Milk Fat and Health Consequences

Robert A. Gibson

FOODplus Australia, University of Adelaide, Glen Osmond, SA, Australia

Abstract
Dairy foods are widely recommended as part of a healthy diet mainly because of the ready availability of calcium but also because they are a good source of protein, minerals and fat soluble vitamins. On the other hand, dairy foods have been viewed with suspicion by many because dairy fats contain saturated fatty acids and cholesterol. It has been thought, particularly by consumers, that dairy fats may increase the risk of coronary heart disease because of the contribution they make to total saturated fat intake. However, dairy fats contain other lipid bioactives (e.g. omega-3 fatty acids, gangliosides, conjugated linoleic acid) that may counteract the effect of saturates in a well balanced diet. Surprisingly, there have been few studies that have addressed this issue.

Dairy Fat Composition
Dairy fats are a complex mixture of lipids, but the bulk (~98%) is contained in the triglyceride form. The fatty acids are made up primarily of saturates and monounsaturates with polyunsaturates present in minor amounts (<3% total fatty acids).

Saturated Fats and Cholesterol
The saturated fats have received the most attention because they contribute to the total saturated fat intake of many people living in Western societies, and this in turn has been associated with elevated risk of cardiovascular disease (CVD) through increased plasma cholesterol and LDL. However, unlike the fats from most animal sources, dairy saturated fats are composed of fatty acids ranging in carbon length from 4 to 20. Because not all saturated fatty
acids are hypercholesterolemic in nature, there is debate about the negative effect of dairy fats on human health. Only lauric (C12:0, 3% total fatty acids), myristic (C14:0, 10%) and palmitic acids (C16:0, 26%) are hypercholesterolemic [1]. Stearic acid (C18:0) is poorly absorbed by the gut and is not considered potent at raising cholesterol levels in humans [2]. Furthermore, it has recently been proposed that stearate-rich fats are suitable replacements for trans fatty acids (TFAs) and possibly other hypercholesterolemic fats [3]. The short- and medium-chain saturates including butyrate (C4:0, 6%), caproate, (C6:0, 3%), caprylate (C8:0, 3%) and capric (C10:0, 3%) are not thought to be hypercholesterolemic. In fact, caprylic and caproic acids are the major constituents of medium chain triglycerides (MCT oil) that are widely used in clinical nutrition as highly available sources of energy since they directly enter the portal system and bypass the liver [4]. The role of butyric acid in foods is less well known. It is interesting to note that the protective effect of dietary fiber against bowel cancer is thought to be mediated by butyric acid produced by commensal bacteria. Butyrate induces transcriptional changes in human colonic mucosa, nucleotide binding and oligomerization domain 2-dependent mucosal immune responses, and is reported to stimulate rumen development in calves [5–7]. There are only limited studies that address the role of dietary butyrate in humans.

Cholesterol and some plant sterols are present in milk fats, and again, the effect of dietary cholesterol is controversial. While it is scientifically accepted that dietary cholesterol contributes little to plasma cholesterol levels, foods containing cholesterol are often grouped as unhealthy. However, cholesterol is present in human breast milk, and because there is emerging evidence to suggest that dietary cholesterol could play a positive role in the growth and development of infants, some manufacturers are including cholesterol in their infant formulas. There is no doubt that animals (e.g. rats, pigs) fed cholesterol can be shown to accumulate cholesterol as measured by increases in cerebrum weight and cholesterol level, but there is little in the way of functional data to show that this can result in a practical difference in brain function [8]. There are no data relating to the brains of breast milk-fed infants compared to the brains of formula-fed infants in the way that was used to establish a need for DHA in infants [9, 10]. It is important to note that human infants thrive on cholesterol-free diets. Smith-Lemli-Opitz syndrome, marked with extremely low serum cholesterol, has served as a human model for the evaluation of dietary cholesterol [11] in the same way that Zellweger syndrome enabled the definition of DHA requirement for neural function.

**Effect of Dairy Fats in the Diet**

Of major interest is the role of dairy foods in the whole diet. Gibson et al. [12] recently conducted a systematic review that had the specific
Milk Fat and Health Consequences

aim to assess the effect of dairy foods on coronary heart disease using all available prospective cohort studies. They found 12 studies that were eligible for inclusion assessing in total over 215,000 subjects. Most studies had close to or greater than 80% follow-up rate, made adjustment for three or more confounders in the statistical analysis and used standard criteria to determine CHD/IHD end points. About half the studies used a validated food frequency questionnaire (FFQ), administered the FFQ more than once, or had a follow-up duration of 20 years or more. Less than half the studies involved subjects with characteristics representative of the general population. Eight of twelve studies reported no association between dairy intake and CHD/IHD. Four of twelve studies suggested some association between some aspect of dairy intake and CHD/IHD. It is important to note that very few studies were designed specifically to address the issue of dairy consumption and heart disease. In most of the studies, the information for dairy intake was collected as part of FFQ, and these tools do not robustly assess dietary fatty acids. In general, attempting to ascribe effects of a single food to multifactorial events such as CVD is extremely difficult. However, in general the studies show that high intakes of saturated fats from all foods are associated with increased risk of CHD, and generally vegetarian diets were protective.

Cohort studies are beset by confounders or effect modifiers including social factors and changes to diet and other risk factors over time. For example, eight of the studies were set up prior to the introduction of low fat dairy products. The Nurses Health Study examined the effect of low fat vs. high fat dairy products in the diet [13]. The study indicated that the ratio of high-to low-fat dairy was positively associated with increased CHD and that the effect could be mainly ascribed to C16:0 and C18:0 in the diet. However, dairy only accounts for 15% total saturates in the diet and 10% of the C16:0 and C18:0 from all foods. Therefore, there appears to be a lack of clarity about the contribution dairy foods make to the risk factors for CVD in our diets. In conclusion, this assessment of twelve prospective cohort studies indicated that there is no consistent evidence in support of the concept that dairy intake is consistently associated with higher CHD/IHD risk.

Most studies support the concept that high saturated fat intake is associated with higher risks of CHD/IHD, but corrections for effect modifiers is not always complete. Thus, it is almost impossible to tease out the relative effects of single food constituents, such as dairy fats. These conclusions have been broadly confirmed by a recent report from Australia. When subjects with the lowest intake of full-fat dairy were compared with participants with the highest intake (median intake 339 g/day), the latter had reduced death due to CVD (HR: 0.31; 95% CI: 0.12–0.79; p for trend = 0.04) after adjustment for calcium intake and other confounders [14]. In contrast, a recent meta-analysis of cohort studies included all studies regardless of whether dairy was mentioned [15]. Surprisingly, this review could not find
significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD. This result challenges the strong belief that many consumers and health care professional have that CHD/CVD is mediated through high intakes of saturated fat that result in elevated plasma cholesterol levels.

To put this in context, there is still uncertainty over the actual role of diets with low polyunsaturated fat to saturated fat (P/S) ratios. In a systematic review and meta-analysis of randomized controlled trials, Skeaff and Miller [16] determined that the relative risk of fatal CHD was not reduced by either low-fat diets or high P/S diets. However, when they restricted the meta-analysis to intervention trials of P/S diets in which mean serum cholesterol concentration was significantly lower in the treatment group, the risk of fatal CHD was significantly reduced by the P/S diets. Similarly, high P/S diets reduced the risk of CHD events. Whether the benefit of high P/S diets is independent of cholesterol lowering deserves attention.

Trans Fatty Acids

Dairy fats also contain TFAs that are also thought to be hypercholesterolemic. However, there is debate as to the relative effect of the ‘natural’ TFAs in milk fats at the typical consumption levels that arise from rumen microbiota and so-called industrial TFAs that arise from industrial transesterification of polyunsaturated fats. Chardigny et al. [17] reported on the results of the TRANSFACT study in which the consumption of TFAs from industrially produced sources was compared with TFAs from natural sources among 40 normolipidemic subjects (19 men and 21 women). In this 3-week study, the subjects were fed 11–12 g/day of these TFAs, and the natural or ruminant TFAs led to increased HDL and LDL cholesterol in women but not in men. Importantly, this intake level represented about 10 times that normally consumed (~5 vs. 0.5%en). The mechanism for this is not clear, but the data point to our limited understanding of one aspect of dairy fats. Finally, conjugated linoleic acid (CLA) is also found in bovine milk. While the efficacy of the use of CLA in the diet of animals is well documented, the effect of this fatty acid on human health remains debatable.

Omega-3 Long-Chain Polyunsaturated Fatty Acids

The importance of dietary omega-3 fats in reducing the risk of CHD/CVD has attracted worldwide attention. Metcalf et al. [18] recently demonstrated the close relationship between dietary omega-3 intake, adequate intake status as measured by the level of omega-3 fatty acids in RBC and the level of omega-3 fatty acids in cardiac tissue. There have been few attempts to
examine the effects of dairy diets on omega-3 long-chain (LC)-PUFA status. This is surprising for two reasons. Firstly, although dairy fat is low in PUFAs, the balance of the essential fatty acids linoleic acid (18:2n-6) and α-linolenic acid (18:3n-3) at 2:1 is considered desirable as it allows the endogenous conversion of these PUFAs to LC-PUFAs. In addition, dairy fats contain low levels of two important omega-3 LC-PUFAs, namely eicosapentaenoic acid and docosapentaenoic acid. Each is a precursor of the very important DHA (docosahexaenoic acid) that has proven health benefits when provided in an adequate amount in the diets of infants. There are clues that a low intake of both precursor fatty acids may result in better omega-3 LC-PUFA status. Clark et al. [19] demonstrated that if the linoleic acid:α-linolenic acid ratio of infant formulas was lowered from the levels of 10:1 to around 3–4:1, the DHA status of infants improved. Equally, pertinent are the findings of others who have shown that infants fed formulas based on dairy fats [20] or indeed evaporated milk [21] have LC-PUFA status midway between those fed formulas enriched with vegetable oils and those fed breast milk. Finally, in their interesting monastery study, Lasserre et al. [22] reported that the level of omega-3 LC-PUFAs in nuns consuming a dairy fat-based diet was superior to the same group when they consumed a sunflower oil-based diet. Confirmation of these findings comes from animal studies. When rats were fed butter, as a model of a saturated fat diet, their omega-3 LC-PUFA status was better than those fed plant oils [23]. Clearly, the influence of dairy fats in a well-balanced diet needs to be investigated in regard to omega-3 LC-PUFA status and the metabolites they produce.

Bioactive Phospholipids

Some of the LC-PUFAs are located in the phospholipid and glycoprophospholipid fractions of cell membranes. These components contribute about 1% of the total fats, and contain some interesting bioactive compounds that have putative health benefits. Those compounds include ceramides, cerebrosides and gangliosides. Gangliosides are particularly interesting. They are naturally present in milk and have been shown to increase ganglioside levels in tissues, including gut and brain (human and animal data). Dietary gangliosides have also been reported to enhance learning ability in animals [24]. Park et al. [25] reported that animals fed gangliosides have increased gangliosides in their retinas and alterations in membrane phospholipids. Interestingly, their work points to an interaction with dietary LC-PUFAs since they also showed an increase in retinal gangliosides in animals fed LC-PUFAs [26]. There are no good human intervention studies with gangliosides, although it is established that breastfed infants have higher levels of brain gangliosides than formula-fed infants.
Conclusions

The paucity of data that relate to the biochemical, physiological and health effects of dairy fats in the diet is surprising considering the ubiquitous nature of messages from learned organizations to include 3–4 serves of dairy as part of a healthy, well-balanced diet. Unraveling the relative health benefits of all the lipid constituents of bovine milk will provide a challenge for researchers for many years to come.

References

Milk Fat and Health Consequences


Discussion

Dr. Hernell: You pointed out that there is a difference between unsaturates. We often talk about saturated fat and lump saturated fatty acids together, and likewise we talk about dairy fat as a lump. But there are clearly differences between the various saturated fatty acids. Is it just too simple to talk about saturated fats or dairy fats? Shouldn't we be more cautious and differentiate between the various saturated fatty acids?

Dr. Gibson: I think that's the point I was trying to make. Dairy fats are very peculiar in the sense that their saturated moieties have molecular weights that are quite small and ones that are quite large. That is in contrast, for example, in meat in which the smallest would be around about C14 and they range through to C20. In dairy fats, the fatty acids are as small as C4, which we know have beneficial effects if they go through the gut. All of the literatures lump everything together in terms of saturated fats, and thus misunderstanding has occurred. I don't believe that dairy fats have been looked at in a fair and a logical manner, particularly given their range of nutrients. Particularly in infant nutrition I think that's where we have missed out enormously. I was one of the proponents many years ago of saying we have got to get the dairy fats out of infant formulas and replace them with vegetable oils, and I think I was dead wrong about that. I think we need to do the trials and look again at what the relative benefits of dairy fats are. I haven't had time to talk about cholesterol, but people are now starting to put cholesterol back into infant formulas as you know, and that's because we think there is now a role for dietary cholestrol in infant nutrition but cholestrol in the diet is something we have been avoiding. So, I think that in past years we have grouped all saturated fats together. Now we know that it's not fair. For example, stearic acid doesn't seem to be absorbed very well, so it can't do much harm, and there are other fatty acids that are not hypercholesterolemic. We are even starting to question the whole cholesterol hypothesis, that is, that saturated fats increase your cholesterol level.
Dr. Hernell: You mentioned infant formulas, and that we have been very careful to get rid of all milk fat when formulas are manufactured. Some companies now use milk fat in formulas. How much dairy fat, in your opinion, should formulas contain? Because there is still the problem with trans fatty acids in bovine milk fat.

Dr. Gibson: A popular combination used to be to have about 80% of the total fat from dairy, and then about 20% vegetable oil was added. What we’ve tended to do is add an awful lot of linoleic acid in the form of corn oil or soy oil or whatever and ignore the fact that linoleic acid is such a strong inhibitor of two processes: the synthesis of omega-3 long-chain polyunsaturates on the one hand and the incorporation of long-chain polyunsaturates in the cells, so that if I eat a piece of fish, for example, I can get more benefit out of it if I eat it cooked in saturated fat than I would have if cooked in polyunsaturated fat because linoleic acid can compete for the incorporation. So then, what vegetable oil would we use if we added it to the 80% dairy fat? I would be advising to be putting in the minimum you can to comply with the regulations about linoleic acid but not so high as to swamp the whole system and prevent any endogenous synthesis.

Dr. Saviano: Would you comment on the ability of the feed stuffs that animals are fed to modify the lipid composition of the milk?

Dr. Gibson: Are you talking about changing the diet of the cow, for example? There is a lot of talk about. You can change the composition of milk slightly, naturally by different diets, for example grass vs. corn and so forth, but the changes are small due to the fact that almost everything that the cow eats goes into one of four different stomachs and gets churned up, and most of the fats that we see that are coming to milk fat are not originated from the grass that they eat but in fact from the biota which is in the gut of the ruminant. So, we are looking at ruminant type fats, that’s why so many of them have got small molecular weight. We can’t change them very much without actually doing something tricky. You can give protective fats, you can wrap them up in activated proteins and get them through to another part of the ruminant to allow that there is some absorption of long-chain polyunsaturates, for example, to enrich them. There is a lot of controversy about whether that’s the sort of thing we want to be doing to the animal and whether the milk is actually safe, but you can do that.

Dr. Mølgaard: What was your final conclusion on the industrial trans fat? I think I missed it.

Dr. Gibson: No, you didn’t miss it, I was carefully avoiding it. Absolutely, I have read the review, I have read the paper and I have read the follow-up reviews, and I am totally confused about that one way or the other. Fortunately Dr. Clemens is going to elucidate on that.

Dr. Melnik: You did not mention in your talk the branched-chain fatty acids. There is some concern in the field of prostate cancer. Correlations between phytanic acid intake and prostate cancer have been reported [1]. Dairy products are a rich source of branched-chain fatty acids, especially phytic acid. Can you comment on that?

Dr. Gibson: I would like to have a bit more expertise before I commented it definitively. My understanding is the branched chains are there absolutely. We measured them ourselves. But they are there in small amounts, and when people say there is a rich source of something, I often wonder what they actually mean by that because about 98% of all the fats are in triglyceride form of standard known fatty acids, so there can’t be much more than point something of a percentage. That also brings us to the point of trans fatty acids. Many of the studies that have been performed about trans fatty acids have used the sort of levels that it’s impossible to eat even if you ate a very high dairy diet, and hydrogenation of fats to make them more solid for the use of making margarines and so forth ceased a long time ago and we now use randomization
procedures to make fats harder. So, many of the studies that have raised these issues with feeding large doses of a single fatty acid, whether it's a trans or a phytanic acid, is somewhat spurious. I think anything, if you give it in huge doses, is going to have deleterious effects on health. It's a personal viewpoint.

Dr. Johansson: You mentioned the different reactions in relation to the trans fatty acids, and my question is if there is anything known about other fatty acids or types of fats. The reason I am asking is that we found a protective effect of dairy products in women, but not men, based on biomarkers measured in plasma and also food frequency questionnaire data.

Dr. Gibson: Thank you for the question, and I don't want to be flippant but I will point out to you that there was a book that came out some years ago that men are from Mars and women are from Venus. I think it was supposed to be about our different characters. The number of reports that are coming out in the literature at the moment about different responses of males and females to different dietary conditions is truly amazing, and I don’t think that I can explain it. In the DINO trial which we reported in JAMA, we got a strong beneficial effect of increasing the DHA level in the breast milk or the formula up to around 1% of the total fatty acids, which is about three times the level that is normally present. The benefit was mostly in very small infants as you would expect, but it was almost exclusively in the girl babies and not the boy babies. Now, why would this be so, why would girls respond and boys not? In the trans fat study there were strange effects that benefited the women but not the men. I don't have an answer for you, but I think we are increasingly becoming aware that the studies need to be large enough and have enough power so that you can actually determine whether there is a gender effect.

Dr. Prentice: A very quick question about the ontogeny of the desaturases. Are newborn babies able to desaturase sufficiently for this mechanism to be useful in young babies?

Dr. Gibson: Absolutely. We know that in adults these is a relatively a slow rate. In fact, the conversion is reported to be somewhere between point zero zero something and one or two percent depending on who you believe. But all those studies have been done with a background of very high levels of linoleic acid in the diet. They haven’t done what our animal data are telling us, that we have got to lower the total PUFAS out of it. If you have an appropriate ratio of omega-6 to omega-3, the total level of PUFA must also be low, otherwise you flood the desaturase system and shut down all of the activity of the enzyme. Having said that, there was a theory around for many years that preterm babies and babies in the first months of life had very low delta-6 desaturate activity and they therefore needed preformed fatty acids, but that has proven to be false. There are good conversion rates being found in preterm babies, and we have shown that in term babies.

Dr. Thorsdottir: I just want to comment on the discussion about long-chain omega-3 in the diet and the concentration in milk. There are several studies in breastfeeding women that show the consumption of omega-3 long-chain fatty acids is mirrored in breast milk. We also know very well that in the dietary studies the concentration of omega-3 in red blood cells is strongly associated with the intake. About milk in general, you indicated that giving omega-3 long-chain fatty acids to the cows would not be a suitable way to increase its concentration in cow's milk. Could this be because of the generally high PUFA intake? Is that possible?

Dr. Gibson: It could be, I think it has more to do with the fact that they are ruminants and that most fat or energy that goes into the ruminant is going into these four stomachs, each of which has huge biota which are converting it to other things.

Dr. Thorsdottir: The fact is that we have seen this in the Nordic cow's milk from Iceland, where the cow's diet contains fish, and we see higher DHA and EPA than in...
the milk collected in Scandinavia and Finland. I thought that was simple, I have not done any intervention or study on that except collected the milk and measured the content. We thought that was because of a different diet.

**Dr. Gibson:** It is from the different diet, and there is some accumulation of EPA and DHA from fish meal which is often given to some animals in the winter time. So, you can increase the levels of EPA and DHA in the cow’s milk, but it’s considered of low efficiency and most of it is getting chewed up by the biota.

**Dr. Haschke:** I would like to follow up a little bit on Dr. Prentice’s question. You said that dairy products are beneficial because it’s possible that the endogenous omega-3 synthesis will be promoted. From which age on would you say it is beneficial? We have discussed what happens in the premature infant and the term infant, but from the fatty acid synthesis side, from which age on do you see a benefit of giving perhaps dairy products with low LC-PUFA levels?

**Dr. Gibson:** This is a great controversy. The one thing that I can stand here with my hand over my heart and say is that my data or the data that Dr. Makrides and I have produced in preterm infants now convince us that long-chain polyunsaturates of the omega-3 variety have a beneficial effect on cognitive outcomes and visual outcomes in children, we know at least to 18 months, if they are born preterm. We started the 7-year follow-up of those infants, and we will know whether this effect disappears or is enhanced. With term infants, as you know, we have also done a number of studies, some of them with Nestlé, about the inclusion of long-chain polyunsaturates into infant formula and compared them with breast milk. The studies haven’t been anywhere near the size that we think is necessary. We suspect that to see any true effects, that is to correct for all possible confounders, the sort of sample size will have to be in the excess of about 3,000, that is about 1,500 per group according to our calculations. But I don’t see any data that convince me that term infants from well-nourished mothers actually benefit from the inclusion of long-chain polyunsaturates of the omega-3 variety in the infant formulas.

**Dr. Gibson:** Dr. Makrides, do you have anything to add?

**Dr. Makrides:** The only thing that I will add comes back to clarifying Dr. Prentice and Dr. Haschke’s questions relating to when the infant is able to synthesize and accumulate DHA. The Clark study from 1992 started with infants from birth, and the changes that we saw in plasma and red cell EPA and DHA were seen in the first 6–10 weeks of life [2]. By simply modifying the balance of vegetable oils in the formula, the concentrations of EPA and DHA in infant blood were increased, although they didn’t exactly match the concentrations of the breastfed infant. So, there was evidence of synthesis and accumulation of EPA and DHA from a very early age.

**Dr. Okolo:** I want to ask if the composition of dairy products varies from location to location. The reason why I ask this is that we analyzed the milk of mothers from northern Nigeria and discovered that the levels of DHA and linoleic acid were on the low side. We wanted to look at what they consume and if they consume more products from their cows; butter oil is the common oil they use for cooking. When we analyzed the butter oil, we discovered that it had a very low level of linoleic acid and DHA, even though the level of linolenic acid was high. So I wonder if the composition of dairy products varies from location to location based on what the cows are fed.

**Dr. Gibson:** I think from looking at the studies around the world, it seems that the fat composition of a milk from dairy cows is pretty independent of the variety of cows, whether they are long horn or short horn, whether they are Friesians or Jerseys. Concerning butter in the diet of the mothers that you are talking about, we’ve shown a number of times now that the level of DHA in the diet is directly proportional to the level of DHA that you can see in the breast milk. Whether there is better conversion of
the α-linolenic acid that women might be getting from other sources, from vegetables and so on, allows better conversion of their bodies to make ALA into DHA for their breast milk, I do not know.

References
