the sternomastoid in spasmodic torticollis) can also be injected.[13 14] Nevertheless, large doses are required for treating bulky muscles and may cause systemic side effects besides stimulating antibody production.[15] A further benefit has been for spastic dysphonia,[16] but less satisfactory results have been obtained with other small muscle groups such as in the hand and detrusor-sphincter abnormalities.[17]

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Regular Review

Calcium supplementation of the diet—I

Not justified by present evidence

O, reason not the need: our basest beggars
Are in the poorest things superfluous:
Allow not nature more than nature needs,
Man's life's as cheap as beast's.—*King Lear*

It is commonly believed that the amount of calcium in our diet is critically important and that many people are deficient in calcium because of an inadequate dietary intake.[1-6] From this arises the view that supplements of calcium confer benefits to the community. In 1986 about $166m was spent in the United States on calcium supplements,[7] and the cost could rise to $1·7 billion.[8] In Britain a statutory obligation on millers to add calcium to the flour used for making bread ensures that the whole population has a daily supplement.

The "calcium lobby" has been countered by those who hold that even low dietary intakes of calcium are sufficient to maintain the skeleton.[9-12] The growing awareness of the clinical and economic impact of osteoporosis in countries with increasing numbers of elderly people has led to arguments on whether to supplement the dietary calcium intake of both patients with osteoporosis and those at risk from osteoporosis in later life.

The arguments have been intense, and in this article and next week's we examine the way in which these diverging views arose and re-examine the evidence. It shows how theoretical dogma may persist long after empirical observations have shown it to be unsound, a lesson taught to medical students by William Cullen 200 years ago.[13]

History of calcium nutrition

Present concepts of the importance of calcium in the diet are a product of our heritage, and so it is instructive to examine the conclusions of the past and the manner in which they arose. Influential American textbooks of nutrition published at the beginning of this century encouraged the idea that calcium deficiency was common. Lusk's *The Science of Nutrition* stated that the ordinary American diet in respect of calcium presented "a sorry spectacle": its calcium content was only 700 mg/3000 kcal, one quarter of the amount consumed by Finns.[14] The Finnish figure came from a paper by Tigerstedt, a well known physiologist.[15] He had recorded diets in a rural area where the average daily milk consumption was 1570 ml among men and 913 ml among women. Lusk gave no evidence that the Americans were disadvantaged because they drank less milk. Biblical tradition would, however, have informed him and his readers that milk was a desirable food (Exodus iii.8).

In six editions published between 1920 and 1950 Sherman's *Chemistry of Food and Nutrition* contained the statement that "the ordinary mixed diet of Americans and Europeans, at least among dwellers in cities and towns, was often more deficient in calcium than in any other chemical element."[16] This conclusion was based on a review of 97 measurements of calcium balance in healthy adult men and women.[17] The apparent daily calcium requirement of young men was 450 mg and ranged from 270 mg to 829 mg (mean 450 mg/70 kg body weight). An analysis of the diets of 225 typical Americans showed that one in six contained less than the indicated requirements of calcium.

It is instructive to examine the major assumptions from which these figures were derived. Firstly, the requirement was calculated as the sum of the calcium balance and the dietary intake after abrupt changes (generally a decrease) in diet over three to eight day periods. It was assumed therefore that in subjects with a negative balance the addition of the apparent requirement of calcium to the diet would restore the balance. This implies that intestinal absorption of the extra calcium would have been 100%—a notion now known to be erroneous. This fallacy is illustrated in the apparent relation between dietary intake and "requirements" for calcium calculated in this way (fig 1)—the higher the calcium intake the greater the apparent requirement, a view that even the calcium protagonists might not consider reasonable.

Secondly, the balance technique used relied on analysis of food and faeces and overestimated retention.[20] Thirdly, it was assumed that a decrease in calcium balance resulting from a decrease in dietary intake would be perpetuated indefinitely,

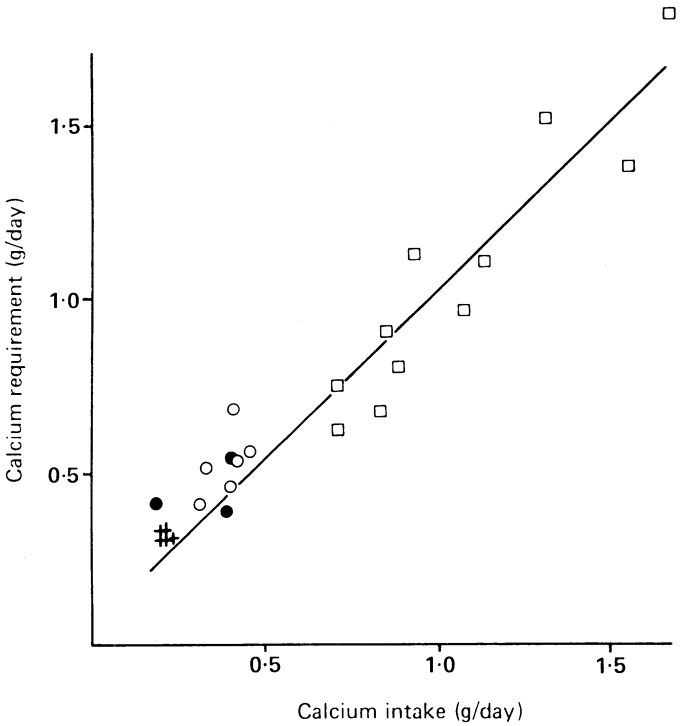

FIG 1—*Relation between calcium intake and apparent requirement computed from balance studies. Solid line shows relation found in perimenopausal women*[18] *and corresponds closely with data of Nordin in similar women* (□).[19] *Apparent calcium requirement for given intake is greater in young adults* (+●○; *data from Sherman*[17]).

but we now know that people adapt to changes in dietary calcium.

Erroneous studies of the 'thirties and 'forties

By 1937 it was appreciated that not all the calcium in the diet was absorbed,[21-23] which led to new approaches to determining the calcium requirements in humans. The first was to examine the relation between dietary intake and metabolic balance in populations. In 1939 Mitchell found that men given a low calcium diet lost calcium whereas those with higher intakes did not.[24] The intercept where the balance was zero was 9·75 mg calcium/kg/day, which is equal to a daily requirement of 570 mg (range 245-760 mg), an advance on the figures of Sherman.[17]

An extension of this type of analysis was to study subjects on a low calcium diet and then to supplement the dietary calcium until balance was obtained.[23] This led to calculations of requirement based on the fractional utilisation of dietary supplements. Not surprisingly, such calculations increased the apparent requirement as the fractional utilisation of calcium ranged from 0·15 to 0·3.[25] Mean requirements in young adults were 662 mg daily (range 500-1000 mg).

A third approach was to examine the relation between dietary intake and output (faecal and urinary) in subjects over a range of manipulated dietary intakes.[23] Women were always in negative calcium balance below an intake of 135 mg daily and had an even chance of being in balance with an intake of 550 mg. By extrapolation no woman would be in negative balance with an intake of 1600 mg calcium daily, yet another advance on the figures of Sherman.[17]

All these studies in the 1930s and 'forties, carried out by investigators of highest repute, promoted the view that a high dietary calcium intake was needed, but in many of them the dietary intake of calcium differed from that normally taken. Thus adaptation was ignored despite emerging evidence for its existence.[26-28] Experiments by Malm in a Norwegian gaol showed that prisoners transferred from a high to a low calcium diet were at first in negative balance for calcium, but after a long period (usually weeks but sometimes months) nearly all came into balance (fig 2).[29] This adaptation was caused by more efficient intestinal absorption of calcium—presumably mediated by calcitriol (1,25-dihydroxyvitamin D). It may, however, take not months but years to attain a new steady state if changes in dietary intake affect skeletal turnover. Calcium deficiency might be expected to stimulate secretion of parathyroid hormone, activate bone resorption, and subsequently increase bone formation—a sequence that may take two to three years to be complete. Thus the true nutritional effect of an altered intake may be determined only in long term studies. Calculations based on sudden decreases in calcium intake would overestimate requirements substantially. It is ironic that this was intuitively appreciated by Sherman himself when he stated that "only those [balance] experiments in which there was a reasonably close approach to equilibrium of lime can be taken as indicating the lime requirement," but it had been forgotten by 1920. Nevertheless, the work of Sherman and his colleagues led enthusiasts in the United States in the 1930s to advocate the drinking of a quart (about 1 litre) or more of milk daily to ensure an adequate intake of calcium.

Not surprisingly, in 1943 the first report of the United States Food and Nutrition Board on recommended dietary allowances set the allowance of calcium for an adult man at 1000 mg.[30] In their ninth report in 1980 the board reduced this to 800 mg. In a new version by the advisory committee, which has not yet been approved by the board but has been leaked to the press, the figure remains but the allowance for an adult woman is raised from 800 mg to 1000 mg.[31] The consensus conference sponsored by the National Institutes of Health in 1984 supported a dietary intake of calcium of 1000 mg for premenopausal women but said that postmenopausal women who are not treated with oestrogen require about 1500 mg daily.[2] This recommendation was made largely on the basis of balance experiments.

The history of calcium nutrition in Britain is shorter than the American history but similar. Adding calcium to flour was made statutory during the second world war. Many ships were being lost in the battle of the Atlantic. Most British bread was then made from white (70% extraction) flour, and

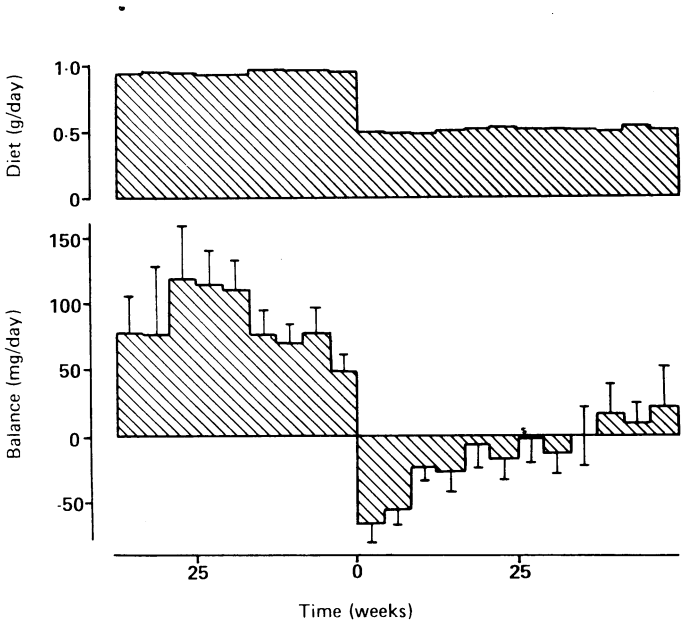

FIG 2—*Mean (SEM) dietary calcium and calcium balance in healthy prisoners. Dietary calcium intake was decreased at time 0, when calcium balance became negative. Note slow attenuation of negative balance thereafter. Data calculated from Malm.*[29]

to save space on ships it was decided that bread should be made only from flour of 85% extraction or higher. McCance and Widdowson showed in balance studies of a few weeks' duration that a change from bread made from white flour to the "national loaf" made from higher extraction flour led to a reduced absorption of calcium and a negative balance.[32,33] The experiments were subject to the same flaws as those of Sherman. Yet after the war, when white bread was again permitted, the obligation to add calcium to flour was retained and still continues under pressure from health enthusiasts despite nutritional advice.[34]

Enthusiasm for calcium nutrition waned in the 1940s and 'fifties when Albright *et al* proposed that osteoporosis was related to a defect in the formation of collagen matrix—caused in some cases by oestrogen deficiency.[35] A revival followed shortly afterwards[35-38]—based once more on balance studies—and since then has never gone away.

The flaws in interpreting early balance studies were appreciated as long ago as 1962, when the Food and Agriculture Organisation and World Health Organisation committee stated that high intakes of calcium were unnecessary and suggested a "practical allowance" for adults of 400-500 mg daily.[20] Many countries, including Britain, follow the recommendations of the committee, whereas other countries follow those of the United States.[39]

Resurgence in the calcium lobby in the 'eighties

The 1980s have seen a resurgence of enthusiasm for calcium nutrition in relation to osteoporosis.[1-6] The consensus conference organised by the National Institutes of Health in 1984 concluded that calcium was one of the "mainstays in prevention and management of osteoporosis,"[2] a view that a more recent conference organised by the National Institutes of Health has done little to dispel.[40] The increasing prevalence of osteoporosis and the cost of its complications have many implications for public health (Pracon Inc report to Rores Pharmaceuticals, Fort Washington, Pennsylvania),[41] but they also place responsibilities on investigators. The question arises whether these views on calcium represent a consolidation of mythology or whether new evidence has emerged indicating that a high calcium intake is important in maintaining skeletal mass.

Calcium in the diet and skeletal mass at maturity

Over 99% of body calcium is in the skeleton. Thus the size of the developing skeleton is proportional to the amount of calcium retained during growth, though not necessarily dependent on it. As skeletal mass continues to increase during growth—and, indeed, after longitudinal growth has ceased—it has been proposed that a high calcium intake increases skeletal mass at maturity. This is an important issue because skeletal mass after the menopause depends on both bone loss after the menopause and the skeletal mass before ovarian function stops. The risk of an osteoporotic fracture may therefore be in part determined by peak skeletal mass.

This view has been strengthened by several observations. The intake of calcium is habitually low in humans compared with that in many mammals, suggesting that a daily dietary intake of 3-4 g might be phylogenetically appropriate.[18,24] Secondly, reports of experimental osteoporosis in animals fed diets deficient in calcium[42] support the view that dietary calcium determines bone mass. But experimental calcium deficiency in growing primates induces osteomalacia rather than osteoporosis,[43] an observation consistent with clinical findings in growing children and young adults.[44-48] Moreover,

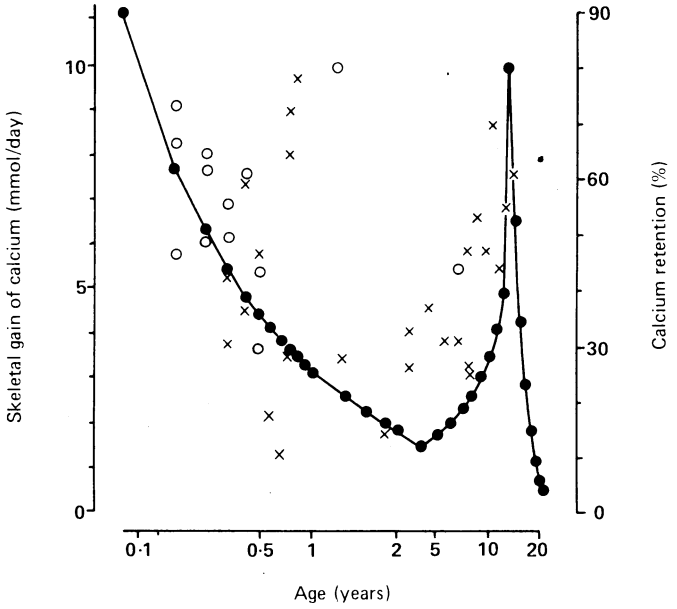

FIG 3—*Estimated daily skeletal gains of calcium in females (●—●) during growth (data from Mitchell[24]). Right ordinate shows the percentage of daily dietary intake of 500 mg that must be retained. Data points show observations from healthy children with high (x) or low (○; less than 500 mg daily) intakes of calcium.*[24]

prolonged calcium deficiency in adult cats also produces the biochemical and histological changes of osteomalacia.[42]

No prospective studies of calcium deprivation in children have been reported, and studies of the effects of calcium supplementation in children are equivocal. Calcium supplements given to children with low calcium diets generally have no effect on the speed of growth.[46,49,50] Short term studies of calcium supplementation in school children have shown small and inconsistent changes that may have been related to changes in energy intake of their diets.[51,52]

Some perspective of the problem may be gained by examining the amount of calcium that must be retained for normal skeletal growth (fig 3). Peak requirements occur during the first months of life and during the adolescent growth spurt, when up to 400 mg daily may be retained. At other times retention is much lower—less than 20 mg daily. Minimum requirements of calcium are dictated by these factors, but actual requirements depend on the amount in the diet, the efficiency of absorption, and the obligatory losses in urine, faeces, and sweat. The efficiency with which the body must retain calcium to cope with skeletal demands throughout growth may be computed for any dietary load and may vary from 5% to 8%. Children are usually capable of such adaptations.[22] Even if calcium deficiency at these critical times affected skeletal growth this does not necessarily have implications for osteoporotic fractures unless it could be shown that short stature was a risk factor, and in reality the converse may be true.[53]

Several other factors have obvious effects on peak skeletal mass in man. These include some hormones—for example, oestrogens and thyroid hormone—as well as physical activity and genetic factors.[54-57] If calcium intake was important we would expect population studies to show differences in bone mass between populations with different intakes of calcium, and studies in the United States, Denmark, Central America, and Switzerland show that this is not so.[10,58-62] The effect of genetic and environmental factors on bone mass may thus be greater than that of dietary calcium.

The most quoted work purporting to show a relation between calcium intake and bone mass and fracture has been widely misinterpreted. Two communities in Yugoslavia were compared, and the people in the one with the higher

calcium intake had the greater bone mass and fewer femoral fractures.[63] There was no difference in the rate of forearm fractures between the two communities. Clearly shown in the paper but not commented on by the authors was the finding that where the calcium intake was higher the energy intake was also higher. Lower energy intake in a population with a similar body weight indicates less physical activity, and diminished activity is a factor affecting skeletal mass. Indeed, in worldwide surveys of rates of fractured neck of femur the differences cannot be accounted for by differences in dietary intake of calcium but may relate more to physical activity.[59-62 64]

Several other surveys have shown small differences in bone mass or density or in cortical width between subjects with high or low calcium intakes, but in each instance physical activity or other nutritional factors may have been the more important determinant.[61 65-71]

There are no prospective controlled studies to show whether an increase in calcium intake increases peak bone mass independently of energy intake. Neither are there any to show whether an increased calcium intake after longitudinal growth has ceased has any effect on skeletal consolidation and the subsequent rate of bone loss or fracture, or both. Studies of metabolic balance after short term changes in dietary intake do not address this question,[36] but it is relevant that the "apparent calcium requirement" for normal subjects in some investigations was less than 300 mg daily.[72 73]

This article is continued next week, when we consider skeletal loss at the menopause and in the elderly and the relation between calcium and fractures.

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