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The health aspects of milk

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Abstract: Cow's milk is not only an important source of calcium, high-value protein, zinc, magnesium and vitamins, but has also scientifically proven health-promoting 'functional' properties. This chapter deals with assured and potential beneficial effects of an adequate milk intake on bone and teeth health, prevention of osteoporosis, the metabolic syndrome, hypertension, and the cardiovascular risk, on overweight and obesity and on gastrointestinal well-being and gut health. Finally, each section of this chapter addresses the question whether the health-promoting value of milk can be or should be enhanced by fortification, modification of the feeding regimen of cows, or addition of components, e.g. probiotic bacteria or prebiotic carbohydrates, to milk products.

Key words: health effects of milk, calcium for bone health and osteoporosis prevention, hypertension and overall cardiovascular disease (CVD) risk, overweight and obesity, probiotics, prebiotics and gut health.

2.1 Introduction

The high nutritional and health-promoting value of milk and fermented milk products has long been known. An Islamic medical textbook recommended (which according to current knowledge may be not quite correct) 'to drink milk, for it wipes away heat from the heart, strengthens the back, increases the brain, augments the intelligence, renews vision and drives away forgetfulness' (cited according to Huth *et al.*, 2006). A Persian version of the Old Testament (*Genesis* 18:8) tells that Abraham owed his longevity to the consumption of sour milk,

and in 76 BC the Roman historian Plinius recommended the administration of fermented milk products for treating gastroenteritis (reference cited in Bottazzi, 1983).

Cows' milk is the major source of calcium in many Western-style diets and an important source of some other minerals, of high-value protein and of several vitamins. Milk and milk products (except butter) contribute relevantly to the US food supply of protein (19.4%), calcium (72.1%), phosphorus (32.4%), zinc (16.2%), magnesium (15.8%) and the vitamins B₂ (26.1%), B₆ (8.7%), B₁₂ (21.6%) and A (15.3%) (Gerrior and Bente, 2002).

Furthermore, milk and milk products have a number of health-promoting properties. The beneficial effects on bone and teeth health, hypertension, the metabolic syndrome and cardiovascular disease (CVD) risk, on overweight and obesity and on gastrointestinal well-being and gut health are described in more detail in the following sections. This high nutritional and health-promoting value of milk needs to be maintained during all technological processes to which milk is subjected. If possible, the value should be enhanced by suitable processing technology, by fortification, by modifying the cows' diet or by adding components such as probiotic bacteria or prebiotic carbohydrates to milk products.

2.2 Bone and teeth health

2.2.1 Calcium and osteoporosis

Osteoporosis is an age-related disease characterized by loss of bone mass, mainly trabecular bone, deterioration of the architecture of bone tissue, and consequently increased bone fragility. Estrogen deficiency exacerbates this effect. Accordingly, women after menopause are at higher risk to suffer from bone fractures than men. Osteoporosis is an increasing health problem not only in industrialized countries but also in threshold countries. In Europe the number of osteoporotic fractures and their total direct costs were estimated at 3.79 million cases and €31.7 billion in 2000 (Kanis and Johnell, 2005). In the USA, the economic burden was estimated at more than 2 million fractures and costs of \$17 billion in 2005 (Burge *et al.*, 2007). In Germany, the total direct costs attributable to osteoporosis amounted to €5.4 billion in 2003 (Häussler *et al.*, 2007). Some major reasons for this are increasing life expectancy, sedentary lifestyle, improved medical care and changing eating habits, whereas physical activity, especially weight-bearing exercise, sufficient exposure to sunlight to ensure an adequate vitamin D synthesis, and a balanced diet providing enough vitamin D and calcium of high availability, may contribute to prevention of osteoporosis.

Thus, calcium is a lifelong, critical nutrient with respect to bone health. It accounts for 1–2% of adult human body weight. Over 99% of total body Ca is found in the bones and teeth, where, incorporated as hydroxyapatite, it brings about rigidity and also serves as a reservoir for metabolically used calcium. An adequate intake of calcium during childhood and youth increases peak bone

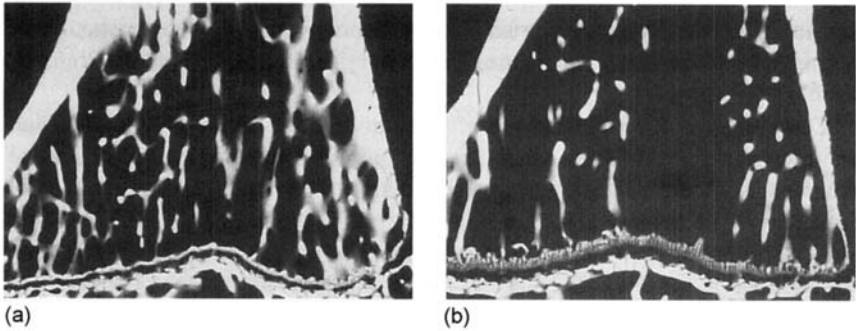


Fig. 2.1 Trabecular structure of (a) a healthy and (b) an osteoporotic tibia in an osteoporosis rat model (Scholz-Ahrens *et al.*).

mass, whereas in adults and aging people calcium may delay and/or slow down bone resorption, alleviating the risk of reaching a critical or threshold value for bone mineral density, when fracture risk increases exponentially (Weaver, 2008; Dontas and Yiannakopoulos, 2007; Heaney *et al.*, 2000; Fig. 2.1).

2.2.2 Calcium requirements and bioavailability

Metabolic balance studies have shown that average absorption rate from whole mixed meals in adults is about 30–35%, and may vary between 25 and 50% depending on age, sex, postmenopausal state, pregnancy, lactation, and calcium and vitamin D status of the body. Calcium homeostasis is regulated by calcitropic hormones, particularly 1,25-dihydroxycholecalciferol, parathyroid hormone and calcitonin. Based on these estimates and considering the adequate safety margins, the recommended dietary allowance (RDA) or adequate intake for calcium varies between 350 and 1300 mg/d (see Table 2.1) to balance the inevitable calcium losses in feces, urine and skin of around 300 mg/d. Actually, men and in particular women ingest calcium at levels which are below these recommendations. The dietary reference intakes (DRI) in the United States are higher than in Europe. At present there is debate on whether current calcium recommendations for adolescents are higher than needed (Atkinson *et al.*, 2008).

2.2.3 Regulation of calcium homeostasis

The varying intestinal fractional absorption rates (or availability) of calcium from different foods depend, in addition to the non-nutritive factors mentioned above, on the physico-chemical form of calcium in the food matrix itself. For absorption calcium has to be present in a soluble form. There are two mechanisms by which soluble calcium is absorbed from the gut (Bronner and Pansu, 1999): (1) the passive, nonsaturable transport is based on paracellular diffusion, vitamin D-independent, and has a similar activity throughout the whole intestine; and (2) the active, saturable calcium transport is transcellular, active already at low calcium concentration, displays its main activity in the

Table 2.1 Recommended Ca intakes in different countries

US (1997)		UK (1998)		D-A-CH (2000) ^c	
Age group (years)	AI/DRI ^a (mg/d)	Age group (years)	RNI ^b (mg/d)	Age group (years)	DRI (mg/d)
1–3	500	1–3	350	1–4	600
4–8	800	4–6	450	4–7	700
		7–10	550	7–10	900
9–18	1300	11–18 m ^d	1000	10–13	1100
		11–18 f ^{d,e}	800	13–19	1200
19–50	1000	19–50 ^e	700	19–50	1000
>50	1200	>50	700	>50	1000

^a Dietary Reference Intakes 1997.^b Reference nutrient intake (Department of Health, 1998).^c German, Austrian and Swiss dietary reference intake (Deutsche Gesellschaft für Ernährung, 2000).^d m = male; f = female.^e An extra amount of calcium (+ 550 mg/d) is recommended for lactating women.

upper small intestine and can be increased by the active form of vitamin D (1,25-dihydroxycholecalciferol), which stimulates the expression of calcium transporters like calbindin D9k.

Thus vitamin D plays an essential role in calcium homeostasis and bone remodeling. Dietary vitamin D (vitamin D₃, cholecalciferol) contributes only little (10–20%) to the maintenance of an adequate vitamin D-status, as measured by circulating 25-hydroxycholecalciferol. The majority of 25-hydroxycholecalciferol is of endogenous origin, when 7-dehydrocholesterol is converted to previtamin D₃ in the skin upon sunlight (UV) irradiation. Previtamin D₃ spontaneously isomerizes to vitamin D₃. Vitamin D₃, of either dietary or endocrine origin, is hydroxylated in the liver to 25-hydroxycholecalciferol, and the latter in the kidney to its active form, 1,25-dihydroxycholecalciferol, also called vitamin D-hormone (Roux *et al.*, 2008; Dawson-Hughes and Bischoff-Ferrari, 2007). In suckling infants calcium is absorbed by a passive, nonsaturable and vitamin D-independent mechanism. After this period, when calcium density in the diet decreases, the active saturable process gains importance. At low intake levels (<300 mg/d) passive calcium diffusion tends toward calcium secretion into the small intestine. In times of increased calcium requirements, i.e. during pregnancy and breastfeeding, a two-fold increase in calcium absorption rate and a decreased renal calcium excretion maximizes calcium absorption efficiency and minimizes maternal bone loss. Therefore most nutrition councils did not consider increments for pregnancy and lactation in their recent recommendations (see Table 2.1).

In the elderly, in particular in people more than 60 years old, vitamin D status deteriorates as a consequence of less exposure to sunlight, less intake of vitamin D from foods and a decline of renal conversion of 25-hydroxycholecalciferol into the active vitamin D-hormone. Consequently, calcium absorption and utilization decrease and calcium balance becomes negative, which entails a loss

of bone mineral and an increased fracture risk. Calcium and vitamin D are thus critical nutrients in this age-group.

2.2.4 Bioavailability of calcium from milk and milk products

Milk, yogurt and (ripened) cheese are the most important sources of calcium in Western culture (Table 2.2). These milk products have a high mineral density (mg Ca/kJ), contain calcium in a highly absorbable form, and can be more easily incorporated in sufficient amounts into a diversified diet than other inexpensive calcium sources like kale, parsley or sesame seed. In Western diets about 60% of calcium is provided by milk and milk products (Huth *et al.*, 2006).

Milk contains 1320 mg calcium per liter and is the food with the highest nutrient density for calcium. One half-liter of milk, yogurt or kefir provides approximately 65% of the recommended daily allowance of calcium of 1000 mg for adults. This calcium is highly absorbable and bioavailable (see Table 2.3).

It is widely assumed that the bioavailability of calcium in milk and dairy products is markedly higher compared with other foods or inorganic calcium salts. This has been explained by the physico-chemical form of calcium in milk, which is micellar and colloidal, and the favorable Ca:P ratio; furthermore the occurrence of calcium absorption-enhancers like caseinophosphopeptides, lactose, citrate, and vitamin D, and the absence of antinutritive factors like phytate and oxalate contribute to its high bioavailability. As a matter of fact

Table 2.2 Calcium concentration in foods

Product	Serving size (g)	mg Ca per 100 g product	mg Ca per serving
Fresh milk (3.5%)	200	120	240
Yogurt (3.5%)	150	120	180
Skim milk yogurt (0.2%)	200	140	210
Cream/Crème fraiche (30%)	30	80	26
Fruit whey drink	200	100	200
Buttermilk	200	110	220
Cheddar (50%)	30	900	270
Gouda/Edam/Tilsiter (45%)	30	~800	240
Camembert (50%)	40	350	140
Feta (50%)	40	450	180
Curd cheese (20%)	50	120	60
Mozzarella	50	450	225
Curly kale (raw)	200	212	424
Fennel	200	109	218
Broccoli/leek	200	87	174
Parsley	15	246	37
Oranges/berries	200/150	33/44	65
Bread (pumpernickel)	50 (1 slice)	110	55
Whole grain bread	50 (1 slice)	84	42
Hazelnuts/almonds	50	240	120

Table 2.3 Calcium bioavailability from food and calcium salts

	Ca/100 g (mg)	Fractional absorption (%)	Reference
Milk	125	32	Weaver <i>et al.</i> (1999)
Cheddar	720	32	Weaver <i>et al.</i> (1999)
Yogurt	125	40	Weaver <i>et al.</i> (1999)
Beans (red)	23	24	Weaver <i>et al.</i> (1999)
Broccoli	50	61	Weaver <i>et al.</i> (1999)
Curly kale	212	40	Weaver <i>et al.</i> (1999)
Spinach	135	5	Weaver <i>et al.</i> (1999)
Mineral water		32	Couzy <i>et al.</i> (1995)
Calcium lactogluconate	11	37	Werner <i>et al.</i> (1999)
Calcium citrate malate	30	36	Heaney <i>et al.</i> (1990)
Tricalcium phosphate	38	25	Heaney <i>et al.</i> (1990)
Calcium carbonate	40	30	Heaney <i>et al.</i> (1990)

fractional absorption from milk products is much higher than from most foods of plant origin. Moreover, the daily dairy servings required to meet a defined amount of calcium are much smaller and thus their incorporation into the daily diet is easier to achieve than solely from staple foods like beans, kale, spinach, potatoes or bread (Weaver *et al.*, 1999).

With respect to availability, the majority of studies do not show physiologically relevant differences between calcium from milk and milk products or from highly soluble, simple or complex calcium salts like calcium chloride, tricalcium citrate, calcium-citrate-malate or calcium lactogluconate. Even calcium salts that are poorly water-soluble like calcium carbonate, calcium oxide or calcium monophosphates are accepted low-cost sources of calcium, except in cases of achlorhydria, and provided that the single dose does not exceed 500 mg (Nickel *et al.*, 1996; Straub, 2007).

Explanations for this are that other factors negate or overcompensate for the effect of solubility, that the poorer absorption of calcium from carbonate may be leveled out in acidic gastric medium, and that calcium phosphate and the calcium-casein complex in milk are present as colloidal aggregates, which are reported to be similarly or even better absorbed than ionic calcium. To date, the assumption that fermented milk products exhibit better calcium bioavailability than milk because of their lactic acid content has not been confirmed.

The Ca:P ratio of the diet and the content of calcium and phosphorus in absolute terms both affect calcium and bone metabolism (Masuyama *et al.*, 2003; Koshihara *et al.*, 2004). An increase of dietary calcium due to strategies for osteoporosis prevention should consider adequate intake of phosphorus. Recent reports underline that 10–15% of older women have intakes of less than 70% of the recommended daily allowance of phosphorus (Heaney, 2004). This

point should receive more attention because there is an increasing demand and a large market for calcium supplements, and these are mainly carbonate or citrate salts (Heaney, 2004). In contrast to calcium from milk, the use of isolated mineral supplements may exceed the dietary Ca:P ratio and, moreover, may imbalance other minerals and trace elements and thus impair their absorption. Milk and milk products contain phosphorus, mainly in the form of phosphate and phosphoric acid esters. The Ca : P ratio in milk is 1.3 w/w and is thus very close to the national guidelines of Germany, Austria and Switzerland of 1.4 w/w (Referenzwerte für die Nährstoffzufuhr, 2000), which is optimal to build up hydroxyapatite. Hydroxyapatite is essential for mineralization, rigidity and structure of bone, and its Ca : P ratio is about 1.7 w/w. Furthermore, phosphorus may counteract protein-induced hypercalciuria.

However, when considering bone health, excess phosphorus intake should be avoided, because the resulting high serum phosphate concentration causes a (transient) drop in serum-ionized calcium and increased PTH secretion, and thereby potentially causes bone resorption. Adolescents are at risk of not achieving an optimum peak bone mass when they change dietary habits, i.e. when they exchange milk for soft drinks, because the latter contain high amounts of phosphorus but no calcium. With respect to bone health, some milk products should be preferred compared to those that contain higher amounts of phosphorus or sodium, for technological reasons.

Milk contains other minerals and vitamins relevant for bone health. Half a liter of milk supplies a large percentage of the recommended daily intakes of many minerals and vitamins, such as magnesium (16%), potassium (15%), zinc (20%), and vitamin D (9%) (Dietary Reference Intakes, 1997, 2001, 2005).

Intestinal absorption of calcium may be affected by concomitant ingestion of digestible carbohydrates. A stimulating effect of lactose is well documented in children, whereas in healthy adults there was little or no effect. Whereas increased calcium absorption due to lactose ingestion has been described in lactose absorbers, impaired calcium absorption has been observed in lactose maldigesters (Obermayer-Pietsch *et al.*, 2007).

A high protein intake increases renal calcium excretion (Kerstetter and Allen, 1994) due to a significant increase in the glomerular filtration rate and a decrease in renal tubular reabsorption rather than to increased calcium absorption (Benable and Martinez-Maldonado, 1991). This calciuric effect depends mainly on acidogenic components of dietary protein, especially on the sulfur-containing amino acids, which are metabolized to sulfate. Milk protein, however, contains less sulfur-containing amino acids than typical animal proteins and is considered to be 'neutral' rather than acidogenic. Any remaining calciuric protein effect may be compensated by the hypocalciuric effect of phosphate in milk.

Casein, the major milk protein, is hydrolyzed in the digestive tract, where encrypted phosphopeptides ('caseinophosphopeptides', CPP) are liberated. CPP have been found to increase the solubility of calcium in the small intestine (Matsui *et al.*, 1997), a pre-requisite for its absorption. Depending on the experi-

mental conditions, this effect was demonstrated in some but not in all studies (Scholz-Ahrens and Schrezenmeir, 2000; Bouhallab and Bouglé, 2004; Möller *et al.*, 2008).

Other encrypted peptides or protein fractions that improve bone health have been described. It was shown that whey protein, especially its basic fraction (the so-called ‘milk basic protein’, MBP) or some of its components, promoted bone formation and suppressed bone resorption (Aoe *et al.*, 2001, 2005) at intakes of less than 50 μg MBP per day. The underlying mechanisms are not yet fully understood. Moreover, it is not clear whether the quantity of MBP that is ingested with normal intakes of milk contributes significantly to a health effect on bone. The presence of encrypted MBP within milk could, however, be a partial explanation for the greater beneficial effect of milk and milk products on bone health in some studies, as compared to calcium supplements.

2.2.5 Calcium and milk products for bone health and prevention of osteoporosis

To fulfill their many functions such as adaptation to varying skeletal strain patterns, repair of bone microdamage or maintenance of calcium homeostasis, bones are subject to lifelong ‘remodeling’, a coupling of bone resorption and formation by specific cells (osteoclasts and osteoblasts, respectively) with little change in shape. Calcium intake or dairy consumption is positively associated with bone mineral density, a predictor of bone fracture risk (see Fig. 2.2). There is considerable evidence from intervention studies and less stringent evidence from observational studies showing that a lifelong, high calcium intake together with sufficient physical activity and strain on bones (1) increases gain of bone mineral and peak bone mass in adolescents and young adults, (2) preserves bone density in adults, and (3) attenuates bone loss in the elderly, particularly in women after the menopause (Heaney *et al.*, 2000; Heaney, 2007; Adolphi *et al.*, 2009).

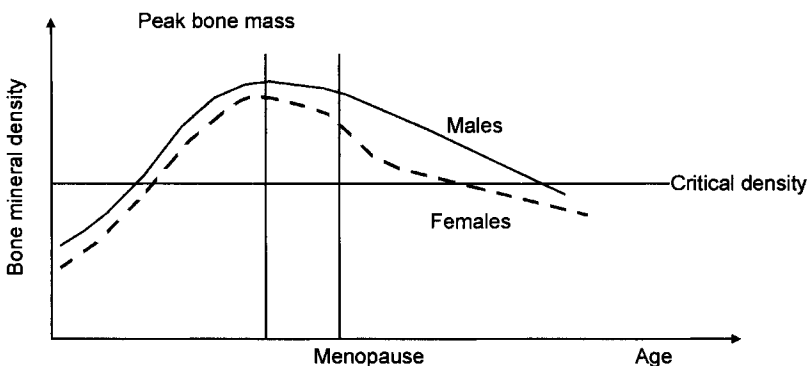


Fig. 2.2 Course of bone mineral density (BMD) throughout life. Critical bone mineral density is achieved earlier in females than in males because of an accelerated loss of bone mineral with the onset of menopause due to the decline in estrogen production.

Some intervention trials, however, failed to show relevant effects of high calcium or dairy intake on bone health (Lanou *et al.*, 2005), and some meta-analyses showed only a weak association between calcium or dairy intake and bone mass, fracture rates or the incidence of osteoporosis (Tang *et al.*, 2007; Winzenberg *et al.*, 2006). The reason for this is the slow development of osteoporosis over years and the large number of risk factors and confounders that are involved but are difficult or impossible to control, like the calcium and/or vitamin D status of the study participants, their habitual diet with great variation of the amount and source of calcium, and other foods that interfere with calcium absorption. The study period may have been too short, and investigation of the 'wrong' bone may have played a role: strained bones (tibia, fibula) profit predominantly from physical activity, while non-strained bones (humerus, ulna, radius) profit more from an increased calcium intake, and for the femur only physical activity plus calcium shows a significant positive effect (Wosje and Specker, 2000).

2.2.6 Milk products and teeth health

Tooth enamel is composed largely of hydroxyapatite ($\text{Ca}_5(\text{PO}_4)_3(\text{OH})$) crystals and is therefore susceptible to acids and calcium-complexing agents. It is always attacked if fermentable sugars are metabolized to organic acids by certain plaque bacteria (especially *Streptococcus mutans*), which decreases the pH of the tooth surface below 5.6.

Milk is only weakly cariogenic or probably not cariogenic at all (Bowen and Lawrence, 2005). Only half of the lactose molecule (namely glucose) is quickly fermented. Therefore, lactose decreases the pH less than an equivalent amount of sucrose or glucose. The high calcium and phosphate content of milk and the buffering capacity of milk proteins inhibit enamel dissolution and demineralization of the teeth and promote or increase remineralization. Ripened cheese and particularly hard and semi-hard cheese is even considered to be the most anticariogenic food and protective against coronal as well as root caries (Kashket and DePaola, 2002). This may be due to one or more of the following mechanisms: stimulation of saliva by cheese chewing, buffering of cariogenic acids, inhibition of enamel demineralization and enhancement of remineralization through the high concentrations of casein, calcium and phosphate, which are higher in cheese than in milk, and the bacteriostatic or even bacteriocidal properties of milk proteins or calcium.

2.2.7 Improving bone- and teeth-protective properties of milk and dairy products

Many individuals do not consume the amount of calcium recommended for prevention of osteoporosis. Milk and calcium-rich dairy products can contribute significantly to the supply of adequate calcium intake of the population, either by increased consumption of dairy products or by offering new functional milk products that are fortified with calcium and/or absorption enhancers.

In populations with a high incidence of lactose maldigestion and intolerance, dairy consumption could be raised by means of lactose-reduced or lactose-free dairy products, particularly cheese and lactose-hydrolyzed and fermented milk products containing active microbial β -galactosidase (see page 53). Whether removal of lactose has a measurable negative impact on intestinal calcium absorption has not been demonstrated to date.

Several measures are conceivable to improve calcium absorption and bioavailability. These include (1) fortification of milk and dairy products with CPP or other relevant peptides; (2) addition of prebiotic fructo-oligosaccharides, i.e. undigestible carbohydrates, which, upon ingestion, will be fermented by the intestinal microbiota, leading to acidification of intestinal contents and improved calcium solubility and absorption (Scholz-Ahrens *et al.*, 2001, 2002, 2007; Scholz-Ahrens and Schrezenmeir, 2007); and (3) vitamin D fortification of dairy products. The latter is effective and is used frequently in many Western countries to improve calcium bioavailability in addition to the aimed improvement of vitamin D status in general. In other countries (e.g. Germany) vitamin D fortification is forbidden because of the risk of exceeding the tolerable upper intake levels (UIL) of 50 μ g vitamin D in Europe and the USA (Przyrembel, 2005; Dietary Reference Intakes, 1997).

2.2.8 Conclusions: calcium-fortified milk products – redundant or helpful

In Germany and some other countries, calcium fortification of milk products is rejected by health authorities. It is argued that milk already contains a high concentration of available calcium, and milk-avoiders, who are most exposed to the risk of low calcium intake, would not profit from these products. It is also thought that calcium fortification of milk products would increase the risk of exceeding tolerable UILs for calcium, i.e. 2500 mg/day in Europe and the USA (Przyrembel, 2005; Dietary Reference Intakes, 1997). On the other hand, fortification is promoted with the argument that many persons would find it difficult to reach the newly recommended intake of up to 1300 mg/d without calcium supplements or fortified foods. Furthermore, the risks of exceeding the UIL for calcium are lowest when dairy foods are fortified, as they are known to be good sources of calcium even without fortification, instead of arbitrarily fortifying a random selection of foods. This question needs further discussion.

2.3 Hypertension and overall cardiovascular disease (CVD) risk

2.3.1 General aspects

It is now recognized that a number of factors contribute to an enhanced risk of cardiovascular disease (CVD). A cluster of metabolic disorders that enhance CVD risk is termed the metabolic syndrome (MS). These include obesity, hypertension, hyperlipidemia (increased low-density-lipoprotein (LDL) and/or decreased high-density-lipoprotein (HDL) cholesterol and increased triglyceride

Table 2.4 Defining the metabolic syndrome

Parameter	Threshold	
	ATP III ^a Insulin insensitivity (high glucose) plus two or more of the following symptoms	IDF (Europeans) ^b Three or more of the following symptoms
Waist circumference (cm)	≥102 (m), ≥88 (f)	≥94 (m), ≥80 (f)
Blood pressure (mm Hg)	≥135/85	≥130/85
Glucose (mg/dl)	≥100	≥100
Triglyceride (mg/dl)	≥150	≥150
HDL-cholesterol (mg/dl)	≤42 (m), ≤50 (f)	≤40 (m), ≤50 (f)

^a Adult Treatment Panel III (National Institutes of Health 2001); m = males, f = females, mg/dl = milligrams per deciliter.

^b www.idf.org

levels), insulin insensitivity or diabetes, and atherosclerosis. Obesity is at the forefront, and insulin insensitivity is the core phenomenon. According to the Adult Treatment Panel of the American Heart Association (ATP III) (Grundy *et al.*, 2005), a metabolic syndrome is established if insulin resistance comes together with two or more of the other disorders. The limits defined by the International Diabetes Federation are even stricter (Table 2.4). Beyond that, there are other disorders like high homocysteine or uric acid levels that may play a role in MS.

CVD refers to a class of diseases that involve the heart or blood vessels related to atherosclerosis. According to the ‘response to injury’ theory (Ross, 1993), pathogenesis of atherosclerosis starts with endothelial dysfunction in blood vessels induced by the aforementioned factors, as well as smoking and bacterial toxins. These factors excite a chronic inflammation as a defense reaction. Over years or even decades, advanced lesions (atherosclerotic plaques) develop and narrow the lumen of the blood vessels. Sudden plaque rupture causes acute myocardial infarction and stroke.

Epidemiological data give little indication that milk and dairy consumption is linked with increasing risk of CVD. A number of studies even indicate that the risk may be reduced with increasing dairy intake. A meta-analysis of 10 studies published before 2002 found that all but one study suggested a lower risk in subjects with the highest intake of milk compared to subjects with the lowest intake (Elwood *et al.*, 2004). Relative risk compared to subjects with the lowest consumption was 0.87 for heart disease and 0.83 for stroke. These results relate to the consumption of mainly full-fat milk, as at the time when these studies were carried out more full-fat than low-fat milk was on the market. More recent cohort studies confirmed these findings. Case-control studies observed also a significant inverse association between yogurt consumption and coronary heart disease (Tavani *et al.*, 2002) and between milk intake and the risk of a first myocardial infarction (Warensjö *et al.*, 2004).

2.3.2 Milk and hypertension

Hypertension is a major risk factor for CVD. Individuals with high blood pressure are three to four times more likely to develop coronary heart disease. Hypertension is the strongest risk factor for stroke. Even persons with high-normal blood pressure have a significantly increased risk of CVD compared to persons with ideal levels. Weight loss, reduction in sodium intake, increased physical activity, and limited alcohol intake are established recommendations that reduce blood pressure.

A number of prospective studies suggest that dairy intake may favor low blood pressure. In the CARDIA study population, the risk for 10-year cumulative incidence of hypertension in the highest dairy intake category (≥ 35 times per week) was less than 50% of that in the lowest category (< 10 times per week). The inverse relation was more obvious in obese persons (Pereira *et al.*, 2002). A follow-up study over 15 years, including a total of 4300 subjects, found an inverse trend for dairy intake ($p = 0.06$). Food subgroup analysis showed a significant inverse trend for milk and dairy desserts, but not for cheese (Steffen *et al.*, 2005). The publication gives no information as to what types of cheese the participants consumed, but as this is a study from the USA, it may be assumed that more fresh and less ripened varieties were consumed. Only the latter may contain relevant amounts of hypotensive peptides (see below). For more detailed coverage see reviews by Jauhiainen and Korpela (2007) and Pfeuffer and Schrezenmeir (2007). A DASH intervention trial (Dietary Intervention to Stop Hypertension) showed that a diet rich in fruits, vegetables and low-fat dairy foods reduces blood pressure significantly more than the respective diet without dairy foods in individuals with both optimal and elevated blood pressure (Appel *et al.*, 1997). Inclusion of dairy products nearly doubled the effect of fruits and vegetables. The benefit of following the DASH dietary pattern was shown to apply throughout the range of sodium intakes (Sacks *et al.*, 2001). In another study a supplement of skim milk decreased blood pressure in subjects with both optimal and elevated blood pressure (Buonopane *et al.*, 1992).

Several components of milk and dairy products may contribute to the blood pressure-reducing effect. The role of antihypertensive milk peptides is without question. Peptides containing up to 10 amino acids may be released from milk proteins through the proteolytic activity of lactic acid bacteria, and are thus found in fermented dairy products, or they may be released during the digestive process in the gut. The hypotensive potential of the peptides requires that they reach target sites without being degraded, through, for example, intestinal or plasma peptidases. Probably the most important underlying mechanism of the antihypertensive effects of milk peptides is inhibition of angiotensin-converting enzyme (ACE) (FitzGerald and Meisel, 2000). Milk peptides may also exert an effect via endothelin release-inhibitory activity. A blood pressure-reducing effect in hypertensive rats was obtained by feeding milk fermented with *Lactobacillus helveticus* CP 790 or *Saccharomyces cerevisiae*, or by feeding two purified tripeptides, Val-Pro-Pro and Ile-Pro-Pro. Fermented milk products in amounts of 95–150 ml/d reduced blood pressure in humans. A powdered, *Lb.*

helveticus CM4-fermented milk, providing 13 mg Val-Pro-Pro and Ile-Pro-Pro per day, reduced systolic blood pressure in subjects with high-normal and mildly elevated blood pressure (Aihara *et al.*, 2005).

Furthermore, calcium in milk may have a blood pressure-reducing effect. Numerous animal and human epidemiologic and intervention studies observed an inverse relationship between dietary calcium and blood pressure. Besides calcium, intake of magnesium and potassium is inversely correlated with blood pressure (Massey, 2001). It was assumed that calcium may suppress circulating vasoactive, calcium-regulating hormones. Lactose, citrate, milk proteins and peptides may improve bioavailability of calcium from milk.

Conjugated linoleic acid (CLA) supplementation reduced blood pressure in spontaneously hypertensive rats (Inoue *et al.*, 2004) and prevented onset of hypertension in fatty, diabetic rats (Nagao *et al.*, 2003). The effects were attributed to the ability of CLA to regulate the production of adipocytokines, such as adiponectin, leptin and angiotensin. There was no effect of CLA on blood pressure in most human studies. Only in pregnant women who consumed 600 mg calcium plus 450 mg CLA daily was pregnancy-induced hypertension significantly reduced (Herrera *et al.*, 2006).

2.3.3 Other factors in milk and milk products with a positive impact on the CVD risk

Obesity

The relationship between milk and obesity is addressed in Section 2.4.

Lipids

Unlike the situation some years ago, low HDL cholesterol and high triglyceride levels rather than high total plasma cholesterol levels are now the main biomarkers used when assessing CVD risk factors (Grundy *et al.*, 2005; Table 2.4). Milk is often considered a potential promoter of atherosclerosis and CVD because it is a source of cholesterol and saturated fatty acids. Butter consumption increases not only total cholesterol, but also HDL cholesterol, such that the ratio of total to HDL cholesterol (or of LDL to HDL cholesterol) is usually not impaired, i.e. not increased. Furthermore, early intervention studies showed that skim milk or yogurt consumption might actually decrease plasma cholesterol levels, while whole milk had neither a hypo- nor a hypercholesterolemic effect. Recent observational studies confirm that higher consumption of milk products is associated with lower cholesterol levels (Pereira *et al.*, 2002; Samuelson *et al.*, 2001). The DASH dietary regimen decreased total and LDL cholesterol beyond the control diet containing no dairy foods (Obarzanek *et al.*, 2001).

It is not clear yet what component(s) play the part of a hypocholesterolemic ‘milk factor’. Calcium, milk peptides and phospholipids are prime candidates. Calcium might have a hypolipidemic effect by decreasing intestinal absorption of cholesterol, of bile acids, and of fat (Shahkhalili *et al.*, 2001). Arguments for the role of milk proteins or peptides are that, at equal fat content, cheese

consumption decreased total and LDL cholesterol as compared to butter (Biong *et al.*, 2004), and that fermented milk products decreased cholesterol levels more than non-fermented products (Agerhol-Larsen *et al.*, 2000). Certain strains of (probiotic) bacteria seem to be more efficient than others (Xiao *et al.*, 2003). Phosphatidylinositol (contained in soy as well as in milk phospholipids) increased levels of HDL cholesterol and apolipoprotein A1 (major apolipoprotein of HDL) and decreased plasma triglycerides. The effect was more pronounced when the preparation was administered together with a light meal (Burgess *et al.*, 2005). Unlike plant phospholipids, milk is also a rich source of sphingomyelin. Sphingomyelin is an inhibitor of pancreatic lipase–colipase and may also decrease micellar solubilization of cholesterol and thus its absorption efficiency. Probably due to its higher degree of saturation, milk sphingomyelin was more effective than egg sphingomyelin in inhibiting absorption of cholesterol and fat in rats (Noh and Koo, 2004). It is not clear if this mechanism is relevant in humans. During processing, phospholipids remain largely with the protein rather than with the fat fraction. Therefore, both full-fat and low-fat milk possess hypolipidemic potential. Butter is relatively depleted of phospholipids.

Dairy fat can be enriched with mono- and polyunsaturated fatty acids at the expense of saturated fatty acids by modified cow feeding regimens. Consumption of modified as compared to a regular milk fat reduced total and LDL cholesterol by 7.9% and 9.5%, respectively, in healthy, normo-cholesterolemic and normal-weight men (Poppitt *et al.*, 2002). The effect was more pronounced than would be predicted from the change in the fatty acid pattern. More studies are needed to explore this effect further. That small changes in the milk fatty acid pattern may have measurable effects on lipid levels is supported by studies that examined the effect of small amounts of long-chain $\omega 3$ fatty acids (eicosapentaenoic acid, 20:5 $\omega 3$, and docosahexaenoic acid, 22:6 $\omega 3$) added to skimmed or semi-skimmed milk. Consumption of 0.5 l/d of such milks, providing between 200 and 300 mg/d $\omega 3$ fatty acids and administered for several months, reduced lipid levels (Carrero *et al.*, 2007; Benito *et al.*, 2006).

Plasma triglyceride levels increase after a fatty meal and return to baseline 6–12 hours later. A high post-meal triglyceride response is associated with increased CVD risk (Cohn, 1998). It is higher in obese and insulin-resistant than in lean and non insulin-resistant subjects, due to an accumulation of triglyceride-rich atherogenic remnant lipoproteins. This post-meal triglyceride response is usually more pronounced with saturated rather than polyunsaturated fatty acids. But frequently the response to milk fat in a mixed meal was comparable to, or less than, that produced by an oil rich in polyunsaturated fatty acids. This attenuated response is most probably due to short-chain and medium-chain fatty acids in dairy fat (see Marten *et al.* 2006 for more details).

Insulin sensitivity

As mentioned before, insulin insensitivity or insulin resistance is the core phenomenon of the metabolic syndrome. In the Health Professionals Follow-up Study, which followed 41,254 healthy male participants for 12 years, each

serving-per-day increase in total dairy intake was associated with a lower risk for type 2 diabetes (relative risk 0.91). The corresponding relative risk was 0.88 for low-fat dairy intake (Choi *et al.*, 2005). In an observational study, fasting glucose and post-meal glucose increase also was lower with higher fat intake from milk and cream (Smedman *et al.*, 1999). A DASH dietary pattern in humans improved insulin sensitivity beyond the effects of the control diet not including low-fat dairy foods (Ard *et al.*, 2004).

Milk proteins, especially whey protein, probably play a role in these effects. When insulin-resistant rats were fed whey or meat protein diets, whey protein reduced plasma insulin and increased insulin sensitivity (Belobrajdic *et al.*, 2004). When rats were fed a high-fructose diet together with probiotic yogurt containing *Lb. acidophilus* and *Lb. casei* (dahi), levels of glucose, insulin and glycated hemoglobin (HbA1c) were reduced as compared to fructose-fed control rats. Indicators of oxidative stress and lipid levels were also significantly improved, but weight increase was identical to that in the fructose-fed control group (Yadav *et al.*, 2007). In rats given a sucrose-rich meal, substitution of α -lactalbumin for whole milk protein attenuated the post-meal glucose increase and improved insulin sensitivity. Non-milk proteins were not tested in this study (Blouet *et al.*, 2007).

Dairy fat is unusual in that it contains a relatively large amount of short-chain (4:0) and medium-chain (6:0-12:0) fatty acids, on average 3.6% and 9.7%, respectively, by weight. Medium-chain fatty acids may affect insulin sensitivity directly, through regulation of glucose metabolism, and indirectly, through regulation of adipose tissue metabolism. Mechanistic studies indicate that longer-chain, saturated fatty acids impair glucose metabolism, but medium-chain fatty acids can actually improve it (for more details see Marten *et al.*, 2006). Evidence that medium-chain fatty acids affect adipocyte metabolism beneficially will be outlined in the section on obesity.

Inflammation

Insulin resistance and diabetes, obesity, hypertension and also dyslipidemia (especially low HDL-cholesterol levels, together with low apolipoprotein A1 levels) are associated with a proinflammatory state of the body. Elevated homocysteine levels (tHcy) are an indicator of such a proinflammatory state (Gori *et al.*, 2005). Hypertensive subjects have higher levels of tHcy as well as lower levels of the endogenous antioxidant, glutathione (GSH) (Rodrigo *et al.*, 2007). Conversely, homocysteine-induced endothelial dysfunction can be reversed by increasing the concentration of GSH. The tripeptide GSH (L-glutamyl-L-cysteinyl-glycine) is the most important intracellular antioxidant of the body.

Observational studies indicate that higher consumption of dairy foods is associated with lower homocysteine levels (Lutsey *et al.*, 2006; more references in Pfeuffer and Schrezenmeir, 2007). In a DASH intervention study, including milk products in the diet reduced serum homocysteine levels beyond those of a diet rich in fruits and vegetables only (Appel *et al.*, 2000).

Among milk components, proteins and phospholipids may have a beneficial role. Whey proteins, especially α -lactalbumin, are a rich source of cysteine. Whey protein (45 g/d) increased plasma GSH levels in humans (Micke *et al.*, 2002) and abolished fructose-induced impaired GSH status in rats (Yadav *et al.*, 2007). Phosphatidylcholine also improved GSH levels in children with cystic fibrosis (Innis *et al.*, 2007) and decreased homocysteine levels in healthy subjects (Olthof *et al.*, 2005). Some effects of phospholipids are probably independent of the source, i.e. independent of phospholipid fatty acid pattern. But in some respects phospholipids rich in saturated fatty acids (present in milk) may be more effective than more unsaturated phospholipids (predominant in soybean oil). In a mouse model, dimyristoyl-phosphatidylcholine (found in milk phospholipids) increased apolipoprotein A1 levels and HDL-cholesterol and prevented atherosclerotic lesions in mice more than equivalent amounts of egg or soy phospholipids (Navab *et al.*, 2003).

Medium-chain fatty acids may attenuate or protect from inflammation (see Marten *et al.*, 2006). The clinical relevance of these findings remains to be established. An interesting aspect is that medium-chain fatty acids have a beneficial effect on serum and tissue levels of long-chain ω 3 fatty acids, which have anti-inflammatory properties. Furthermore, a number of studies indicate that dairy foods may improve the bioavailability of folate. Higher dairy consumption was associated with higher folate levels in observational studies. The DASH dietary regimen not only decreased serum homocysteine levels but also increased folate levels (Appel *et al.*, 2000). In other studies, low-dose ω 3 fatty acids (up to 350 mg/d) combined with low-dose folic acid (150 μ g/d) supplements in 500 ml/d milk decreased homocysteine and increased folate levels (Carrero *et al.*, 2007; Benito *et al.*, 2006) and improved plasma levels of long-chain ω 3 fatty acids markedly (Carrero *et al.*, 2007). Cell culture and animal studies suggest that CLA has anti-inflammatory properties (Bhattacharya *et al.*, 2006). In human studies, however, no such effects were observed.

Obesity and the metabolic syndrome change the serum phospholipid fatty acid pattern toward higher levels of saturated and lower levels of ω 3 fatty acids (Klein-Platat, 2005). Although milk fatty acids may increase serum cholesterol, they apparently have no negative effect on serum phospholipid fatty acid pattern in humans. This was shown for butter as compared to soybean oil (Lichtenstein *et al.*, 2003). Higher consumption of dairy fat (indicated by the concentration of pentadecanoic acid) was associated with higher levels of long-chain ω 3 fatty acids in serum phospholipids and cholesterol esters in an observational study (Smedman *et al.*, 1999). Some reports suggest that conjugated linoleic acid (CLA) improves metabolism of ω 3 fatty acids (Attar-Bashi *et al.*, 2007).

2.3.4 Conclusions: milk products protecting from hypertension and CVD risk

Milk is a whole food with many beneficial components and should therefore be an essential component of a varied healthy diet. Differently processed products

have different effects. There are interactions between milk products and other foods. Therefore not much can or needs to be done to improve milk products. Fermented products may be particularly effective in reducing blood pressure. Low-fat products carry almost all the benefits, as phospholipids remain largely with the protein fraction. When it comes to milk fat, it may be a promising approach to induce a shift in the fatty acid pattern by modifying feeding regimens of the cows, e.g. by including rapeseed cake, in order to reduce the content of saturated fatty acids somewhat and to increase the concentration of vaccenic, oleic and conjugated linoleic acid.

2.4 Protection from obesity

2.4.1 Milk and obesity

The potential association between dairy product consumption and body weight regulation has been the subject of several recent publications. Data from cross-sectional epidemiological studies (Zemel *et al.*, 2000; Carruth and Skinner, 2001; Pereira *et al.*, 2002), rather than prospective studies, and randomized controlled intervention trials with sufficiently large subject numbers showed an inverse association between a high intake of milk and milk products and body weight or body fat accumulation. In a small study, body mass and waist circumference were inversely related to milk fat intake (Smedman *et al.*, 1999).

One may argue that high consumption of milk and milk products might be a marker of a healthier lifestyle, and that methodological weaknesses like insufficiently precise recording of the true intake of individual dairy products and of the nutritional differences between them might have biased the study results. It should also be mentioned that the energy density of many dairy products is actually very low (Table 2.5). But, on the other hand, many of the available data support – though not unequivocally – the hypothesis that one or more milk constituents, e.g. calcium, CLA, medium-chain fatty acids or appetite-regulatory whey proteins and bioactive peptides released from the proteins, are causally related to lower fat mass deposition by decreased absorption and/or higher utilization of fat or energy, respectively.

2.4.2 Calcium

Evidence for an inverse relation between calcium intake and obesity

Observations showing an inverse relationship between calcium intake and obesity have been published since the end of the 1980s, but this hypothesis became more popular in the scientific community following the seminal paper by Zemel and co-workers (Zemel *et al.*, 2000). This publication was based mainly on investigations in obese and insulin-resistant mouse mutants ('agouti mouse') and led to an intensive re-examination and extended interpretation of data from several epidemiological studies.

Table 2.5 Energy density of selected foods

Product	Fat (g/100 g)	Energy density (kJ/100 g)	Product	Fat (g/100 g)	Energy density (kJ/100 g)
Milk (3.5%)	3.5	278	Beef fillet	4.0	506
Milk (1.5%)	1.5	206	Pork fillet	2.0	445
Milk (0.2%)	0.2	153	Chicken breast	6.0	605
Yogurt (3.5%)	3.5	308	Salami	50	2191
Yogurt (1.5%)	1.5	212	Wiener	22	1150
Yogurt (0.2%)	0.2	176	Herring, cooked	17	972
Fruit yogurt (3.5%)	3.5	473	Coalfish, cooked	1.0	377
Fruit yogurt (0.2%)	0.2	363	Chicken egg, whole	11	636
Whipped cream (30%)	30	1296	Pasta prepared with eggs	2.7	1505
Milk ice-cream	2.4	356	Potatoes, cooked	0.1	71
Kefir	3.5	290	Rice, not hulled	2.2	1463
Curd cheese (40%)	11	692	Salad vegetables	0.2	12
Curd cheese (20%)	5	470	Broccoli	0.2	27
Curd cheese (2%)	0.5	319	Leek	0.4	26
Brie (60%)	33	1622	Legumes	1.4	280
Chester (50%)	32	1765	Wholemeal bread	1.0	841
Emmental (45%)	30	1741	with sunflower seeds	3.0	901
Mozzarella (45%)	20	1162	White bread	1.3	240
Gouda (45%)	30	1616	for toasting	3.4	1080
Camembert (40%)	20	1223	Apple, fresh	0.4	221
Parmesan (30%)	22	1601	Hazelnuts	62	2849
Cottage cheese (10%)	2.9	376	Milk chocolate	31	2241

Source: German nutrient database II.3, 2007.

Data from US NHANES III (National Health and Nutrition Examination Survey; Zemel *et al.*, 2000), the CSFII study (Continuing Survey of Food Intake by Individuals; Albertson *et al.*, 2003), the CARDIA study (Pereira *et al.*, 2002), the Quebec Family Study (Jacqmain *et al.*, 2003) and the HERITAGE Family Study (Loos *et al.*, 2004) showed a significant inverse relationship between calcium consumption and body weight, the body mass index ($\text{BMI} = \text{body weight divided by the square of body length (kg/m}^2\text{)}$), body fat distribution, and the prevalence of obesity, respectively. The results were independent of whether calcium intake itself was estimated in the respective study or milk was taken as a measure of calcium intake.

Further evidence came from several clinical observational or controlled intervention studies, respectively, of which the primary focus was the calcium effect on bone mass (summarized by Davies *et al.*, 2000 and Heaney *et al.*, 2002), from studies relating nutrient intake to body composition and from some controlled intervention trials explicitly testing the calcium effect on body weight, fat and the efficacy of weight reduction diets (summarized by Scholz-Ahrens and Schrezenmeir, 2006). Whereas these studies consistently revealed that a high calcium intake in childhood and adulthood independent of the

Table 2.6 Effect of a 300 mg increment in regular calcium intake on body weight and fat

Group	Change in body weight	Change in body fat	Reference
Children		–1.0 kg	Carruth and Skinner (2001)
Young women	–2.5 kg		Davies <i>et al.</i> (2000)
Adult women	–3.0 kg		Zemel <i>et al.</i> (2000)
African-American men		–4.9 kg	Zemel <i>et al.</i> (1990)

calcium source (dairy, supplements, other foods) was positively associated with a lower body weight or BMI, respectively, as well as with a shift from fat to lean body mass and a slower age-dependent weight gain in midlife, other human studies failed to show positive effects of calcium on body weight and composition (Wosje and Kalkwarf, 2004; Bortolotti *et al.*, 2008) or positive calcium effects failed to reach statistical significance (Boon *et al.*, 2007).

A quantitative re-analysis of available data (Davies *et al.*, 2000) using simple bivariate and multivariate regression models revealed that calcium intake accounted for ~3% of the variation in BMI in young women and that every 100 mg increment in daily calcium intake decreased average BMI by 0.3 kg/m². Other studies showed somewhat more pronounced effects in adults (Table 2.6). But regarding population means these effects gain more weight. In young women, an increase in calcium intake from 500 to 1100 mg/d caused a drop in mean BMI by 1.8 kg/m² (–8%) but decreased the predicted prevalence of overweight/obesity (BMI ≥ 25 or 30 kg/m² respectively; WHO, 2000) substantially by 78% and 84%, respectively (Heaney *et al.*, 2002). Midlife weight gain decreased from 0.4 kg/year to 0.01 kg/year when comparing women below or at the 25th percentile of calcium intake with those at recommended calcium intake (Heaney, 2003), and one additional serving of calcium per day (300 mg) led to a decrease of 3.5–4.5% (–20%) of body fat in pre-school boys and girls (mean body fat ~18% or 21%, respectively) (Carruth and Skinner 2001).

Mechanisms of the anti-obesity effect of calcium

How does calcium work? Although the physiological or cellular basis for the changes in body weight and body fat has not been fully elucidated, several hypotheses have been developed. The oldest one starts from the chemical nature of calcium and postulates that the divalent cation calcium prevents intestinal absorption of part of the dietary fat and increases fecal lipid loss and sterol excretion by forming insoluble fatty acid soaps and bile salts in the gut (Denke *et al.*, 1993; Vaskonen, 2003). It is assumed that low calcium absorption (or bioavailability) in the intestine combined with a high calcium intake and thus calcium concentration in the intestine would be associated with less fat and energy intake (or rather availability to the body) and consequentially with a lower body weight.

Another convincing idea developed by Zemel and co-workers (Zemel *et al.*, 2000) is based largely on experiments in obesity-prone (so-called agouti) mutant mice (Shi *et al.*, 2002; Zemel, 2002). According to this hypothesis, increased circulating Ca^{2+} due to the consumption of relatively large amounts of dietary calcium decreases counter-regulatory serum concentrations of the calcitropic hormones PTH (parathyroid hormone) and calcitriol (1,25-dihydroxy-vitamin D3), which in turn down-regulates Ca^{2+} influx into adipocytes and thereby intracellular calcium. Decreased adipocyte intracellular Ca^{2+} stimulates lipolysis, fatty acid oxidation and, in some studies, the expression of uncoupling protein 2 and thereby thermogenesis. At the same time, lipogenic gene expression and fatty acid synthase activity are inhibited, but a contribution of *de novo* lipogenesis in the development of obesity in humans remains doubtful. All these effects result in decreased adipocyte lipid accumulation (Shi *et al.*, 2001), weight and body fat reduction and an overall shift of dietary energy from adipose tissue to lean body mass.

A third possible mechanism, which may weakly contribute to weight reduction as well, has recently been proposed (Ping-Delfos *et al.*, 2004). In a randomized, blind, controlled, crossover study in 11 overweight or obese subjects, a high calcium intake did not change hunger and satiety immediately after a meal, but did significantly reduce spontaneous food intake over the next 24 hours.

Relevance of the anti-obesity effect of calcium

Although the contribution of the different mechanisms to the overall anti-obesity effect of calcium is not clear, there is substantial evidence from animal and human studies that a high calcium intake decreases body weight and fat by a small but significant and relevant amount. However, the results of studies are contradictory in whether an increase of the calcium supply beyond recommendations of ~1000–1300 mg/day, which were set up in order to reduce the osteoporosis risk, would be able to increase the calcium effect on body weight further. Therefore, these effects can be achieved by milk and diets naturally rich in calcium and also by consuming calcium supplements and calcium-fortified food, paving the way for new nutritional concepts to fight obesity (Gerstner and de Vrese, 2007). However, calcium from milk and dairy products seems to be more effective than pure calcium preparations (Lin *et al.*, 2000; Zemel, 2002). This suggests that other milk constituents also contribute to the anti-obesity effect of milk.

2.4.3 Conjugated linoleic acid (CLA)

Dairy fat is the major natural source of conjugated linoleic acid (CLA), and CLA is a major dietary ruminant *trans*-fatty acid. Whereas studies in animals (hamsters) indicate that CLA may have beneficial effects on lipid parameters and body weight by reducing fat mass and increasing lean body mass (Larsen *et al.*, 2003; Bhattacharya *et al.*, 2006), early human trials lasting between 9 and 18

weeks and using CLA doses of about 3 to 3.5 g/d failed to confirm this (Zambell *et al.*, 2000; Whigham *et al.*, 2004) or showed only trends towards lower body fat mass, up to -1 kg (Malpuech-Brugère *et al.*, 2004; Taylor *et al.*, 2006). Animal studies suggest that the *trans*10,*cis*12-CLA isomer has a greater bodyweight-reducing potential than *cis*9,*trans*11-CLA, which is the dominant isomer in dairy fat. But a human study found comparable effects on body fat mass with both the *c*9,*t*11 and *t*10,*c*12 isomers (Malpuech-Brugère *et al.*, 2004). CLA was associated with increased resting energy expenditure and β -oxidation and a significant decrease of body weight or at least body fat and a concomitant increase in lean body mass (Nazare *et al.*, 2007). CLA did prevent an increase in body weight during winter, which was observed with safflower oil (linoleic acid rich) as control (Fig. 2.3; Watras *et al.*, 2007). The most pronounced effect of CLA was observed when combined with additional body weight-reducing measures, i.e. physical exercise, in young, normal-weight subjects: 1.8 g/d CLA plus a 90-minute vigorous run three times a week reduced in 12 weeks the body weight by -1.9 kg and the fat mass by -20% as compared to control subjects who did not receive CLA (Thom *et al.*, 2001). A meta-analysis in 2007 concluded that with 3.2 g/d CLA a moderate reduction of body fat can be achieved (Whigham *et al.*, 2007). The available data do not allow an estimate to be made of the amount of CLA required to achieve beneficial effects concerning weight and body fat reduction. This makes it difficult to give recommendations concerning an optimal milk fat consumption, or a reasonable CLA fortification of milk fat to be achieved either by modified feeding regimens of the cow or by adding isolated or chemically produced CLA.

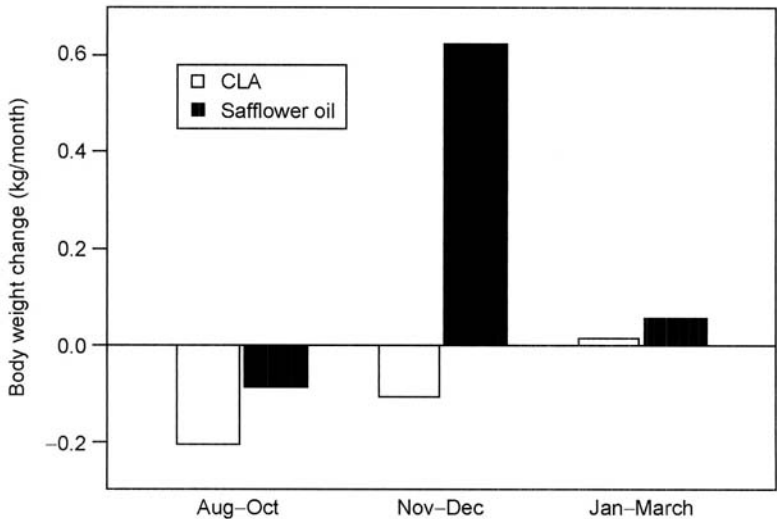


Fig. 2.3 Effects of fatty acids and season (or holidays, respectively) on body weight in overweight subjects (18–44 years, $n = 40$). Results of giving 3.2 g/day CLA for 6 months in a randomized, double-blind, placebo-controlled study (Watras *et al.*, 2007, with permission of the authors).

2.4.4 Medium-chain fatty acids

Medium-chain fatty acids (MCFA) are naturally found in milk fat and coconut oil. Medium-chain triglycerides (MCT) are produced from coconut oil. Triglycerides with short- or medium-chain fatty acids have a higher proportion of carbon and hydrogen in the molecule and therefore a lower energy density than triglycerides with fatty acids with 16 or 18 C atoms (Smedman *et al.*, 1999). This is, however, not sufficient to explain the reductions of body fat mass induced by medium-chain fatty acids in several human studies (Tsuji *et al.*, 2001; Han *et al.*, 2007), and one must postulate an independent effect of MCFA.

Potential mechanisms are: (1) a preferential β -oxidation of medium-chain fatty acids rather than deposition in adipose tissue triglycerides; (2) an increase in resting glucose and lipid oxidation and in postprandial lipid oxidation and energy expenditure following administration of MCT or butterfat, respectively, to obese subjects or animals; and (3) down-regulation of adipogenic genes. Some of these findings add to the idea that medium-chain fatty acids may especially assist in the dietary management of existing obesity (Marten *et al.*, 2006; Rolland *et al.*, 2002).

2.4.5 Effects of milk (whey) protein and appetite-regulatory bioactive peptides

Milk (whey) protein has potential to contribute to the regulation of body weight by inducing satiety signals that affect both short-term and long-term food intake regulation. Although the role of individual whey proteins and peptides is not fully understood, it seems that whey protein reduces short-term food intake compared with placebo, carbohydrates and other proteins affecting satiation and satiety by the actions of whey protein fractions *per se*, bioactive peptides and/or amino acids released during digestion. Whey protein ingestion activates many components of the food intake regulatory system, it is insulinotropic, and peptides derived from whey affect the renin-angiotensin system, which may influence body weight (Sharma, 2008; Sarzani *et al.*, 2008). However, it is unclear whether measurable effects of whey on satiety and food intake and, therefore, potentially on obesity and its co-morbidities (hypertension, diabetes type II, hyper- and dyslipidemia) can be obtained through normal levels of consumption of dairy products. The effects described have been observed in short-term experiments and only with high amounts of whey protein (Luhovyy *et al.*, 2007; Anderson *et al.*, 2004).

2.4.6 Conclusions: is milk a fat burner?

Beside the relatively small energy density of milk and the possible association between high dairy consumption and a healthy lifestyle, some dairy constituents have direct, positive effects on body weight and body fat. Overall these effects are small and the study outcomes are not sufficiently consistent, such that one cannot name milk, calcium or CLA as 'fat burners'. The individual consumer of