion importante de calcium; *iii)* une faible absorption de calcium peut provenir d'une carence modérée en vitamine D; et *iv)* une excrétion importante de calcium peut être due à des facteurs alimentaires (apports protéiques et sodiques, par exemple) ou hormonaux (tels qu'une insuffisance œstrogénique). Dans ce contexte, on comprend mieux le profil mondial de l'ostéoporose, mais on n'obtiendra une image complète de la situation que si on réalise des études de terrain soigneusement ciblées.

El calcio en relación con la salud y la enfermedad

La función del calcio y de la vitamina D en la nutrición humana en general y en la osteoporosis en particular ha suscitado notables polémicas. En el presente artículo se examinan las funciones del calcio en el organismo, se describen las principales conclusiones de los estudios sobre el calcio realizados durante el último siglo y se exponen los debates en curso.

Las sales de calcio que proporcionan rigidez al esqueleto constituyen además una reserva muy amplia para el mantenimiento de la concentración de calcio en el agua extracelular del organismo. La hormona paratiroidea y la vitamina D protegen esta concentración, lo que evidencia la función decisiva que el calcio desempeña en el sistema neuromuscular, en la regulación cardíaca, en las reacciones en las que intervienen enzimas y en muchos otros procesos metabólicos.

El calcio se acumula en el esqueleto durante el período de crecimiento y maduración de éste, es decir hasta que el individuo tiene poco más de 20 años. Durante la edad adulta, el calcio en el organismo se mantiene en equilibrio más o menos estable; a partir de los 50 años aproximadamente en los hombres y de la menopausia en las mujeres, el equilibrio óseo se altera y en todas las partes del esqueleto se producen pérdidas óseas. Este proceso está asociado con un aumento notable del índice de fracturas. No se conoce con certeza la causa de la pérdida ósea asociada con la menopausia y el envejecimiento.

El consumo de calcio varía enormemente en el mundo, oscilando entre 800 mg/día o más en los países industrializados y 200-300 mg/día en los países en desarrollo. Paradójicamente, la osteoporosis es más frecuente en los países industrializados.

Las tesis que se formulan en el presente artículo son que la alteración del equilibrio primario del calcio es la causa principal de la osteoporosis, pero no la única; que esta alteración del equilibrio puede ser el resultado de una ingesta insuficiente, de una absorción baja o de una excreción alta de calcio; que una absorción baja de calcio puede ser el resultado de una insuficiencia moderada de vitamina D; y que una excreción alta de calcio puede deberse a factores alimentarios (como la proteína y el sodio) o a efectos hormonales (como la carencia de estrógenos). Desde esta perspectiva, la tipología de la osteoporosis a nivel mundial resulta comprensible, si bien será necesario realizar una labor sobre el terreno con objetivos cuidadosamente seleccionados para completar el cuadro. ♦