



Proceedings of the IDF Word Dairy Summit 2011 Parma, Italy, 12-19 October 2011



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Foreword

Since many years, IDF's annual meetings have featured presentations by invited speakers. These 'special addresses', as they were called in the beginning, are currently scheduled as conferences during the IDF World Dairy Summit. They cover areas of interest to the global dairy sector. This IDF Bulletin comprises a selection of the presentations made during the conferences organized during the IDF World Dairy Summit in Parma, Italy in October 2011.

IDF would like to thank the authors and presenters of these papers whose contribution helped make the event in Parma memorable for the dairy sector and for the many participants. Their written contributions enable those who could not attend to learn about the new information presented at the 2011 IDF World Dairy Summit.

Nico van Belzen, PhD Director General International Dairy Federation Brussels, 7 October 2012

Animal Feeding

1. The link between feeding and welfare in dairy cattle

Cheryl M E McCrindle¹, Beniamino T Cenci Goga²

Summary

The welfare of any animal can be described by considering its state of well-being. Animals, including dairy cattle, should live in reasonable harmony with their environment, have adequate fulfilment of their physical, health and behavioural needs and not be subjected to unreasonable pain or distress. Lactating dairy cattle are particularly susceptible to the effects of feed on their metabolism and well-being. In this presentation, the manner in which feed can compromise the welfare of dairy cattle will be discussed in relation to protein-energy malnutrition, water deprivation, mineral deficiencies and imbalances, fast fermenting sugars and starches, roughage and forage composition and feeding behaviour. Disease syndromes related to feed and feeding, that may compromise dairy cow welfare, include starvation resulting in suboptimal body condition score, laminitis, arthritis, acidosis, abomasal displacement, milk fever, calving difficulties and retained afterbirth. Each of these impacts on one or more of the five freedoms . Ways in which welfare deficiencies linked to these syndromes can be objectively measured will be described and discussed. It was concluded that feeding systems that do not compromise the well-being of dairy cows are likely to result in better herd productivity. It is strongly recommended that the well-being of dairy cows should also be taken into account when formulating feeding strategies linked to externalities such as environmental objectives or consumer preferences.

Introduction

The International Dairy Federation Guide to Good Welfare in Dairy Production (2008) states that:

"An animal's welfare can be described by considering its state of well-being. Animals should live in reasonable harmony with their environment, have adequate fulfilment of their physical, health and behavioural needs and not be subjected to unreasonable pain or distress".

This definition does not only hold true for the housing and general management of a dairy animal but is also important in relation to feeding. To look at this from a different angle we can also relate feeding to the "Five Freedoms" that characterise animal welfare:

- Freedom from thirst, hunger and malnutrition
- · Freedom from discomfort
- · Freedom from pain , injury and disease
- · Freedom from fear and distress
- Freedom to engage in normal patterns of behaviour

The aspects of feeding that relate to welfare include protein-energy malnutrition (downer cows), deprivation of water, chronic mineral deficiencies or imbalances, excessive fast fermenting sugars and starches, poor quality or insufficient roughage (forage) and ignorance of normal feeding behaviour. Each of these will be discussed in more detail below, indicating how they contribute to contravening the five freedoms and/ or the IDF definition of good dairy cow welfare.

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Protein energy malnutrition and water deprivation

In many parts of the world the rainfall is seasonal with long dry periods. In these countries or areas the smallholder dairy farmer is often more able to survive than a large scale commercial operation. However, this is often a low input/ low output system in order to minimise risk. In the rainy season cows become fat and easily conceive, however in the last two months of pregnancy, if the rain is late, the cow easily goes into a negative energy, protein and mineral balance as the growing calf uses more than can be replaced from feed. The heavily pregnant cow goes down and often dies a lingering death, or is attacked by dogs or jackals. This cruel situation takes quite a while to develop and by the time the cow is a "downer" there is often so little phosphate in the bones that the tail will crumble and she hardly has enough energy to eat. The situation can be complicated by the starving cow, at an earlier phase, eating plastic bags, which interfere with the rumen function. A deficiency of salt in the ration or failure to give a salt lick, can also impair metabolism of protein and energy, exacerbating the "downer cow syndrome") Prevention is by feeding supplements containing protein (or non-protein nitrogen such as urea), energy (molasses is an affordable source) and minerals (calcium and phosphates). In South Africa this supplement is fed , mixed with salt to prevent too much uptake, as a lick. At the same time roughage is fed to stimulate rumen movement. Cows will survive the dry season on maize stover, dried hay or silage and produce a healthy calf.



Plate 1. A lactating cow with calf at foot showing signs of protein-energy malnutrition. The coat is also pale and rough, probably as a result of Vitamin A deficiency as there is no green grass left.

Neglect or failure of a water supply due to depletion of underground reserves in a drought can lead to a very rapid and painful death for high producing dairy cows as 87% of milk is comprised of water. All the conditions just discussed affect the welfare of dairy cattle and link to the first of the five freedoms: *Freedom from thirst, hunger and malnutrition*.

Mineral deficiencies and imbalances

As a dairy cow puts a great deal of calcium and phosphate into milk, as well as into a growing calf, it is relatively easy to see signs of severe deficiency if the pastures and water are deficient

in these minerals. Half of the dry mass of the skeleton and teeth is made up of calcium and phosphorus and . blood also contains these minerals. There is about 10 mg of calcium and 15 mg of phosphorus in each 100 ml of blood. Milk contains approximately 9 g of Ca and 7 g of P per litre.

In low-input, low output or extensive rangeland systems, Ca and P deficiencies can result in severe suffering if these minerals are not supplemented. The signs of phosphate deficiency include severe anaemia, pica (a depraved appetite where the cow eats dry bones of other animals) and osteomalacia, with an arched back (Plate 2). Sir Arnold Theiler diagnosed phosphate deficiency in cattle in South Africa that showed a stiff, slow and painful gait. He linked this disease to botulism, as the affected cows chewed old rotten bones and were poisoned by the Clostridium organisms that grew in the dried out marrow and tendons.



Plate 2. The typical arched back of a Holstein dairy cow with severe phosphate deficiency.

Calcium deficiency, on the other hand, gives rise to rickets in growing calves and lameness due to bruised soles and overgrown hooves. This is common on common on Kikuyu grass pastures, which, when very green inhibit the uptake of Calcium.

In addition to mineral deficiencies, mineral imbalances can cause severe suffering in affected dairy cattle. For instance, there is an interaction between different minerals where excess of one results in deficiency of another. For example, excess potassium (often found in organically fertilized pastures) can depress sodium (salt) levels by 30% and decrease uptake of Calcium and Magnesium. This can give rise to the disease known as "magnesium tetany". Excess molybdenum can cause copper deficiency with anaemia, osteomalacia and hair discolouration. It will also prevent nitrate excretion, leading to fertility problems or , in severe cases, secondary methemoglobinaemia . High levels of copper and sulphur can depress selenium uptake, resulting in "white muscle disease" in calves.

It is very important that dairy farmers pay attention to levels of minerals in water and feed, particularly in pasture based or extensive grazing systems. Mineral supplements are usually affordable and can be used successfully in pasture based systems to improve the well-being of dairy cows. If this is done, the farmer will not only be improving productivity and therefore profit, but also improving dairy cow welfare.

Sugars, starches, effective fibre and acidosis

There has been talk about altering the diet of ruminants to decrease the eructation of methane. One way that has been suggested is to increase the level of short chain carbohydrates and sugars. It should be remembered that rumen microbes ferment carbohydrates to form volatile fatty acids (mainly propionate) that are absorbed from the rumen. Excess propionate reduces pH and encourages lactate-producing microbes. Lactate is a strong acid and lowers the rumen pH.

When a ruminant consumes fast fermenting short chain carbohydrates in excess, this results in acidosis. As a rule of thumb, it is considered that these should not exceed 30% of the ration. To reduce acidosis, slow fermentation is desired and is achieved through feeds with more soluble fibre. Fibre in the ration stimulates rumen movement. Although it can result in higher methane production, it also counteracts acid production through buffering, as salivation is stimulated through chewing and regurgitation.

Acidosis in the rumen eventually results in blood acidity. Affected dairy cows can show chronic, low level bloating and the manure is loose and has a sour smell. Regurgitation and rumen movements decrease or slow down and cows are often depressed and may stop eating. As a result of the decreased pH, there can be fungal over-growth in the rumen, or the acidity can cause ulcers. Other side effects include an increased risk of laminitis and abomasal displacement.

"Forage" is another name for fibre and about 15% of the diet should contain fibrous particles that are about 4cm in length. This stimulates rumination. In the rumen the mat or net of fibre protects fibre digesting microbes. Without effective fibre, acidosis will occur. Fibre stimulates the cow to chew the cud and long hay (that is hay over 12 cm in length) can even be added to a total mixed ration (TMR) to stimulate rumination and prevent acidosis.

Feeding behaviour

High yielding dairy cows need to eat for 4-6 hours a day, lie down to rest to prevent lameness and promote rumination (chewing the cud). External influences can influence feeding behaviour. These include milking times (they should be the same time every day) and social dominance (cows should be separated into different groups according to age, size). In intensive systems, sufficient bunker space prevents aggression and in grazing systems there must be sufficient feeding troughs provided. Sufficient drinking space is essential, if overcrowded, the lower ranking cows in a herd will lie down rather than wait in a queue to eat or drink. Selective feeding can also be a problem, where cows choose the most palatable sugars and starches , which can result in imbalances and acidosis, particularly in the more dominant cows in a herd. This aspect is linked to the 5th of the five freedoms: "Freedom to engage in normal patterns of behaviour".

Diseases linked to feeding

As already mentioned, malnutrition, stunting and acidosis can be directly linked to feeding of dairy cows. There are three other important diseases of dairy cattle where the incidence is greatly influenced by feed. These are lameness (measured by the locomotion index), milk fever, fertility and dystochia. In addition, many toxins that affect the health of cows can be found in poor quality feed. All of these diseases result in avoidable pain and suffering and link to two of the five freedoms (*Freedom from discomfort* and *Freedom from pain*, *injury and disease*).

Locomotion index:

The locomotion index is an objective measure of the severity of lameness in an individual dairy cow. If applied to a herd, the proportion of the herd that shows a grade 1,2,3,4 or 5 lameness can be used as a management tool . Lameness in dairy cattle, although it can be caused by a direct injury, is more often related to pododermatitis, arthritis and laminitis. Laminitis is directly related to rumen acidosis (explained above). Acidic blood decreases oxygen supply in the hoof laminae and endotoxins from acid rumen fermentation cause endotoxaemia and histamine release in the laminae.

Pododermatitis and arthritis are partly due to other management factors, but the primary cause may in many cases also relate to acidosis. Acidotic cows tend not to lie down and rest, thus putting more strain on their hooves and joints. This in turn causes swelling and inflammation of the joints, or arthritis.

Acidotic cows tend to move around very little, causing swelling and poor circulation in the hooves. Although pododermatitis is often linked to wet, muddy pastures or excess manure which soften the skin and hooves, the small sores resulting from cracks or chapping heal slowly if circulation is poor. Poor circulation prolongs healing of inflamed skin between the toes and at the heels and pressure on the hoof wall due to laminitis causes hoof ulcers and promotes secondary infections. These secondary infections, in turn can lead to septic arthritis.

Milk fever:

The efficiency of the parathyroid glands, which regulate the absorption of calcium through the production of calcitonin, decreases during the dry period of the cow, when her requirements are much less than that normally supplied by the feed during that period. The absorption of dietary calcium and phosphorus during the early stages of lactation is often poor owing to low levels of calcitonin, when the requirement of the cow for these minerals is high, as a result of high milk production.

Milk fever can be prevented by decreasing calcium in the last 3 weeks of pregnancy. Some suggest injecting Vitamin D. Recently it has been shown that anionic salts have a positive influence in preventing milk fever and rations or supplements can be designed by specialists in the feed industry to prevent milk fever in a dairy herd. It is also good practice to use the correct ratio of minerals - Ca/P/K/Mg/Se/ Vit E in the feed – which is fairly easy in a TMR system but more difficult in grazing systems, unless these are added to a lick or supplement.

Calving difficulties:

Starvation and mineral deficiencies can result in a late maturing cow that comes into season but is too small to give birth (Plate 3).



Plate 3. Starvation and mineral deficiencies with poor body condition score.

Deficiencies of phosphate can result in a high incidence of dystochia and retained afterbirth in pastoral systems. Compensatory overfeeding of undersized heifers in late pregnancy can result in an overlarge calf resulting in caesarean section or embryotomy.

Toxicity:

Mycotoxins in mouldy feed can not only result in milk residues but also cause low grade liver failure in dairy cattle. Several toxic plants that affect the health and well-being of dairy cattle, for instance ragwort (Senecio spp) can be found in badly managed pastures or extensive grazing. These can also be harvested when hay or silage is made.

Conclusions

It is concluded that paying attention to good feeding practices improves both the welfare and productivity of cows.

Increasing the proportion of highly digestible carbohydrates to increase production (or reduce methane excretion) in the short term, has long term negative welfare and economic implications due to increased acidosis in the herd.

Animal Health

1. The welfare of dairy animals: the perspective of Mediterranean farmers

Paolo Ferrari¹

Animal welfare (AW) in Europe is an increasingly important issue for stakeholders and key actors of the livestock chains.

Promotion of high AW standards has been a primary objective of the European Community Action Plan on the Protection and Welfare of Animals 2006-2010 whose upgrading of existing minimum standards for animal protection and welfare in line with new scientific evidence and socio-economic assessments is a main area of action [Commission of the European Communities, 2006].

There are many ways in which animal welfare can be improved, but the decisions on which routes to follow should be subordinated to their expected impact on society, the livestock industry and the animals themselves [Lawrence and Stott, 2009].

The process of increasing animal welfare standards in EU has evolved through a number of public and private initiatives: legislation, research, education, information campaigns and training; the application of mandatory or voluntary AW schemes.

The level of development of all these kinds of initiatives as well as their level of success have varied between the EU countries. As far as voluntary AW schemes are concerned the collaboration between animal protection organizations, multiple retailers and actors in the production chain often creates the necessary conditions to launch upgraded AW standards on the market.

However the opinions of EU dairy farmers towards AW issues depend mostly on the following features that vary across EU countries:

- farmer education, its professional preparation and experience on farm;
- pressure in society towards upgrading AW standards through the legislation and its enforcement or through information campaigns carried out by animal protection organizations;
- and market segmentation in relation to animal-friendly products and the consequent opportunity for farmers to join AW schemes.

In recent years the opinion of European and Italian dairy farmers about AW issues has been surveyed within the scope of two important EU research projects: Welfare Quality $^{\otimes}$ and EconWelfare.

Milk production in Italy and Spain is concentrated in medium and large size intensive farms located in the Northern regions where forage crop systems are more productive and allow farmers to limit production costs and consequently to be competitive at international level.

Nevertheless the vast majority of holdings in the Mediterranean region are small, although herd sizes fall within a broad range: around 10 on mixed livestock farms, around 50-60 on more commercial dairy operations [WUR, 2010].

In Mediterranean EU Member States national rules about welfare of dairy cows do not go beyond the minimum EU requirements.

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The outcomes of a survey on 471 dairy farmers in Italy, Sweden and the Netherlands [Ferrari and De Roest, 2009] have shown a lower level of professional preparation among the Italian farmers revealed by the lower percentage of those having a degree at an agricultural school compared to their Swedish and Dutch colleagues (22% vs. 46% and 86%, respectively).

With regard to lameness, as an example of specific welfare issue for dairy cows, Italian farmers have been shown to be more concerned than their Swedish and Dutch colleagues (88%, 64%, 54% respectively) owing, on the one hand, to the high prevalence of this problem perceived in their farms and causing them economic damage of which they are aware, and, on the other, to the fact that most of them do not use pasturing systems as a way to reduce the problem because they are operating in the region of the fertile Po valley where pasture is not possible or affordable for technical and economic reasons. Nevertheless most Italian farmers declare themselves to be facing the problem by clipping and disinfecting cow claws regularly (81% instead of 54% and 76% of Swedish and Dutch farmers, respectively) even though the required frequency of claw clipping has been shown much lower on the Italian farms than on the Swedish and Dutch ones (twice a year or more in 32%, 83% and 67%, respectively). In this regard the survey has shown that many more Italian dairy farmers, compared to their Swedish and Dutch colleagues (63% vs. 6% and 36%, respectively), are used to carrying out claw clipping by themselves instead of by external professional hoof trimmers. So most Italian farmers clip cow claws less frequently and do so by themselves. These outcomes indicate quite clearly that most Italian dairy farmers pay less attention to how to reduce the lameness problem, compared to Swedish and Dutch dairy farmers, even knowing that it causes poor cow welfare and economic damage to the farm, and that a reason for this is related to the lower level of education, professional skills and use of external professional hoof trimmers.

A definition of AW, commonly agreed by Italian and also by other dairy farmers of North and Central Europe is related mainly to health, absence of stressful conditions, normal physiology and good production performance.

From the consultation of dairy farmers carried out within the EconWelfare project, a general agreement among the key actors interviewed from the Italian dairy production chain was found about the importance of improving animal welfare beyond the legal requirements, in particular for those aspects producing positive impacts on animal health conditions and productivity. It is a common opinion that the improvement of productivity indexes (birth and replacement rates, live born calves, % of heifers at the first birth) also depend on the level of animal welfare on farm. When AW issues are expressed in these terms, farmers are extremely sensitive to them. For this purpose technical services and advice tailored to the specificities of each farm would be more useful than interventions imposed by regulation because the enhancement of the standards through the introduction of compulsory norms is likely to create trouble for those farmers who are not capable of complying with them. Making the optimal standards compulsory could not be afforded by many farmers, considering the wide range of situations and specificities concerning housing systems, obsolescence of the structures and economic performance. From this point of view the role of regional dairy farmer associations through the services and guidelines provided to their members is extremely important in helping farmers to implement good practices, enhancing welfare conditions in farms. Also the measures of the regional rural development plans aimed at improving animal welfare give farmers the opportunity to approach this topic and to become aware of the importance of some aspects related to animal welfare for good farm management, thereby facilitating the process of learning and increasing awareness of the matter. In the opinion of one farmers' association it is necessary to clarify considerably and implement the current EU rules at national and EU level in order to, on one the hand, improve AW in all EU countries and on the other to avoid distortion of competition between farmers of different EU regions.

A common shared view that arose from key actors in the dairy and meat production chains attending five national workshops organized in the United Kingdom, the Netherlands, Poland, the Former Yugoslav Republic of Macedonia and Italy within the EconWelfare project is that there is no need for more EU AW legislation as the current level of legislation is sufficient to

guarantee a reasonable level of AW. However there is a strong need for uniform enforcement of existing animal welfare regulations in the EU in order to prevent unfair competition.

Another reason to oppose further upgraded legislation is the fear of extra administrative and bureaucratic burdens on farms, as this burden has already become considerable. Alongside the possible increase of production costs these extra administrative costs create a risk of a loss of competitiveness for EU animal production. Some operators in the Italian chain even state that further mandatory regulations are not necessary at all because market forces will steer producers towards certain upgraded standards. In this regard all participants in the chain agree with the statement that voluntary AW schemes combined with labelling, constitute an effective instrument in raising AW issues as they act through the market mechanism and reassure consumers about food safety and AW.

Italian farmers however point out that voluntary quality certification is not always rewarded by consumers owing to lack of information and to production schemes which favour large retailers, and not the producers, and then no appreciable advantages can be expected for Italian farmers given the current national patterns of consumption. The view in Italy of actors in the organic chain differs from that of the actors in the conventional chain because they believe that voluntary standards provide more competitiveness on international market.

The Italian chain actors argue that AW regulations should also include mandatory communication towards consumers. They should be informed that intensive farming per se is not a synonym of poor animal welfare, paying attention to avoiding incorrect or inadequate information that could create negative effects on the market. Emotional, badly informed and inaccurate descriptions of some production systems by some organizations highlight the need for commonly agreed definitions of AW and production systems with the participation of all stakeholders in the food chain.

Most participants in the five Countries agreed that farmers and farmers' groups will only go for higher AW if there are sufficient financial incentives as they need to be rewarded for the capital investment necessary to improve AW. But the Italian farmers' representatives observe that public financial incentives are not able, at present, to encourage a general upgrading of AW standards. Finally the actors in the Italian chain underline that in the near future voluntary schemes may soon effectively become mandatory as they will be required by all of the major abattoirs/processors.

References

- 1. Commission of the European Communities. Communication from the Commission to the European Parliament and the Council of 23 January 2006 on a Community Action Plan on the Protection and Welfare of animals 2006-2010. COM(2006) 13 Official Journal C 49 of 28.02.2006.
- 2. Lawrence A. B., Stott A. W. Profiting from animal welfare: an animal-based perspective. The Oxford Farming Conference 2009.
- 3. WUR Wageningen UR Livestock Research. Animal welfare risk assessment guidelines on housing and management. Technical report submitted to EFSA. August 2010. http://www.efsa.europa.eu/en/supporting/doc/87e.pdf
- 4. Ferrari P. De Roest, K. A quantification in economical terms of job (dis-)satisfaction farmers get from improved welfare measures listed in Step 1. Welfare Quality Deliverable 4.11, subtask 4.5.1, June 2009.

2. Lameness, cow welfare and sustainable farming

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Abstract

A sustainable dairy farming system can be defined as a farming system that takes care of the environment and of animal welfare, in combination with social responsibility and a decent profit. Animal welfare is an important aspect of sustainable dairy farming. Diseases influence both animal welfare and farm profitability. Foot disorders are an important health problem in current dairy farming. Prevalence of foot disorders is high. Eighty percent of all the cows have at least one foot disorder and approximately one third becomes lame. This health problem has major implications for economics and animal welfare. Recently, a dynamic stochastic model to simulate clinical (cows that are visibly lame) and subclinical (foot disorder can be diagnosed but cows are not visibly lame) foot disorders and their effect on economics and cow welfare has been developed. For the Dutch situation, foot disorders cost on average € 53 per cow per year, with milk production losses and premature culling being the most important cost factors. Subclinical cases make up 32% of all costs and approximately 50% of the welfare impact. When looking at the different foot disorders, digital dermatitis is the most expensive foot disorder (€ 17 per cow per year) with also the highest impact on welfare (32 %). By studying the relation between monetary costs and welfare impact, and hence costs, of the different foot disorders, a direction can be given as to what to change on dairy farms to improve profitability as well as animal welfare and thus improve the sustainability of dairy farming.

Introduction

A sustainable dairy farming system can be defined as a farming system that takes care of the environment and of animal welfare, in combination with social responsibility and a decent profit. Foot disorders are an important health problem in current dairy farming because of their high incidence, severity and long duration (Algers et al., 2009, Clarkson et al., 1996, Frankena et al., 2009). It is estimated that in the Netherlands eighty per cent of dairy cows, kept in cubicle housing systems, have at least one foot disorder and approximately one third becomes lame during a year (Frankena et al., 2009, Somers et al., 2003). The majority of the affected cows have subclinical foot disorders (foot disorders which do not cause lameness) (Clarkson et al., 1996, Espejo et al., 2006). Foot disorders and the resulting lameness cause serious economic losses for the farmer (Bruijnis et al., 2010) and are considered to be the most important welfare issue in dairy farming. Because of this combination, foot problems can also be regarded as a serious problem with regard to sustainability.

In this contribution, the effects of foot disorders on both animal welfare and on farm economics will be described and related to each other. Both items are, amongst others, important for a sustainable dairy sector. The welfare and economic impact assessment were based on a simulation model. Therefore first the simulation model is described, followed by the economic impact of foot disorders and the welfare impact of foot disorders. In the final part of this contribution, the economic and welfare impact are combined and compared to each other.

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Modelling foot disorders

A dynamic simulation model has been developed for estimating the consequences of foot disorders (Bruijnis et al., 2010). The model simulates cow characteristics like the parity, stage of lactation and milk production level all of which influence the probabilities of getting a foot disorder (Figure 1). In the second step, the model simulates the dynamics of foot disorders per cow per month for two years, giving the incidence and duration of the foot disorders. Every month each cow has a different probability of changing foot health status, depending on its status in the previous month and cow characteristics. The following events can take place: development of a foot disorder, transition from a subclinical to a clinical foot disorder or cure of a foot disorder. Getting a foot disorder is dependent on the probabilities of transition from healthy to subclinical (P_{HS}) or to clinical (P_{HC}) . These are influenced by parity, stage of lactation and milk production level. For example, a higher producing cow has a higher risk of getting a foot disorder. The subclinical foot disorders have a probability of developing into the clinical phase after one or more months (P_{SC}) or have a probability of cure after foot trimming (P_{SH}). The clinical foot disorders have a certain probability of recovery due to treatment by the farmer, foot trimmer or veterinarian during the year or after foot trimming (P_{CH}) and a probability of culling due to the foot disorder (P_{Cul}) . The state of the cow, Healthy, Subclinical, Clinical and Culled, is determined with a set of discrete distribution functions. PCul is influenced by milk production level and parity.

In the third step, the results of the second year are used for the calculation of the economic consequences and welfare impact for the simulated foot disorders in one year. The fourth step sums cow level results to produce herd level results.

Model parameter settings were derived from reports in relevant literature on prevalence, incidence, and consequences of foot disorders in dairy cattle. Only those papers with criteria relevant to common Dutch dairy circumstances were included for estimation of the input values of the model. These criteria include a cubicle housing system with a concrete (slatted) floor, pasturing during summer, two foot trimming interventions per year and a herd consisting of mainly Holstein dairy cows. These farm characteristics resemble characteristics of many modern dairy farms in other Western countries, and present findings are assumed to describe the situation especially for such farms.

The following foot disorders were modelled: Interdigital Phlegmon (IP), Interdigital Dermatitis and Heel Horn Erosion (IDHE), Digital Dermatitis (DD), Sole Haemorrhage (SoH), White Line Disease (WLD), Sole Ulcer (SUL), and Interdigital Hyperplasia (HYP). IP, IDHE and DD are infectious foot disorders; SoH, WLD, SUL and HYP have physical or metabolic causes or are a secondary foot disorder. Where IP is an acute, painful inflammation, IDHE is an epidermitis of the interdigital skin extending to the dermis up to the heel horn. DD infection affects the epidermis of the hoof skin (Blowey and Weaver, 2003). SoH refers to damage of the corium and classifies as haemorrhage in the sole, being reported in literature under different names like subclinical laminitis and laminitis. WLD identifies haemorrhages and lesions in the white line. SUL mainly occurs after SoH and IDHE and concerns ulcers in the sole, toe and heel. HYP is proliferation of the interdigital skin and originates as a reaction to long lasting inflammation (e.g. DD and IDHE). It is assumed that all cases of IP and SUL occur clinically. For most of the simulated foot disorders (IDHE, DD, SoH, WLD and HYP), it is assumed that the foot disorder first occurs subclinically before developing into a clinical foot disorder.

The total costs due to subclinical and clinical foot disorders comprise costs for milk production losses, costs for culling, costs for a prolonged calving interval, costs for labour of the dairy farmer, costs for the foot trimmer, costs for the veterinarian, costs for treatment, and costs for discarded milk. The costs are calculated monthly and summed up to a year for each cow. The costs for milk production losses due to subclinical and clinical foot disorders are based on the milk production, the percentage of milk production loss and costs for milk production losses. Costs for a culled cow due to clinical foot disorders are based on the retention pay-off value and were dependent on parity and lactation value of the cow. Costs for a prolonged calving interval are calculated by multiplying the number of prolonged days with the costs for each day of pro-

longation. For clinical foot disorders, the extra labour of the dairy farmer is estimated in hours per month per cow. The costs are calculated by multiplying the hours with the hourly rate of a dairy farmer. Costs for the foot trimmer are calculated on the basis of rates per treated cow, and costs for the veterinarian are calculated on that of the price for a visit per treated cow. The costs for the use of antibiotics, costs for the resulting discarded milk, and topical treatments are included in the model as well. A more detailed description of these calculations can be found in elsewhere (Bruijnis et al., 2010).

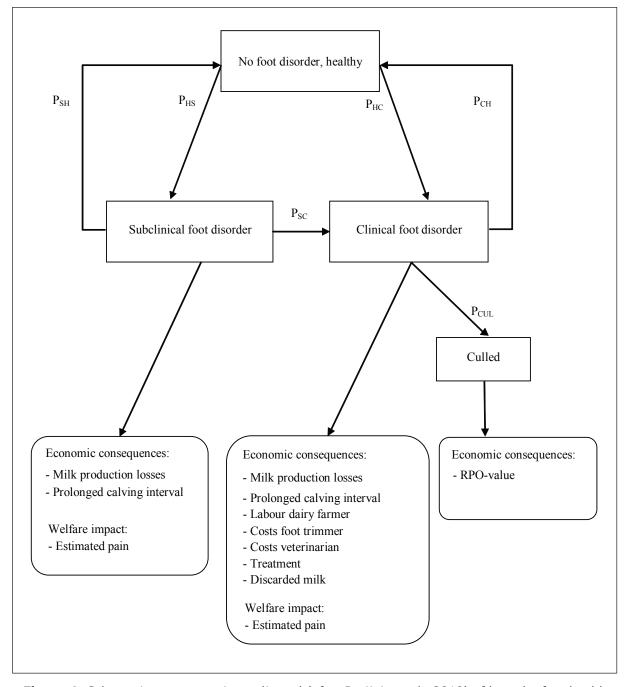


Figure 1. Schematic representation, adjusted (after Bruijnis et al., 2010) of how the foot health status of the cows is determined in the simulation model, including the factors used to calculate the economic consequences and welfare impact.

The welfare impact was assessed using the estimated pain of each foot disorder (Bruijnis et al., 2011), assuming that pain caused by the foot disorders is the basis for the effects on the different aspects of animal welfare as defined by Fraser et al. (1997). Specifically, a cow with a foot disorder will, to a certain extent, have difficulties functioning normally because the pain obstructs the locomotion function, causes negative affective states and impairs ability to perform natural behaviours, constraining natural living. Pain impact for each of the foot disorders in clinical and subclinical state, was estimated by experts according to a scoring scale that is similar to that used in locomotion scoring systems (for example, Bicalho et al., 2007, Garbarino et al., 2004). Literature on pathophysiology of foot disorders and on lameness and locomotion was studied and, in combination with the estimation of experts in the field of dairy cow foot health, the pain impact of a foot disorder in subclinical and clinical state was estimated. The welfare impact was calculated by counting this pain score for each month that the foot disorders were present.

Economic impact

After running the model, the results show that throughout the year the prevalence of foot disorders varies from 43% after foot trimming in October (after grazing) to 80% at the end of the winter in March (before foot trimming) (Bruijnis et al., 2010). Subclinical SoH has the highest prevalence. SoH and IDHE are mainly subclinical: only a few cases become clinical. This is also the case for the less prevalent foot disorders, WLD and HYP. The foot disorders IP and SUL have relatively low total prevalence, but do account for a substantial part of the total prevalence of clinical foot disorders.

The total costs due to foot disorders for a farm with 65 cows in the default situation are €3474 per year (€53 per cow) with a variation between €2282 and €4965. The costs due to subclinical foot disorders are €1107 per year (variation between €883 and €1367), which is 32% of the total costs due to foot disorders (Table 1).

Table 1: Average economic consequences (€/yr) of subclinical (SC) and clinical (C) foot disorders on the default farm (cubicle housing, concrete (slatted) floor, pasturing during summer, two foot trimming interventions per year) classified by cost factors (after Bruijnis et al., 2010).

	Subclinical	Clinical	Total
Milk production losses	864	673	1,537
Culling	0	769	769
Prolonged calving interval	243	175	418
Extra labour dairy farmer	0	410	410
Extra visit foot trimmer	0	105	105
Extra visit veterinarian	0	53	53
Treatment	0	48	48
Discarded milk	0	135	135
Total	1107	2367	3474

On average a clinical case costs €67 and a subclinical case €13. Milk production losses cause 44% of the total costs due to foot disorders, culling 22%, prolonged calving interval 12% and costs for extra labour of the dairy farmer 12%.

IP and SUL cause 23% of the total costs due to foot disorders (Table 2). DD causes the greatest costs, mainly because of the relative high incidence of the clinical stage. For SoH and IDHE the subclinical stage causes most costs.

Table 2: Average economic consequences (€/year) for the different foot disorders, both subclinical and clinical on the default farm (cubicle housing, concrete (slatted) floor, pasturing during summer, two foot trimming interventions per year (after Bruijnis et al., 2010).

	IP	SUL	SoH	IDHE	DD	НҮР	WLD
Subclinical	-	-	473	313	191	48	83
Clinical	339	455	237	272	886	66	113
Total	339	455	710	585	1076	114	195

Welfare impact

On average a cow has a negative welfare impact of 12. Sixty is the maximum score for welfare impact, representing a cow with very severe pain for the whole year, thus, on average a cow is estimated to experience 20% of the maximum welfare impact, which translates to, for example, having severe pain for 3 months (Bruijnis et al., 2011). DD has a relatively high clinical occurrence and has the highest impact on dairy cow welfare, followed by SoH and IDHE (Table 3). SoH and IDHE have a high subclinical score. The total welfare impact of subclinical foot disorders (54%) is comparable to the welfare impact of clinical foot disorders (46%). The welfare impact of IP, the foot disorder which is assessed to be the most painful foot disorder, is negligible (0.5%) particularly at herd level. At cow level, i.e. when excluding the effects of foot disorder incidences, clinical foot disorders have more impact than the subclinical ones. With the approach to cow level, the secondary foot disorders, HYP, SUL and WLD, have relatively higher impact than at herd level, mainly due to its painfulness. Similar to the outcomes at herd level, the welfare impact of DD at cow level is high due to its painfulness, which is also the case for SUL and WLD. The results underline the fact that subclinical foot disorders have a relatively high impact on welfare when taking into account the duration and incidence of a foot disorder, as subclinical foot disorders can be present for a long time (e.g. IDHE) or have a high incidence (SoH). The welfare consequences of subclinical foot disorders may be relatively minor compared to those of clinical foot disorder cases at individual cow level, but substantial at herd level.

Table 3: Relative impact of the different foot disorders (subclinical and clinical) for the average welfare impact (representing herd level impact; pain x duration x incidence (after Bruijnis et al., 2011).

Welfare impact, %	IP	IDHE	DD	SoH	WLD	SUL	НҮР
Subclinical	-	14.8	11.5	21.0	3.3	-	3.2
Clinical	0.5	7.2	20.7	6.3	2.1	7.9	1.6

Comparing economic and welfare impact

Bruijnis et al. (2012) have compared the economic and welfare impact of foot disorders. Subclinical cases make up 32% of all costs and account for approximately 50% of the welfare impact. Digital dermatitis, has the highest impact: almost one third of total impact for both economics and welfare (Figure 3). Sole haemorrhage and interdigital dermatitis/heel erosion, mainly subclinical and of a high prevalence, have a substantial impact on costs due to foot disorders, 20% and 17% respectively, and on welfare, 27% and 22% respectively. Interdigital phlegmon, the foot disorder regarded as most painful (Table 2), but which has a low incidence and short duration, is not very costly, accounting for only 10% of total costs, and has the lowest welfare impact, 0.5%. Together with SUL, IP only occurs clinically and has a relative higher impact on economics than on welfare (Figure 2).

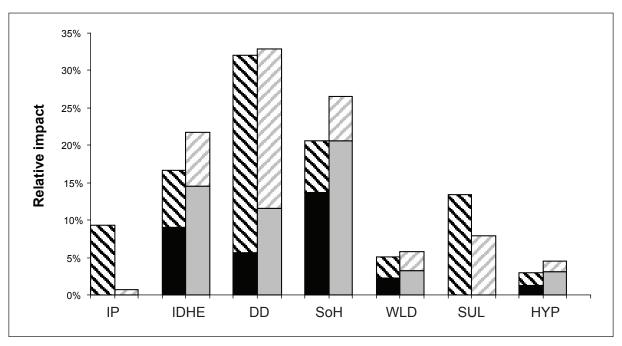


Figure 2. Relative impact at the herd level for each foot disorder of the economic consequences (black bars) and welfare impact (grey bars), divided for the subclinical state (solid pattern) and clinical state (hatched pattern; after Bruijnis et al., 2012).

The outcomes on economics and welfare impact are significantly positively correlated, with a Spearman rank coefficient of 0.64 (p <0.05). Subclinical cases of foot disorders tend to have a relatively higher impact on welfare than the clinical cases (Figure 3).

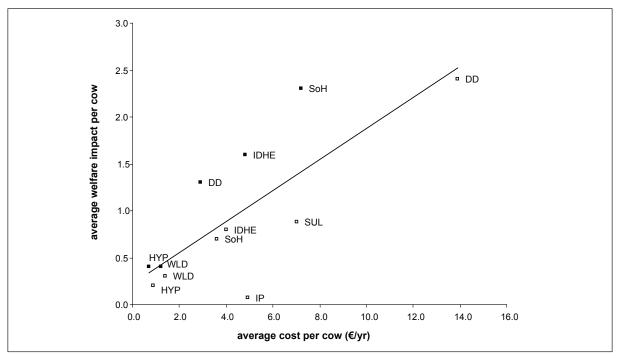


Figure 3. Relation between average costs and the welfare impact per cow in the herd over one year by clinical state (= □) and subclinical state (= ■; after Bruijnis et al., 2012).

Concluding remarks

In Dutch dairy farming with cubicle housing and concrete floors, foot disorders are a major welfare problem with serious economic consequences. At the herd level, DD has highest impact on economics and cow welfare, followed by SoH and IDHE. Subclinical foot disorders, which are the foot disorders not recognised by dairy farmers, account for 50% of the total welfare impact of foot disorders and 32% of the total costs, indicating a considerable impact of undetected or untreated foot disorders. The impact of foot disorders on economics and animal welfare are positively correlated, a finding which can further increase awareness among farmers and stimulate improvements in dairy cow foot health. disorders. An improved level of foot disorders is good for the farmer (fewer losses) as well as for the animal (fewer welfare problems). For a sustainable dairy farming system, therefore, it is important to pay attention to foot disorders.

References

- 1. Algers, B., G. Bertoni, D. M. Broom, J. Hartung, L. Lidfors, J. H. M. Metz, L. Munksgaard, T. Nunes Pina, T. Oltenacu, J. Rehage, J. Rushen, F. Smulders, E. N. Stassen, G. Stilwell, S. Waiblinger, and A. J. F. Webster. 2009. Scientific opinion on the overall effects of farming systems on dairy cow welfare and disease. EFSA J 1143:1-38.
- 2. Bicalho, R. C., F. Vokey, H. N. Erb, and C. L. Guard. 2007. Visual locomotion scoring in the first seventy days in milk: Impact on pregnancy and survival. J. Dairy Sci. 90(10):4586-4591.
- 3. Blowey, R. W. and A. D. Weaver. 2003. Locomotor disorders. in Color Atlas of Diseases and Disorders of Cattle. 2nd ed. Mosby, New York, NY.
- 4. Bruijnis, M. R. M., B. Beerda, H. Hogeveen, and E. N. Stassen. 2012. Foot disorders in dairy cattle: impact on cow and dairy farmer. Animal Welfare, in press.
- 5. Bruijnis, M. R. N., B. Beerda, H. Hogeveen, and E. N. Stassen. 2011. Assessing the welfare impact of foot disorders in dairy cattle by a modeling approach Animal, in press.
- 6. Bruijnis, M. R. N., H. Hogeveen, and E. N. Stassen. 2010. Assessing economic consequences of foot disorders in dairy cattle using a dynamic stochastic simulation model. J. Dairy Sci. 93(6):2419-2432.
- 7. Clarkson, M. J., D. Y. Downham, W. B. Faull, J. W. Hughes, F. J. Manson, J. B. Merritt, R. D. Murray, W. B. Russell, J. E. Sutherst, and W. R. Ward. 1996. Incidence and prevalence of lameness in dairy cattle. Vet. Rec. 138(23):563-567.
- 8. Espejo, L. A., M. I. Endres, and J. A. Salfer. 2006. Prevalence of lameness in high-producing Holstein cows housed in freestall barns in Minnesota. J. Dairy Sci. 89(8):3052-3058.
- 9. Frankena, K., J. Somers, W. G. P. Schouten, J. V. van Stek, J. H. M. Metz, E. N. Stassen, and E. A. M. Graat. 2009. The effect of digital lesions and floor type on locomotion score in Dutch dairy cows. Prev. Vet. Med. 88(2):150-157.
- 10. Fraser, D., D. M. Weary, E. A. Pajor, and B. N. Milligan. 1997. A scientific conception of animal welfare that reflects ethical concerns. Animal Welfare 6(3):187-205.
- 12. Garbarino, E. J., J. A. Hernandez, J. K. Shearer, C. A. Risco, and W. W. Thatcher. 2004. Effect of lameness on ovarian activity in postpartum Holstein cows. J. Dairy Sci. 87(12):4123-4131.
- 13. Somers, J. G. C. J., K. Frankena, E. N. Noordhuizen-Stassen, and J. H. M. Metz. 2003. Prevalence of claw disorders in Dutch dairy cows exposed to several floor systems. J. Dairy Sci. 86(6):2082-2093.

Dairy Policies

1. Protected Designation of Origin - Italian model

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AFIDOP - Italian Association of Cheeses with Protected Designation of Origin

The Italian dairy industry is based on cheese production, particularly traditional cheeses protected by Geographic Indication (GI), i. e. by using the name of the place or region where the cheese was originally produced and reserving the use of the product name for cheese from that place. The legal term is Protected Designation of Origin, PDO. Only milk produced in defined production areas may be used to make these cheeses, following the product specifications. They represent 51% of all Italian milk (50% cow; 80% ewe's & goat; 78% buffalo) resulting from 32 000 dairy farms, with 1.74 million cows; 2.97 million sheep; 274 000 buffaloes; 3000 goats. Their value at origin amounts to 3.4 billion Euro (+ 9.7% in 2010) and 3.8 billion Euro at consumption. The total production of cheese is around 450 000 tons, obtained in 1700 dairy plants. Out of these, 125 000 tons are exported (+16% in 2010). Almost all PDO cheeses show an upward trend and producers are eager to exploit their increasingly positive market image. Italian cheeses were exported to countries where Italians and their descendants were strongly represented. In recent times they are exported where the Italian food style or more generally the Mediterranean diet has become fashionable. However it is crucial for the Italian dairy industry to maintain, develop and protect the system.

Geographical Indications identify a good as originating from a specific geographical region. The characteristic qualities and reputation of these products are essentially attributable to the geographical environment, including natural and human factors of that region. The GIs contribute to rural development by allowing producers to signal to the consumers the exact origin and thus the value and the quality of their products.

At present in Italy there are 42 dairy products protected by PDO: 40 cheeses, and 2 Ricotta (Romana, di Bufala Campana). There is also 1 PGI cheese (Canestrato di Moliterno)

The PDO cheeses are as follows:

- <u>28 Cow's milk</u> (Grana Padano, Parmigiano-Reggiano, Gorgonzola, Asiago, Piave, Taleggio, Provolone Valpadana, Montasio, Quartirolo Lombardo, Fontina, Valtellina Casera, Toma Piemontese, Stelvio, Raschera, Bra, Monte Veronese, Caciocavallo Silano, Casatella Trevigiana, Bitto*, Casciotta d'Urbino*, Castelmagno, Ragusano, Robiola di Roccaverano, Formai de Mut, Spressa delle Giudicarie, Provolone del Monaco, Murazzano*, Valle d'Aosta Fromadzo. (*mixture sheep&goat milk)
- 10 Ewe's milk (Pecorino Romano, Pecorino Toscano, Pecorino Sardo, Fiore Sardo, Canestrato Pugliese, Pecorino Siciliano, Pecorino di Filiano, Piacentinu Ennese, Vastedda Valle del Belice, Formaggio di Fossa di Sogliano)
- <u>1 Goat milk</u> (Formaggella del Luinese)
- 1 Buffalo milk (Mozzarella di Bufala Campana)

The production of traditional cheeses is typical of every Italian region and dates back to ancient times. Tradition is the dynamic dimension of origin. It is the whole of actions that were born in one region and that have been transmitted, improved and changed without any break by the

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continuous evolution of culture, human activity and environment. Traditions are not folklore and are developed and improved in order to know better the link between the origin and the product. The producers are specialists of the management of this link and they developed non-transferable localized knowledge. A similar product produced with the same skills in another area cannot be exactly the same. A product made in the same area without respecting the specific link is also not the same. In this framework new technologies or modern skills are permissible as long as the product is linked and submitted to its natural and pertinent environment. When the cheese is bought the consumer buys this specificity. The consumer has to be protected by the control of the link that means the geographical origin and the specific utilization of its characteristics. Someone who wishes to make the same cheese will have to get installed in the area. All these elements are useful to link origin and notions of intellectual property rights and consumer protection. However, the tradition has to be collective and shared by several actors with specific organizations.

In Italy the common body capable of defending the product's reputation and of maintaining its quality is the *Consorzio di tutela*. The *Consorzio* is the producer's group, a voluntary association of the producers representing at least ¾ of the total PDO quantity, which oversees legal protection, product specification and product advertising and promotion. It is approved by the Ministry of Agriculture. The certification system is managed by independent organizations responsible for auditing the adherence to the PDO's code of practices. The control organizations are accredited by the national body *Accredia*. The system is financed directly by the producers.

The present Italian collective management of Geographic Indications in cheese is the consequence of the International Convention on the Use of Appellations of Origin and Denominations of Cheeses signed in the Northern Italian town of Stresa on 1 June 1951. The signatory countries (Austria, Denmark, France, Italy, the Netherlands, Norway, Sweden and Switzerland) committed themselves to prohibiting the use of the false designations of origin on their territory and to take necessary measures to ensure the application of the Convention. Four geographical indications were considered to be "appellations d'origine" and therefore they were granted a higher level of protection: Gorgonzola, Parmigiano Reggiano, Pecorino Romano and Roquefort. A second group of cheeses, such as Camembert, Danablu, Edam, Emmental or Gruyère had a less extensive protection, since it was considered at the time that these names had become quasi generic and were being used outside their geographic region of origin. As a consequence of the Convention, in 1954 the protection of the geographical indications was enacted with Italian Law N.125/54, containing standards for the protection of designation of origin and typical names of Italian cheeses. That law has been implemented through specific administrative acts with respect to the various qualities and types of traditional cheeses. The first cheeses to be protected were Gorgonzola, Parmigiano Reggiano and Pecorino Romano, followed by Asiago, Fontina, Grana Padano, and Pecorino Siciliano. A subsequent ministerial decree regulated the activity of the Consorzi volontari (voluntary production consortia), foreseen by Law N.125/54 whose function and tasks are similar to those carried out by the consortia of protection of wines. New laws were introduced to adopt the EC legislation on PDOs and PGIs. The laws that preceded the EC legislation remained in force but only in so far as they were compatible with it. Article 53 of Law 128/99 implemented the aspects of EC Regulation 2081/92 that relate to inspection structures stipulating that these should be managed by an independent body. Article 14 of Law 526 of December 1999 redefined the role of the Consorzio di tutela (producer's groups).

Even if the Stresa Convention only attracted a limited number of countries the idea of protection of the use of appellations of origin and denominations of products was confirmed in 1958 by the Lisbon Agreement. Appellations of Origin are defined as: "...the geographical name of a country, region, or locality, which serves to designate a product originating therein, the quality and characteristics of which are due exclusively or essentially to the geographic environment, including natural and human factors".

In the European Community before 1992 there was no common approach on how to protect Geographical Indications. The protection of consumers from false and misleading information and the protection of producers from unfair competition were attained either through specific intellectual property rules or by general rules on unfair rules. The legal protection of GIs was

most fully developed in France, Italy, Spain and Portugal. Council Regulation 2081/92 on the protection of Geographical Indications and designations of origin for agricultural products and foodstuffs was the first legal instrument to cover all EU agricultural products. The present Regulation (EC) N.510/06 is the regulatory framework of PDO/PGI schemes. The success of the system is represented by the number of names which have been registered and by those under scrutiny from the EU member countries as well as from Third Countries. Café de Colombia was the first non EU Geographic Indication recognized in 2007. The Italian sheep's cheese Piacentinu Ennese, produced in Sicily was the 1000th name registered in February 2011 as PDO.

At present in the EU there are 1043 registered GIs; 199 are dairy products (Figure 1). The countries with a long experience of protection of designations of origin top the list. The northern European countries which traditionally have been protecting food products under trademark laws are far behind their southern neighbours and several of the new members still do not have PDO/PGI. However the number of registrations in the EU is increasing even if producers' groups complain about the length of procedures both at national level and at EU level. France remains the country with the highest number of dairy GIs and Italy is the major producer of them (for detailed production data see Table 1).

The on-going debate: generic vs. authentic

"Europe – as the principal beneficiary of 'strong GI's'—should renounce any claims to colonise the language of food and, in accordance with its Doha undertakings, should negotiate in good faith on the liberalization of agricultural market access" (Trademarks or Colonialism? The value of geographical indications Peter Gallagher – Inquit Pty Ltd June 2002).

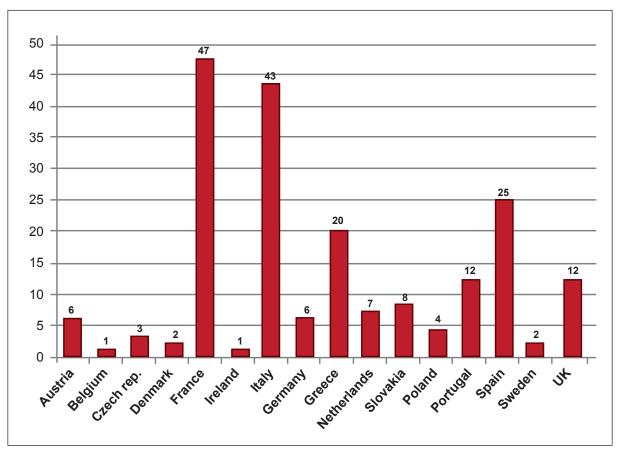


Figure 1. 199 Dairy GIs in the EU.

Table 1: Production volumes of the Italian PDO cheeses (Tons).

		2005	2006	2007	2008	2009	2010	± from 2009
Grana Padano	V	159.607	158.243	158.017	163.341	158.326	163.326	+3,16%
Parmigiano Reggiano	V	118.979	117.410	117.044	116.064	113.436	119.221	+5,10%
Gorgonzola	V	48.480	48.134	48.860	48.721	47.644	48.624	+2,06%
Provolone Valpadana	V	12.745	9.630	9.637	9.615	8.799	7.742	-12,01%
Asiago	V	23.621	23.330	22.649	23.318	23.528	22.669	-3,65%
Taleggio	V	9.196	8.766	8.814	8.800	8.497	8.699	+2,38%
Montasio	V	8.190	7.325	7.144	7.349	7.691	6.871	-10,66%
Fontina	V	3.606	3.735	3.556	3.747	3.527	3.588	+1,73%
Quartirolo Lombardo	V	3.428	3.654	3.747	3.693	3.704	3.805	+2,74%
Valtellina Casera	V	1.464	1.400	1.280	1.360	1.400	1.460	+4,29%
Toma Piemontese	V	1.234	1.116	1.128	1.078	1.067	1.422	+33,26%
Bra	V	1.028	816	758	762	731	783	+7,17%
Raschera	V	994	686	793	780	734	836	+13,91%
Caciocavallo Silano	٧	1.119	1.050	1.008	750	750	738	-1,60%
Monte Veronese	V	537	482	496	589	655	755	+15,27%
Casciotta d'Urbino (70% P)	М	240	250	245	229	220	235	+6,82%
Bitto (10% C)	М	332	310	275	290	264	237	-10,23%
Robiola di Roccaverano	М	76,4	104	78,5	84,2	88,3	109	+23,48%
Castelmagno	V	201	201	201	197	215	227	+5,58%
Murazzano (60% P)	М	26,0	24,6	22,9	21,5	15,8	16,0	+1,27%
Ragusano	V	169	155	137	131	165	160	-3,03%
Formai de Mut	V	60,9	58,6	67,1	71,0	72,0	74,5	+3,42%
Valle d'Aosta Fromadzo	V	4,0	6,0	5,1	4,2	4,6	6,0	+30,43%
Spressa delle Giudicarie	V	137	46,1	98,4	150	58,0	60,0	+3,45%
Castelmagno	М	201	201	201	197	215	227	+5,58%
Stelvio	V				1.112	1.186	1.152	-2,83%
Piave	V					1.183		-0,24%
Casatella Trevigiana	V					467	242	-48,18%
Provolone del Monaco	V					40,0	40,0	0,00%
Total		395.473	386.931	386.062	392.256	383.283	394.281	+3,50%
Mozzarella di bufala campana	В	29.645	33.805	35.640	31.960	33.900	36.900	+8,85%
Total		29.645	33.805	35.640	31.960	33.900	36.900	+8,85%
Pecorino Romano	Р	23.855	24.470	33.425	29.461	26.746	27.477	+2,73%
Pecorino Siciliano	Р	13,1	8,9	15,6	35,0	21,0	24,6	+17,14%
Pecorino Toscano	Р	1.869	1.965	1.943	2.816	2.933	3.092	+5,42%
Fiore Sardo	Р	466	620	600	650	(e) 712	800	+12,36%
Pecorino Sardo	Р	1.600	1.800	1.800	1.960	1.860	1.935	+4,03%
Canestrato Pugliese	Р	107	107	104	106	83,7	28,0	-66,56%
Pecorino di Filiano	Р				8,0	8,0	8,0	0,00%
Total		27.910	28.971	37.888	35.036	32.364	33.365	-0,81%

V: cow's milk; P: ewe's milk; B: buffalo's milk; M: mixed milk

Source: clal.it

Italy is among the principal advocates of greater protection for GIs in the EU and around the world. The discussions around the EU legal milk package and legal quality package show the importance of the quality schemes and of their improvement. Bilateral and multilateral negotiations are necessary to ensure higher protection for GIs around the world. Italian (as well as EU) Geographical Indications face usurpation and misuse in some Third Countries. This may result in problems concerning access to those markets, the cost of fighting against the appropriation or illegitimate use of the name by third parties, loss of potential market shares in those countries when the name is considered generic.

Moreover, it would mislead the consumer.

As globalization spreads, traditional dairy products face a risk of being made uniform to respond to growing competition in the market place. One visible effect is a threat to the diversity of local products. The trends promoted by competition and globalization are resulting in a multiplication of symbols to communicate features of products. The retail trade also adopts personalized source of origin marketing. This favours products where quality is clearly defined at the source and in terms of its specific process. The GIs scheme is used in that context as a marketing strategy. In Italy and elsewhere, GIs have proven to be the key economic engines for rural regions that might otherwise become marginalized in a global economy. A GI product with a high regional economic impact is a matter not just of local pride but also represents an investment for the local people that cannot be moved away to another country, unlike other forms of production.

The on-going debate between what is generic and what remains authentic is sterile and thus unnecessary. The fact that a product is manufactured outside the area of origin does not necessarily imply that the name has become generic. A name that has become generic means a name that has passed into common parlance and characterizes a category of identical products that do not necessarily originate in the region indicated by the name. Therefore the debate should be based on the nature of the schemes to protect product authenticity and therefore ensure producers and consumers on their rights and their responsibilities. The Italian experience with the perpetuation of traditional cheeses shows that this is possible and repeatable in other countries and in other regions of the world.

2. Global milk production

Torsten Hemme¹

1. Milk production and IFCN approach

The IFCN was established in the year 2000 to analyse milk production trends and their determining factors. The focus of IFCN is milk production as it is the key element in the whole dairy chain because it creates the major share of I) the costs, II) resources used, III) emissions created and IV) the political challenges in the dairy chain. Milk production development is quite diverse. In the time frame 2005 - 2010 the IFCN has observed growth rates which have ranged between 0.8 - 3.0% or 5 - 19 million tons of ECM (Energy Corrected Milk, standardised to 4% fat and 3.3% protein). Based on monthly data collection in 49 countries milk production in the first 6 months 2011 grew at a high rate of 3%.

2. Three phases of milk prices

The IFCN milk price indicator, based on SMP and butter prices, exceeded the long-term price range of 11-25 US-\$/100 kg milk in November 2006. In the following 38 months prices had been very volatile in a range from 19 to 58 US-\$/100 kg milk. Since November 2009 we have seen relatively stable prices at an average level of 44.7 US-\$ (+/- 8 US-\$).

With this shift in level in world milk prices and its volatility, all national milk prices are very strongly affected. In most cases the world milk price is the strongest factor for the local milk prices.

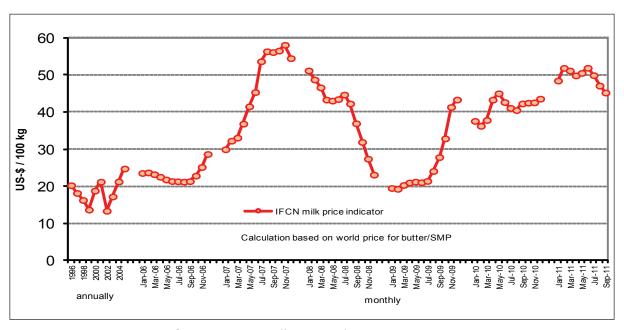


Figure 1. IFCN milk price indicator 1996-2011.

IFCN Dairy Research Center at University of Kiel, Germany.

3. Cost of milk production in 2010

Since 2000 the IFCN has annually been comparing typical farms around the world. In the 2011 farm comparison 157 typical farms from 60 dairy regions in 49 countries were analysed. For simplification, the farms analysed have been clustered into 8 different world regions. Figures 2 and 3 show the average values for all farms analysed within the region.

Two groups of regions can be distinguished based on the milk yield: high yield regions having about 8000 kg ECM per cow per year and more (Western Europe, North America and Middle East) and low yield regions with yields usually below 6000 kg ECM (Africa, CEEC (Central & Eastern European Countries), South America, Asia and Oceania).

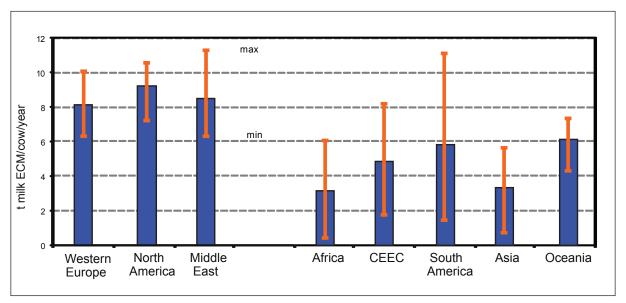


Figure 2. Milk yield in different world regions 2010.

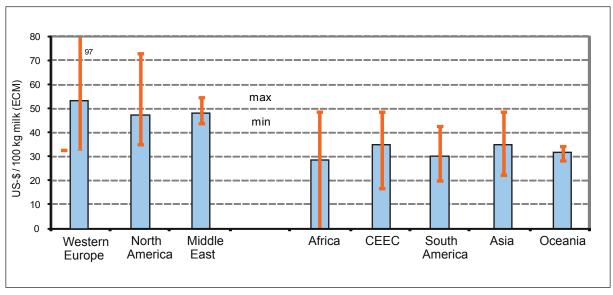


Figure 3. Cost of milk production in different world regions in 2010.

The cost indicator shown in figure 3 represents the concept of full economic costs. Technically it is defined as follows: costs from the profit and loss account of the dairy farm plus opportunity costs for own production factors (family labour, own land, own capital) minus the non-milk returns (returns from cull cows, calves or heifers, returns from manure and returns from coupled direct payments).

The results show a simplified global overview on milk production costs:

- Western Europe, North America and the Middle East had the highest costs.
- Costs in CEEC, South America, Asia and Oceania were on a similar level of 30 to 35 US-\$ per 100 kg milk.
- In Western Europe and North America there exist typical farms which are able to produce milk at cost of about 35 US-\$ per 100 kg milk ECM.
- Compared to the IFCN cost analysis for 2009 in all world regions costs increased greatly in 2010. Western Europe is an exception as costs decreased.
- There is an indication that on a global basis high yield or large farm size is not really a factor for low costs.
- Low costs are more a result of having the right farming system in terms of feeding system, technology, intensity and management skills.

4. Rising feed prices from 13 to 33 US-\$, an increase of 156%

Feed prices have increased from 13 US-\$/100 kg in 2005 to 23 in 2010 (77% increase). In 2011 prices even increased to 33 US-\$ (Ø Jan-Sep) or by 43% compared to 2010.

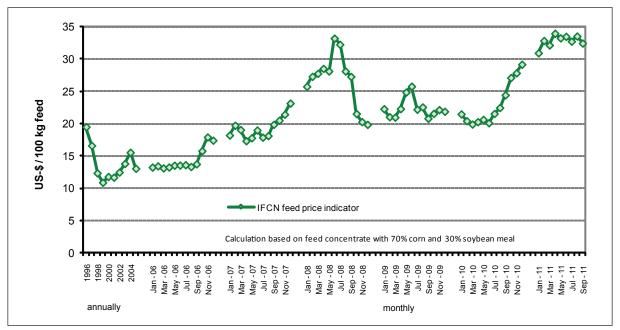


Figure 4. IFCN feed price indicator 1996-2011.

The IFCN has a method to estimate for all typical farms analysed the total feed costs which includes the costs of purchased feed, costs for home grown feed and all costs related with feed and manure handling.

Based on this analysis the average share of feed costs in total costs for all farms was 55% in 2010. The highest share was observed in the Middle East (74%) while the share in Western Europe was at a lower level of 46%.

For 2011 it is expected that the average share of feed costs on total costs will rise to a level of 65%. This means feed prices and feed management will be the most important drivers for competitive milk production.

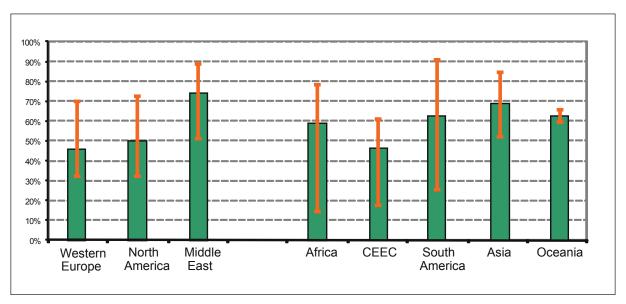


Figure 5. Share of feed cost on total cost.

5. World average dairy farm size is 3 cows

A farm structure analysis is relevant in order to understand possible developments and scenarios in specific dairy regions. It allows one to see the diversity in speed of structural change in countries. In the IFCN Dairy Report 2011 milk production profiles for 90 countries are shown, representing about 98% of milk production worldwide.

These 90 countries have an average herd size of only 3 cows per farm. This is mainly due to the fact that in developing and transition countries many small scale dairy farms with 1 to 2 cows exist. On the other hand only 11 of the 90 countries have an average farm size of more than 100 cows. The extremely high differences in farm structures can be shown via the example of comparing the farm structures of the USA with Pakistan. In the USA twice the amount of milk is produced compared to Pakistan, but this is produced in the USA from only less than 1% of the number of dairy farms Pakistan has.

This year, the IFCN has developed the "IFCN Standard size classes" in order to have comparable farm structure information between countries. In this analysis data from 78 countries are included, representing 95 % of cow and buffalo milk production, and harmonised into seven "IFCN Standard size classes".

The results allow clustering the farms into three categories:

Farm size 1 - 10 cows: 78% of all farms and 56% of the cows are in this category. A large part of the milk produced in these farms is consumed by the family, whereas the rest of the milk is sold locally and often to an informal market. Milk selling provides the daily cash for family subsistence. These dairy farms can be described as "household farms".

Farm size > 10 - 100 cows: 22% of all farms and 28% of the cows are in this category. Most of these farms can be described as "family farms" as most of the work is done by family members. The economic aim of these farms is to generate a sufficient income for the family members.

Farm size more than 100 cows: Only 0.3% of the dairy farms having 16% of the cows are in this size category. These farms can be described as "business farms" as most of the work is done by employees. The main aim of these enterprises is to generate the expected return on investment.

6. IFCN Top 21 milk processors

A view on the ranking of the top 21 processors shows the concentration of milk processing worldwide.

- The top 21 dairy processors source 24% of world milk production which is 39% of all milk delivered to processors worldwide.
- No. 1 milk processor in the world is Fonterra which processes 3% of world milk.
- Compared to the IFCN ranking of 2009 there was no mayor change in the ranks 1 to 10.
- Via mergers Nordmilch & Humana as well as Sodial & Entremont alliance have improved their rank position.
- In Asia the companies Mengniu, Yili and Amul gained position via strong growth in milk intake.
- Some milk processors in the USA showed stable milk intake and lost positions in this ranking.

Table 1: IFCN top 21 milk processors list 2011 (measured by milk intake).

Rank	Company name	Country	Dairy processing plants main location	Milk intake in mill. t	Market share in % of world milk production
1	Fonterra	New Zealand	International	20,5	3,0%
2	Dairy Farmers of America	USA	USA	17,1	2,5%
3	Nestle	Switzerland	International	14,9	2,2%
4	Dean Foods	USA	USA	11,8	1,7%
5	Royal Friesland Campina	The Netherlands	The Netherlands	10,3	1,5%
6	Lactalis	France	International	10,2	1,5%
7	Arla Foods	Denmark/Sweden	Denmark/Sweden	8,7	1,3%
8	Danone	France	International	8,0	1,2%
9	California Dairies Inc.	USA	USA	7,7	1,1%
10	Kraft Foods	USA	International	7,5	1,1%
11	Nordmilch & Humana (DMK)	Germany	Germany	6,7	1,0%
12	Saputo	Canada/USA	Canada/USA	6,2	0,9%
13	Land O' Lakes Inc.	USA	USA	5,8	0,9%
14	Sodiaal & Entremont alliance	France	France	4,2	0,6%
15	Mengniu group	China	China	3,8	0,6%
16	Parmalat	Italy	International	3,7	0,6%
17	Yili group	China	China	3,7	0,5%
18	Amul	India	India	3,4	0,5%
19	Northwest Dairy Association	USA	USA	3,3	0,5%
20	Schreiber Foods Inc.	USA	USA	3,3	0,5%
21	Murray Goulbum	Australia	Australia	3,2	0,5%
	Sum top 21	163,9	24,0%		

Source: IFCN analysis is based on the IFCN Dairy Report 2010 and additional analyses and estimates. Data represents in most cases the year 2009 or 2010. **Explanation**: Milk intake represents milk volume collected, commodity purchase (in milk equivalents) and subsidiaries in other countries. Milk intake figures in mill. tons. In some cases recalculated from liter (1liter = 1.033 kg). **Comments**: Amul (India): milk with high fat content. Nordmilch and Humana merged in 2010 and created new company Deutsches Milchkontor (DMK). Sodiaal and Entremont alliance merged in 2011. Fonterra and Nestle incl. 50% of milk intake of Dairy Partners America (DPA) each. In some cases: double-counting of millk intake possible (companies purchase milk / dairy ingredients from each other).

7. Several dairy regions will come under pressure

In 2011 IFCN has analysed the change of milk production within the countries and their regions. The result was that the change of milk production per year can easily reach 5% and in some cases goes beyond this. This means that within a time frame of 5 years some regions may have 30% more milk whereas other regions may have 30% less milk production. Especially in Europe it can be expected that this speed of change will be even higher in some regions within the coming years.

This fact will be a challenge for milk processors as they have to adjust milk processing capacities in two directions depending on whether they are in growing or declining dairy region. For farm input suppliers, especially feed companies, this will also be the case.

The IFCN analysis 2011 has identified the following criteria for countries, regions or farming systems which will come under pressure at the milk and feed price levels found in August 2011.

The following criteria will increase the pressure:

- a) land prices rise fast or milk production is located in regions which are very favourable for cash crops
- b) economic prosperity is strong this leads to strongly increasing wages and currency appreciation
- c) dairy farms having only a little or no land base to produce their own feed
- d) milk supply in the region is ahead of a shift from either 1) household farms to family farms or 2) from family farms to business farms.

For all stakeholders in the dairy chain this offers two basic options for reaction:

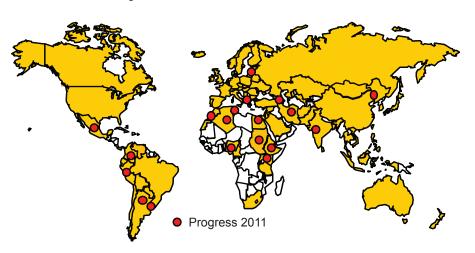
- relocate farms and plants to more competitive dairy regions
- bring all stakeholders together and develop future dairy farming systems which are competitive.

8. Status of the IFCN Network in 2011

Since the year 2000 the IFCN developed out of a PhD thesis towards a global leading organisation in milk production research.

The network consists of researchers in over 90 countries, over 85 dairy related companies and over 18 researchers at the IFCN Dairy Research Center in Kiel.

Research partners from 90 countries







IFCN Institutional developments in 2011

To better guide the future developments in the IFCN in 2011 a board has been established. Six representatives cover the interests of all involved parties of the network.

The members of the IFCN board



Anders Fagerberg Chairman of the IFCN board



Ernesto Reyes Research view elected by researchers



Morelon
Business view elected by companies



Uwe Latacz-Lohmann Academic perspective University Kiel



Olaf Rosenbaum Tax & legal perspective



Torsten Hemme Managing Director IFCN

World dairy companies: restructuring & investments

B. Rouyer¹

1. The dairy leaders in 2010

In 2010, there were 24 groups generating dairy sales exceeding 3 billion USD (see Figure 1). Those 24 groups came from 14 countries located on 4 continents. This geographical breakdown highlights a very significant change that occurred in the dairy sector over the last few years. The dairy leaders' ranking presents currently a wider geographical diversity than before.

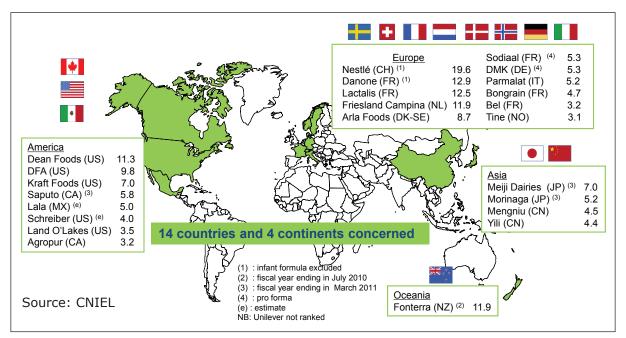


Figure 1. Dairy leaders in 2010 (dairy turnover exceeding 3 billion USD).

2. Reorganization since 1996

Even with a larger number of companies taken into account, the top 40 dairy leaders' ranking established in 2006 did not present such geographical diversity (see Figure 2). Those 40 dairy leaders came from 14 different countries, but only 3 outside Europe. In America all companies ranked in this top 40 exclusively came from the US. No world leaders had yet emerged from Canada and Mexico. The same goes for Asia, all companies belonging to this ranking came exclusively from Japan. No world leaders had yet appeared from China. Actually the majority of the top 40 world leaders were located in Europe, with 27 groups from 11 different countries.

Since 1996 broad reorganisation occurred in many western countries. This is the case in the US, where Mid-America Dairymen and Associated Milk Producers merged in 1997 with two other coops, giving rise to Dairy Farmers of America. Still in the US, Dean Foods also achieved strong

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growth when it merged with Suiza Foods in 2001 and became the main national dairy processor in terms of turnover.

In New Zealand massive reorganization also occurred in 2002. Fonterra was born as a result of the merger between New Zealand Dairy Board and the two major national dairy coops, that is to say Kiwi Dairies and New Zealand Dairy Group.

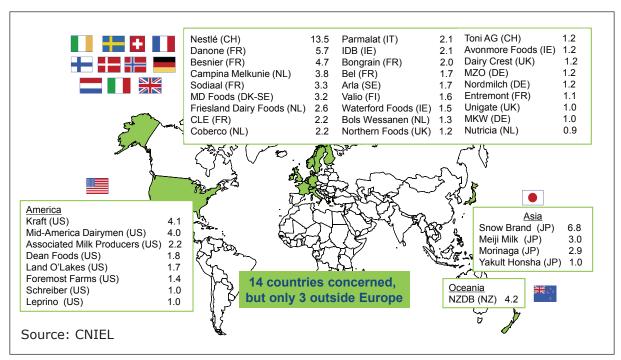


Figure 2. Top 40 dairy leaders in 1996 (dairy turnover in billion USD).

Meanwhile many changes also happened in Europe. The dairy assets of the 27 European leaders identified in 1996 in the top 40 ranking are now integrated in only 15 different companies (see Figure 3). With a few exceptions such as Nestlé, Irish Dairy Board or Valio, those leaders either bought a company belonging to this world top 40 or they were bought by another company belonging to this ranking.

That is the case of the French group Danone, which bought Dutch Nutricia in 2007.

This is also the case of French Besnier, which changed its name to Lactalis in May 1999, and bought Italian Parmalat recently, in 2011.

The Dutch giant Friesland Campina today brings together 4 companies which were part of the world top 40 in 1996. This consolidation took place through different stages. First of all Dutch Campina-Melkunie and German Milchwerke Köln Wuppertal joined their activities in 1997. At the same moment Friesland Dairy Foods and Coberco merged with two other smaller Dutch coops, giving rise to a new group called Friesland Foods. And this Friesland Foods actually merged with Campina three years ago, in 2008, resulting in Friesland Campina.

Sodiaal, the main French dairy coop, bought the cheese maker Entremont in 2010.

Danish MD Foods and Swedish Arla merged in 2000, creating a new group called Arla Foods. Three years later, Arla Foods bought the former dairy assets of the British group Northern Foods. Those assets were pooled in a company called Express Dairies, which was spun off by Northern Foods in 1998.

French CLE (Compagnie Laitière Européenne) was bigger than the French group Bongrain in 1996, but the latter was already a shareholder of CLE. Bongrain actually consolidated CLE in its accounts in 1999.

Fromageries Bel bought the main European dairy assets of Bols Wessanen, that is to say the Dutch Leerdammer cheese company in 2002. On the other hand, the American dairy assets of Bols Wessanen are now part of the American group HP Hood. It bought those assets in 2004 from National Dairy Holding, which had acquired them three years earlier (in 2001).

The two Irish coops Waterford Foods and Avonmore Foods merged in 1997 giving rise to Glanbia

The Swiss group Toni had an eventful development during the last 15 years. Toni merged in 1999 with another Swiss company called Säntis. They created a new group called Swiss Dairy Food group, which collapsed three years later in 2002. The dairy assets of Swiss Dairy Foods were sold to several companies, but mainly to Emmi and Cremo.

British Dairy Crest bought the main dairy assets of Unigate in 2000. At the same moment Unigate changed its name to Uniq and almost left the dairy industry completely.

German MZO and Nordmilch are two of the 4 German coops which merged in 1999, giving rise to a new group called Nordmilch. This new Nordmilch merged recently in 2010 with another coop called Humana and changed its name to Deutsches Milch Kontor.

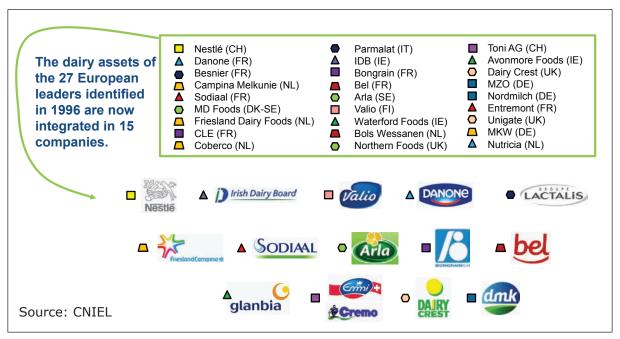


Figure 3. Vast reorganization has occurred in Europe since 1996.

3. Emergence of dairy leaders in Asia

Parallel to this broad reorganization in Europe, important changes took place in Asia. Dynamic demand stimulated the emergence of national dairy leaders, which achieved such growth that they now belong to world dairy leaders. This is the case of Chinese Yili, which multiplied its turnover by 6 within 7 years. This is also the case of Chinese Mengniu, which multiplied its turnover by 9 during the same period (see Figure 4).

Likewise in India Gujarat Cooperative Milk Marketing Federation, which is better known through its main brand Amul, accelerated its growth during the last decade. Its turnover was multiplied by 3 within 6 years (from 0.7 billion USD in 2005 to 2.1 billion USD in 2011), while its growth was previously rather small.

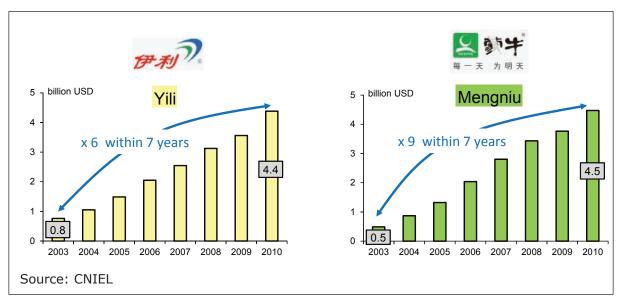


Figure 4. Yili and Mengniu turnover development.

4. Significant growth achieved by western groups

Outside Asia, some dairy groups have also achieved strong growth. This is the case of Canadian Agropur. Its turnover has tripled within 10 years (see Figure 5). This spectacular growth is linked to growing internationalisation of its activities. Since 2002 Agropur has bought several companies in the US which now contribute to more than a quarter of its global turnover.

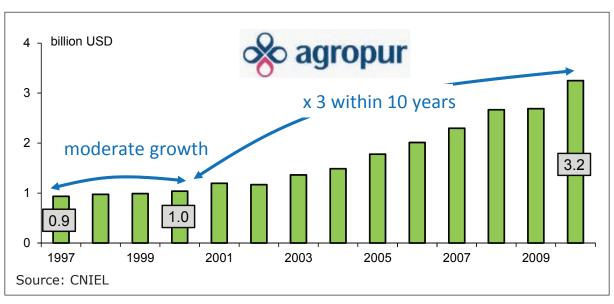


Figure 5. Agropur turnover development.

A similar development occurred in Canadian Saputo, which was a regional company until the mid-90s. Saputo increased its turnover more than tenfold within 15 years. At present Saputo is not only the main dairy processor in Canada, but also a group with many factories abroad, mainly in the US, but also in Argentina and in Europe. Saputo expansion is clearly due to a growing development of its international activities. As an example, its dairy turnover in the US increased from 300 million to more than 2 billion USD within 12 years (see Figure 6).

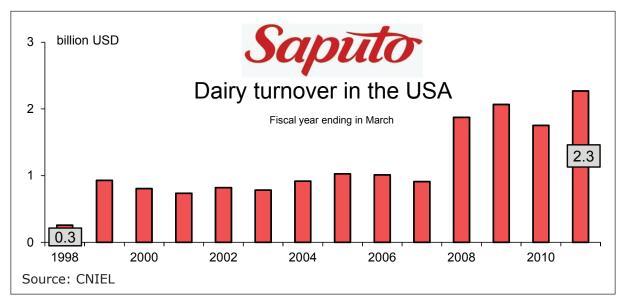


Figure 6. Saputo expansion in the USA.

French Lactalis has also sped up its growth during the last decade. Its turnover was multiplied by 4 within 10 years. Like Saputo, this expansion is the result of a growing internationalisation of its activities. Lactalis is generating around 70% of its turnover outside France in 2011, as compared to only 32% in 1993 (see Figure 7).

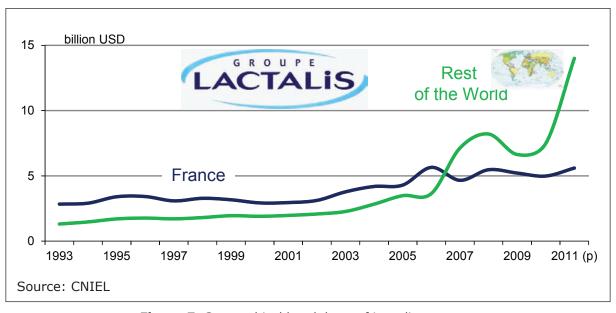


Figure 7. Geographical breakdown of Lactalis turnover.

5. Internationalisation: a common concern

However, industrial internationalisation is no longer a prerogative of western groups alone. As an example, in 2009 Lala (Mexico) became the number two in the liquid milk market in the US. In one single year Lala bought 20 factories, including 18 from National Dairy.

Internationalisation is also a concern for Asian dairy leaders (see Figure 8). In 2010 Chinese Bright Dairy took control of New Zealander Synlait. Also in 2010 Vietnamese Vinamilk established itself in New Zealand, taking over a share in the capital of Miraka, a new dairy operator.



Figure 8. The expansion of Asian dairy groups in New Zealand.

Environment

1. Towards a partnership on benchmarking and monitoring the environmental performance of livestock food chains

Michael MacLeod¹, Pierre Gerber¹

Abstract

The livestock sector is under pressure to improve its environmental performance, while at the same time meet increasing demand for its products. In support of this, FAO has been seeking to set up a global Partnership with the aim of improving the environmental performance of livestock supply chains. The involvement of stakeholders from different sectors is a key feature, and the Partnership will be open to members from the private sector, NGOs, governments, international organizations and technical experts. The Partnership will seek to improve the evidence base for decision-making by pursuing the following activities:

- 1. Developing sector-specific guidelines for the assessment of greenhouse gas (GHG) emissions along the main livestock supply chains.
- 2. Developing analytical tools for the assessment of GHG emissions associated with the production of major feed ingredients.
- 3. Developing indicators of the wider environmental performance of livestock supply chains.
- 4. Providing transparent and balanced communication of the Partnership's findings.

Background

Livestock is a major contributor to food security and provides livelihoods to a large part of the world's poor. But at the same time, the livestock sector places pressure on many ecosystems and contributes to global environmental impacts. The natural resource base within which livestock production must be accommodated is finite, so the continuing expansion of the sector will need be accompanied by substantial efficiency gains.

The need to improve performance is increasingly recognized among producers, civil society and governments, and initiatives have been put in place to improve the efficiency of natural resource use. The lack of broadly recognized frameworks for monitoring and predicting environmental performance is however a bottleneck to effective action. While there are many good quality studies, issues remain, such as:

- Are the methods used comparable and accepted across stakeholder groups?
- How long are the results valid for? Are they replicable?
- Is the work adding-value and moving the debate forward?

Why adopt a partnership approach?

In response to calls from the private sector, FAO decided to explore the potential of a partnership approach to addressing these issues. Initial consultations with stakeholders (in October 2010 and March 2011) confirmed that there was demand for a partnership focusing on benchmarking

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and monitoring the environmental performance of the livestock sector. Key potential strengths of the approach were considered to be:

- Avoiding short-termism improvement in environmental performance requires mediumlong-term strategy (in addition to short-term responses).
- Improving the consistency of approach, and the comparability of results, both between sectors and over time.
- Improving co-ordination and cost-effectiveness, by combining resources and avoiding duplication of effort.
- Providing a more balanced and objective multistakeholder perspective.

Key features

The key features of the Partnership were developed with stakeholders over summer 2011, and are summarized below.

Feature	Summary	
Impact	Improved environmental performance of the livestock sector, while considering economic and social viability.	
Approach	Common approaches to the analysis and communication of environmental performance.	
Outputs	Methods.Data.Analysis and interpretation.Communication.	
Management and implementation	• FAC) reconical facility coordinating input from Partners and experts	

The Partnership will be established for an initial phase of three years, with an expected start in spring 2012. The initial 3 year work programme will be composed of four multilateral components, (described briefly below). There will be scope to undertake additional bilateral projects within this period, which could, for example, address more specific issues such as the GHG emissions associated with processed feed ingredients.

<u>Component 1: Sector-specific guidelines and methods for the Life Cycle Assessment of GHG</u> emissions from livestock food chains.

The overall aim of component 1 is to produce methodologies and sector specific guidelines for the life cycle assessment of greenhouse gas emissions from animal supply chains. These will aim for consistency with existing standards, e.g. ISO, PAS2050, the GHG Protocol Supply Chain Initiative, and build on relevant existing guidelines, e.g. the International Dairy Federation, Agribalyse and CFPan. Methods and guidelines will focus on key issues, such as: emissions allocation; uncertainty; land use change and soil carbon sequestration.

Component 2: Global database of GHG emissions related to feed crops.

Component 2 will develop global sets of GHG Life Cycle Inventory (LCI) data for all major feed crop materials. This activity is of relevance to all livestock sectors. It will lead to a global database on greenhouse gas emissions associated with the production of plant-based feed materials. A thorough review of the existing state of knowledge regarding feed-related emission will be undertaken at the outset of the project and potential synergies with related projects will be

identified and exploited. The work will complement related work being undertaken in the Netherlands (Carbon Foot Printing of Animal Nutrition – CFPAN project), France (Agribalyse) and elsewhere.

Component 3: Measures of non-GHG environmental performance of livestock food chains.

This component will develop indicators and methods that can be used to measure the wider environmental performance of livestock on a global scale, specifically: (i) water consumption and scarcity, (ii) perturbation of the nutrient cycles (with emphasis on the impacts on water quality) and (iii) biodiversity. The work will build on the findings of previous work at FAO and other relevant initiatives such as the UNEP/SETAC Life-Cycle Initiative and the Water Footprint Network. Many of the approaches to assessing the wider impacts are not readily applicable on a global scale. This activity will produce measures that can be applied at a global scale, and are based on a consistent set of explicit assumptions.

Component 4: Communication strategy.

The Partnership deals with issues that are complex, and potentially controversial. Its work could be easily misinterpreted, or deliberately misrepresented. It is therefore important that the Partnership communicates its work in a way that minimizes these risks. Component 4 will devise a communication strategy which focuses on measuring progress and identifying options for improvement. It will also seek to explain the work of the Partnership in ways that are transparent and promote scrutiny and discussion.

Concluding remarks

The response to the Partnership has been positive and it is anticipated that it will start in the Spring of 2012. The Partnership is not an easy option: it will not provide quick fixes, and it will be a new way of working for many of the partners. However, FAO is committed to improving the evidence base over time and believes that longer term, collaborative approaches are required given the complexity and urgency of the issues faced.

Food Safety

1. The Biology of Antimicrobial Resistance - Where Does It Come From and How Does It Spread?

Glenn F. Browning¹

The focus of this paper is the science, rather than the politics, of antimicrobial resistance, but both are critical in developing an appropriate approach to the issue. All consideration of controls to reduce the development and spread of antimicrobial resistance needs to be based on the fact that ongoing, but prudent, use of antimicrobials is a cornerstone of modern animal heath and welfare that can and should be preserved.

This paper considers why antimicrobial resistance should be seen as a critical issue in veterinary medicine, how bacteria resist the effects of antimicrobial drugs, where the resistance genes they use to achieve this come from, how these genes can spread between bacteria, what multiple resistance is and how it arises, and finally what the critical control points might be for controlling this problem. The key considerations are that the occurrence of resistance cannot be prevented, but that it is possible, and necessary, to aim towards limiting the development of multiple resistance and its spread.

The Tragedy of the Commons?

Antimicrobial resistance has been described as a typical case of "The Tragedy of the Commons" - classical overutilization of a public resource from which everyone wants to gain as much advantage as possible while they can, but for which no one accepts responsibility for maintenance [1]. The pessimistic view that this is inevitable is not necessarily correct, but it is essential to ensure that all the users of this "commons" appreciate how to use it sustainably.

As this view suggests, the central consideration in antimicrobial resistance is that we are utilizing a common resource, so it is inappropriate to focus on any one animal production system, but rather on antimicrobial usage and resistance as a shared issue in animal and human health.

Any consideration of the "tragedy of the commons", requires an understanding of what the "commons" look like. Many publications provide a list of the different classes of antimicrobial drugs that are currently registered for use in animals and humans and the date that each class was first registered for use. This presents a depressing picture of a past golden age of antimicrobial drug discovery that all but ended in the early 1960s. Since 1962 only two entirely novel classes of antimicrobial drugs, the oxazolidinones and daptomycin, have been commercialized, and at present it seems unlikely that these would make their way on to the animal health market. Both have quite restricted use even in human medical treatment [2].

However, is the picture quite this bleak? There are at least forty antimicrobial compounds currently in active development [2]. Of these, one that is in phase III evaluation (fidaxomicin) belongs to a novel class, and a further five in phase II trials and six in phase I trials are in novel classes, while the remaining 28 are variants of known classes of antimicrobial drug.

The development of novel classes of antimicrobial drugs is crucial because, in many cases, if resistance develops to one drug in a class, the bacterium is resistant to most or all other drugs in that class. Thus, each novel class of antimicrobial is an alternative option for therapy once resistance develops.

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While the potential future availability of a number of new classes of antimicrobial drug suggests the future might not be quite as bleak as some have suggested, it cannot be assumed that availability of new drugs will solve the problem. It is increasingly unlikely that new classes of antimicrobials will be introduced into veterinary medicine, and many of these "new" agents were first identified many years ago and do not, in fact, represent a new golden age of discovery.

There is a common perception, particularly among in the medical community, as well as among much of the public, that agricultural usage of antimicrobials is responsible for most of our problems with antimicrobial resistance in medically important pathogens. While veterinary and agricultural usage does bear the blame in some cases, the majority of these problems have probably been generated by poorly controlled medical usage. There remain very few cases where veterinary treatment is becoming limited by multiple resistance in significant pathogens, unlike in human medicine. The reason for this is not likely to be that those of us involved animal health have been particularly virtuous in our antimicrobial usage, but rather because we do not tend to use large quantities of multiple antibiotics on the same population at the same time - a situation that is common in large tertiary care medical centres.

However, deciding who bears the blame is something that should only be addressed after considering the factors that have contributed to the problem. Furthermore, attributing blame is often extremely difficult, as the development of multiple resistance is complex and conclusions are often reached on quite tenuous data.

Ultimately this is a problem with multifactorial origins and any solutions will need to be similarly complex and will require an integrated approach by all the users of antimicrobial agents.

What Is Antimicrobial Resistance?

Antimicrobial resistance is generally defined as reduced susceptibility to therapeutic drugs at concentrations achievable during treatment. It can be an innate property of all members of a particular bacterial species or can be a property acquired by only some strains. Acquired resistance may or may not be transferable to other bacteria.

The problem that is of major concern and which needs to be controlled is acquired resistance, particularly when it is transferable. Furthermore, while there is a tendency to focus most attention on resistance against drugs, resistance can also be acquired against disinfectants and metals.

Intrinsic or innate resistance occurs in bacteria that lack a target for, or are impermeable to, some antimicrobial drugs and that will therefore always be resistant to these drugs [3]. Acquired resistance occurs when normally susceptible bacteria become resistant to a specific drug. Transferability is the capacity of some resistance genes to readily spread from one bacterium to another. Other resistance genes cannot spread and thus are not infectious.

Multiple resistance occurs when genes are accumulated by some bacteria, generating organisms that are resistant to a multiplicity of drugs, and this is the major problem that we need to address. This multiple resistance can include resistance to disinfectants and heavy metals.

Consequences of Multiple Resistance

Multiple resistance has resulted in reduced efficacy of antimicrobials across a range of pathogens and increasingly limits options for veterinary and medical treatment. It causes food safety and environmental concerns and can result in concerns about the consequences of animal ownership, and about occupational health and safety in farm workers and farming families.

Unfortunately, like climate change, if we wait and debate until we have the ultimate proof that a particular practice is to blame for a particular antimicrobial resistance problem, it will be too late to bother acting. Thus, we need to extrapolate from what we now know if we are to ensure the continued utility of the "commons" we are sharing.

It is useful to consider this problem as a series of critical points that may or may not be

controllable: the origins of resistance genes; their spread; the development of multiple resistance; the spread of resistant bacteria and their selection; the reservoirs of resistant bacteria in animals and in the environment; and, finally, those factors that lead to infection of animals and humans with resistant bacteria.

Mechanisms Involved In Antimicrobial Resistance

Although there are hundreds of different specific mechanisms involved in antimicrobial resistance, they can be broadly defined them into five different categories - changes in the target of the drug that stop it being able to perform its usual function, enzymes that modify or destroy the drug so that it can no longer function, efflux pumps that remove the drug from the bacterial cell before it can act, and overproduction of the target of the drug, so that higher concentrations of it will be required to have an effect.

Origins of Resistance Genes

Resistance can result from and does arise from random mutations in chromosomal genes that result in decreased susceptibility. These genes are less commonly transferable to other bacteria. Alternatively, resistance can arise from acquisition of genes from other organisms, raising the question of the original source of these transferable genes. They could come from: the organisms used to produce antibiotics; from the usually harmless commensal bacteria living on the surfaces of the bodies of animals; from other pathogenic bacteria in animals; or from environmental organisms.

As the micro-organisms used to produce antibiotics need some protection from the toxic products they produce, it has been suggested that this may be a source of the resistance genes that have been transferred to pathogens. If this were the case, there is the risk that crude antibiotic preparations might be the original source of acquired resistance [4]. The other most likely source is that they come from environmental organisms, as these organisms may need to compete with antibiotic producers in the complex microbial communities found in soil.

Investigation of this issue has suggested that the ultimate origin of many of the transferable resistance genes found in pathogenic bacteria has probably been environmental bacteria [5], and that antibiotic producing micro-organisms used in manufacturing have not been the source. In fact, recent studies have detected resistance genes in 30 000 year old soil samples, long before industrial production of antimicrobial drugs [6].

There are very large reservoirs of different resistance genes in environmental bacteria and some environmental bacteria can even live off antibiotics as a source of nutrition [7]. It likely that the primary function of many of these genes may not be to deal with the antibiotics we use therapeutically, but rather to deal with other toxins in the environment.

These recent studies suggest we are not likely to be able to control the source of antimicrobial resistance genes. However, once these genes have been acquired by a commensal or pathogen they are then further transferable.

Spread of Resistance Genes

Many resistance genes are carried on mobile or mobilizable DNA elements, called plasmids, transposons and integrons [3]. These mobile elements can shift in and out of bacterial chromosomes and from bacterium to bacterium, thus effectively ensuring that resistance is infectious. Even resistance genes that are not on transferable elements can be transferred by: transformation, a mechanism used by some bacteria to import DNA from dead bacterial cells; transduction, which is achieved by bacterial viruses; or conjugation, which is essentially sexual transfer, from one bacterium to another. While all of these mechanisms can contribute to the infectious spread of resistance genes, conjugation is particularly efficient, and many resistance genes are carried on conjugative plasmids that can ensure their own transfer to other bacteria.

Transfer most commonly occurs between close relatives, but can also occur between quite distantly related species, and can be promoted by exposure to some antimicrobial drugs. The prevalence and efficiency of transfer is such that this again is an aspect of development of resistance that we are unable to control readily.

Development of Multiple Resistance

Multiple resistance results from the accumulation of resistance genes in the one bacterium, and often because the resistance genes are accumulated in the one transferable element. The mobile elements carrying resistance genes can be accumulated by bacterial cells, resulting in clusters of resistance genes, as well as other genes beneficial to the bacterium, on the chromosome, in plasmids and in integrons. Integrons, in particular, seem to be able to capture multiple resistance genes at the same site on a bacterial chromosome [8]. Once these clusters have developed, they then tend to be transferred as a block. The development of these clusters of resistance genes is likely to be promoted by environments where multiple antimicrobials are used simultaneously or in close succession, as this will provide a selective environment that is quite specific for multiple-resistant bacteria. These environments could be within the bodies of animals, in waste, or in soil and water.

Dissemination of Multiple Resistance

While it is possible for resistance genes to be dispersed as naked DNA, typically they will travel within the more protected environment of bacterial cells, so the factors that we usually think of as associated with spread of infectious disease are also involved in dispersal of multiple resistance. These include physical forces, such as wind and water, particularly for environmental bacteria, movement of contaminated soil, food and water, of animals, and, particularly, movement of people. Multiply resistant human pathogens have had by far the most rapid and the greatest dispersal around the globe, because humans are the most mobile element in our environment.

Effect of Ongoing Exposure to Antimicrobial Drugs

Once resistance has been acquired, continued antimicrobial exposure provides a selective advantage to resistant bacteria, allowing them to increase in number by limiting growth of susceptible competitors. In addition, continued antimicrobial exposure can concurrently enhance resistance gene transfer to non-resistant strains of bacteria.

Multi-resistant strains can be selected by any one of the antimicrobials they are resistant to, enhancing the likelihood of their dominance. Co-selection of multiple resistance gene cassettes can also enhance their spread.

A further point that is often overlooked is the duration of the effect of a single period of antimicrobial use on a bacterial population - resistant strains are likely to dominate in the intestine of animals for many weeks after treatment has stopped, and in a large population of animals treated simultaneously, this effect is likely to be even more prolonged, potentially lasting months [9, 10].

Reconstructing the History of Development of Antimicrobial Resistance

The development of multiple resistance in a single pathogenic bacterium can have a very complex history, with multiple mechanisms responsible for introducing resistance genes into a single bacterium and for aggregation of collections of resistance genes within a pathogen: transduction by a phage; transformation of naked DNA from a dead bacterial cell; introduction of these genes into a conjugative plasmid, then efficient transfer to other strains; transposition to other plasmids or the chromosome; fusion of plasmids, aggregating large numbers of genes; then dissemination of large multiple resistance plasmids through conjugation and co-selection into multiple strains or bacterial species. Reconstructing this complex history once we have the final result is very difficult. We may have glimpses of part of the history written in genetic signatures

in multiple resistance plasmids, but we should be careful of attempts to interpolate the full history from knowledge of just a few stops along the way. Furthermore, when we are interpreting the history we are biased by the relatively large amount of information we have on pathogens and the relatively small amount of information we have on the much more numerous commensal and environmental bacteria.

Reservoirs of Multiple-Resistant Bacteria

Reservoirs of multiple-resistant organisms can be environmental or commensal bacteria or pathogens, and they may reside in wildlife and feral animals, in other species in mixed farming systems, or in humans. One particularly important point to note is that carriage of most resistance genes does not diminish fitness sufficiently for rapid selection against resistance – once they have been acquired they tend not to be lost for a long time [11].

Key Points to Consider in Controlling Antimicrobial Resistance

Resistance existed well before the use of antimicrobials, so we cannot stop it arising. However, we can probably limit the aggregation of resistance genes and the dissemination of these clusters of genes. Judicious limitation of antimicrobial use now is likely to delay, and possibly prevent, imposition of future limitations, which are likely to be both legislative and biological. Even if a particular animal production system was not responsible for the original multi-resistant organism, antimicrobial use will influence the likelihood that it will cause that system a problem, so there is a strong element of self interest in judicious use of antimicrobials. However, judicious antimicrobial use requires an emphasis on the longer term consequences rather than the apparent short term (and often illusory) benefits of inappropriate use.

All attempts at control of use need to recognize that there are a large number of selective environments that could be contributing to the development of multiple resistance, possibly in concert [3]. These include: animal agriculture, products and by-products; medical hospitals and patients in the community, veterinary hospitals and patients in the community; plant agriculture and products; aquaculture; waste water treatment plants; biocides in households; and pharmaceutical manufacturing wastes. Furthermore, multi-resistant organisms may have arisen by passing backwards and forwards between several of these environments.

Pharmaceutical wastes warrant particular comment. Near Hyderabad, in India, where there is considerable concentration of antimicrobial manufacturing, surrounding lakes and groundwater have been found to be heavily contaminated with a variety of antimicrobials, in some cases at concentrations at least as great as those seen in the plasma of animals under treatment [12].

In each of these environments the development of multi-resistant bacteria will be influenced by contamination of food or water with active drug residues, resistant bacteria and resistance genes, as well as other selective agents such as metals and biocides.

Options for Control of Antimicrobial Resistance

Any control of antimicrobial resistance will clearly need to be multifactorial, as there is unlikely to be a single critical control point. To control dissemination of multiply resistant clones of bacteria, the only option is the biosecurity measures we currently recognize as having value in control of infectious disease. To reduce selection and co-selection of resistance genes, we need to consider limiting our antimicrobial usage. To limit transfer of multiple resistance across both bacterial and animal species, both biosecurity and antimicrobial usage controls are likely to be important, and to reduce the significance of reservoirs in the environment and other animals, again both biosecurity and antimicrobial usage control will play a role.

To a large extent the appropriate approach to take in controlling antimicrobial use has not changed for many years. The key principles are to: use them only when they will make a difference; use the most appropriate antimicrobial for the case, which includes using the antimicrobial most closely targeted to the pathogen we need to treat; and use the drug at the right dose and only

for as long as necessary. The should be a strong element of self-interest in adopting these principles, as using an antimicrobial to which a pathogen is resistant could exacerbate disease.

Our collective responsibility for, and global consequences of, antimicrobial resistance, are well illustrated by three recent case studies. The recent occurrence of New Delhi metallo-beta-lactamase 1 (NDM1) associated resistance demonstrates rapid spread of multiple resistance genes across a wide range of bacterial species and to multiple countries. The carriage of multiply resistant *Staphylococcus aureus* in pigs in the Netherlands demonstrates the spread of a resistant strain between animal species. The development of multiple resistance in association with aquaculture demonstrates the impact of antimicrobial use across agricultural sectors and in integrated systems.

New Delhi Metallo-Beta-lactamase 1

This novel resistance gene was first detected in *Escherichia coli* in 2008, initially in several different countries, but in individuals with a recent history of travel to India [13]. It appears that this resistance gene first entered *E. coli* in India. The gene itself encodes a potent beta-lactamase that is capable of destroying all the beta-lactam antimicrobials - the penicillins and the cephalosporins. The gene is carried on plasmids with up to 14 other resistance genes, and these plasmids thus confer resistance to a very broad range of antimicrobial drugs. These plasmids are now found in a very wide range of Gram negative bacteria, some quite distantly related to *E. coli*, including significant pathogens, in water sources in New Delhi, but these plasmids are being recovered from pathogens in humans throughout the world [14].

Multiple-resistant Staphylococcus aureus in Europe

A specific strain of multipl-e-resistant Staphylococcus aureus has recently been found, initially in pigs in the Netherlands [15]. This strain is variably resistant to amoxycillin, cefoxitin, ciprofloxacin, clindamycin, erythromycin, gentamicin, methicillin, penicillin, sulphonamides/ trimethoprim and tetracycline. Although initially detected in The Netherlands, it is now being detected across North America, Europe and Asia. The strain can be transmitted from colonized livestock, particularly pigs, to farm workers, abattoir workers and veterinarians. It has been suggested that a specific gene in the resistance plasmid indicates that the spread of the plasmid could have been promoted by use of zinc in pig food [16]. Epidemiological data shows a close concordance between the areas of the Netherlands used for pig farming and the occurrence of human infection with this strain [15]. Infections with other strains of multiple-resistant Staphylococcus aureus in the Netherlands are distributed in concordance with the distribution of people. Some notable aspects of this outbreak include the fact that this strain is not associated with significant disease problems in pigs, that it is also being isolated from veal calves and there have been a few reports of it causing bovine mastitis, although some of these cases have no clear association with pig farms [17]. Epidemiological studies show that people are more likely to be colonized by this strain the longer they have had contact with veal calves, that the higher the prevalence of carriage by calves on the farm, the greater the likelihood of carriage by people working with the calves, and that treatment of the calves with antimicrobial drugs increases the likelihood that they will carry this strain [18].

It is important to note that this strain does not appear to persist for very long on people if they don't have ongoing animal contact [19], and that most cases of multiple-resistant *Staphylococcus aureus* infection are associated with strains that appear to have developed exclusively in humans - the pig associated strain is responsible for well under 1% of the multiple-resistant Staphylococcus aureus cases in the Netherlands.

Antimicrobial Resistance Associated with High Intensity Integrated Farming Systems

High intensity integrated farming systems incorporating aquaculture can be a sustainable solution to managing waste from terrestrial animals, but could also result in high levels

of exposure and cycling of a wider range of antimicrobials and resistant organisms [20]. The recent occurrence of a specific strain of multi-resistant *Salmonella enterica* serovar appears likely to have been selected in African fish farms, and amplified through integrated fish and poultry farming [21]. This organism carries a multiple resistance cassette protecting the bacterium against amoxycillin, streptomycin, spectinomycin, gentamicin, sulphonamides and tetracycline that it appears to have acquired in 1996. Since then it has acquired two subsequent mutations that render it resistant to ciprofloxacin. This strain has now been found in cases of disease in humans throughout Europe and the Middle East, as well as Africa, now in association with chickens.

These three case studies should be considered examples of the range of responsibilities in the communities using antimicrobials, rather than as a basis for blame. The generation of multiple resistance and its spread is probably a relatively rare event, and apportioning blame, rather than focusing on collective responsibility may serve no purpose other than to deflect attention from the shortcoming of all antimicrobial user communities.

Practical Considerations in Controlling Antimicrobial Resistance

The majority of resistance issues in medical practice have no association with agricultural use, including most hospital and community acquired multiple-resistant *Staphylococcus aureus* infections, vancomycin resistant enterococcal (VRE) infections in North America, where avoparcin was never licensed for use in animals, but vancomycin was more commonly used for medical therapy, and resistance in human streptococci, to name only a few. However there is very strong evidence that agricultural use resulted in VRE problems in Europe and the occurrence of fluoroquinolone resistance in campylobacters in North America [22].

Ultimately it is important to remember that bacteria often do not respect geographical or species boundaries and that we all share the problem. Prudent use should be implemented voluntarily throughout the animal health community. Safety and efficacy have been central considerations in the use and regulation of antimicrobial drugs for many years, but a third consideration must be added to this - need. It is important to examine very closely whether there is a good case for need for some of the newer broad spectrum antimicrobials, including fluoroquinolones and newer generation cephalosporins, in production animal health. If there is already an adequate drug already available for targeted treatment, are additional antimicrobial agents needed? While ease of use, including less frequent administration, is one indication offered for introduction of some of the newer antimicrobials, the driver for adoption of newer drugs should be therapeutic need. Although it is not generally a problem in agricultural systems, a potential concern is the increasing use of custom-made antimicrobial formulations in companion animals, sometimes driven by the marketing of compounding pharmacies.

Any use of antimicrobial drugs that might be better addressed by alternative disease management approaches should be reconsidered. One of the best solutions for antimicrobial resistance is the development of effective vaccines, which can replace much of the need for antimicrobial administration, so vaccine development and use should always be considered an important component of prudent antimicrobial use.

References

- 1 Anonymous. Antimicrobial resistance: revisiting the "tragedy of the commons". Bull World Health Organ. 88: 805-806 (2010).
- 2 Butler, M.S. & Cooper, M.A. Antibiotics in the clinical pipeline in 2011. J Antibiot (Tokyo). 64: 413-425 (2011).
- 3 Davies, J. & Davies, D. Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev. 74: 417-433 (2010).
- 4 Hopwood, D.A. How do antibiotic-producing bacteria ensure their self-resistance before antibiotic biosynthesis incapacitates them? Mol Microbiol. 63: 937-940 (2007).

- 5 Aminov, R.I. & Mackie, R.I. Evolution and ecology of antibiotic resistance genes. FEMS Microbiol Lett. 271: 147-161 (2007).
- 6 D'Costa, V.M., King, C.E., Kalan, L., Morar, M., Sung, W.W., Schwarz, C., Froese, D., Zazula, G., Calmels, F., Debruyne, R., Golding, G.B., Poinar, H.N. & Wright, G.D. Antibiotic resistance is ancient. Nature. 477: 457-461 (2011).
- 7 Allen, H.K., Donato, J., Wang, H.H., Cloud-Hansen, K.A., Davies, J. & Handelsman, J. Call of the wild: antibiotic resistance genes in natural environments. Nat Rev Microbiol. 8: 251-259 (2010).
- 8 Cambray, G., Guerout, A.M. & Mazel, D. Integrons. Annu Rev Genet. 44: 141-166 (2010).
- 9 Ginns, C.A., Browning, G.F., Benham, M.L., Anderson, G.A. & Whithear, K.G. Antimicrobial resistance and epidemiology of *Escherichia coli* in broiler breeder chickens. Avian Pathol. 25: 591-605 (1996).
- 10 Cavaco, L.M., Abatih, E., Aarestrup, F.M. & Guardabassi, L. Selection and persistence of CTX-M-producing *Escherichia coli* in the intestinal flora of pigs treated with amoxicillin, ceftiofur, or cefquinome. Antimicrob Agents Chemother. 52: 3612-3616 (2008).
- 11 Andersson, D.I. & Hughes, D. Antibiotic resistance and its cost: is it possible to reverse resistance? Nat Rev Microbiol. 8: 260-271 (2010).
- 12 Fick, J., Soderstrom, H., Lindberg, R.H., Phan, C., Tysklind, M. & Larsson, D.G. Contamination of surface, ground, and drinking water from pharmaceutical production. Environ Toxicol Chem. 28: 2522-2527 (2009).
- 13 Nordmann, P., Poirel, L., Walsh, T.R. & Livermore, D.M. The emerging NDM carbapenemases. Trends Microbiol. 19: 588-595 (2011).
- 14 Walsh, T.R., Weeks, J., Livermore, D.M. & Toleman, M.A. Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. Lancet Infect Dis. 11: 355-362 (2011).
- 15 van Loo, I., Huijsdens, X., Tiemersma, E., de Neeling, A., van de Sande-Bruinsma, N., Beaujean, D., Voss, A. & Kluytmans, J. Emergence of methicillin-resistant *Staphylococcus aureus* of animal origin in humans. Emerg Infect Dis. 13: 1834-1839 (2007).
- 16 Cavaco, L.M., Hasman, H. & Aarestrup, F.M. Zinc resistance of *Staphylococcus aureus* of animal origin is strongly associated with methicillin resistance. Vet Microbiol. 150: 344-348 (2011).
- 17 Vanderhaeghen, W., Cerpentier, T., Adriaensen, C., Vicca, J., Hermans, K. & Butaye, P. Methicillinresistant *Staphylococcus aureus* (MRSA) ST398 associated with clinical and subclinical mastitis in Belgian cows. Vet Microbiol. 144: 166-171 (2010).
- 18 Graveland, H., Wagenaar, J.A., Heesterbeek, H., Mevius, D., van Duijkeren, E. & Heederik, D. Methicillin resistant *Staphylococcus aureus* ST398 in veal calf farming: human MRSA carriage related with animal antimicrobial usage and farm hygiene. PLoS One. 5: e10990 (2010).
- 19 van Cleef, B.A., Graveland, H., Haenen, A.P., van de Giessen, A.W., Heederik, D., Wagenaar, J.A. & Kluytmans, J.A. Persistence of livestock-associated methicillin-resistant *Staphylococcus aureus* in field workers after short-term occupational exposure to pigs and veal calves. J Clin Microbiol. 49: 1030-1033 (2011).
- 20 Dang, S.T., Petersen, A., Van Truong, D., Chu, H.T. & Dalsgaard, A. Impact of medicated feed on the development of antimicrobial resistance in bacteria at integrated pig-fish farms in Vietnam. Appl Environ Microbiol. 77: 4494-4498 (2011).
- 21 Le Hello, S., Hendriksen, R.S., Doublet, B., Fisher, I., Nielsen, E.M., Whichard, J.M., Bouchrif, B., Fashae, K., Granier, S.A., Jourdan-Da Silva, N., Cloeckaert, A., Threlfall, E.J., Angulo, F.J., Aarestrup, F.M., Wain, J. & Weill, F.X. International spread of an epidemic population of *Salmonella enterica* serotype Kentucky ST198 resistant to ciprofloxacin. J Infect Dis. 204: 675-684 (2011).
- 22 Wassenaar, T.M. Use of antimicrobial agents in veterinary medicine and implications for human health. Crit Rev Microbiol. 31: 155-169 (2005).

2. The concerns of the dairy industry in relation to public health and market access

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Abstract

Although the use of antibiotics is strictly controlled and monitored by the dairy industry there is a need to continue to challenge existing practices, to ensure a robust defence against ill-informed attacks.

Introduction

Although antibiotics are used to treat sick animals and any residues are below Maximum Residue Limits (MRLs), the dairy industry is concerned that consumers may perceive that milk contains antibiotic residues, and that the need for antibiotics results from poor and avoidable farming practices. Consumers may additionally be concerned that these antibiotic residues could affect their health, and might increase human antibiotic resistance.

Media reactions

The popular press needs to come up with sensationalist stories, with eye-catching headlines, and the antibiotic issue can provide ammunition for addressing consumer concerns. In the UK in June 2011 the publication of a scientific paper reporting findings of a novel strain of meticillin-resistant Staphylococcus aureus (MRSA) (1) in the UK dairy herd and in some people, resulted in front page headlines (2) of "Death wish", and accusations "As Europe and the US face up to the menace of antibiotic-resistant superbugs, UK farmers have dramatically increased their use of the drugs most likely to cause these lethal strains". Information on increased drug use was provided though this in fact indicated that antibiotic usage in cattle was relatively modest. This did not prevent the paper claiming that routine use of vital antibiotics on farms was threatening human health, and blaming intensive farming and market forces for reckless practices.

Realities

The realities are that antibiotics are used to treat sick animals, and the antibiotics are licensed, and prescribed by veterinarians. Withdrawal periods are set such that any residues entering the milk are within Maximum Residue Limits, and these limits have large safety factors built in.

In addition milk supplies are tested regularly by industry. For example in the UK milk from farms is sampled and tested weekly, so that with 15 000 dairy farms some 780 000 tests are carried out annually. Farmers are severely penalised if their milk fails the antibiotic test, and are not paid for their milk but in addition may have to pay for the tanker load or silo. This testing by industry is supplemented by official surveillance by government, using tests capable of detecting a wider spectrum of residues, and no issue is found.

Weaknesses

Nevertheless there are weaknesses in our position. Farmers do very occasionally make mistakes over withdrawal periods or milking. Antibiotics do sometimes get into milk at a very low level, and antibiotics may be prescribed too readily.

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What can be done at the farm?

There are no simple solutions but there is a need for industry to keep challenging itself. Would better farm management reduce the need for antibiotics? Would better management reduce the incidence of antibiotic failures? Are tests which are faster, wider spectrum or with greater sensitivity required?

What can be done at the veterinary level?

Again veterinarians need to keep challenging current practices. Is there a need for tighter rules applying to the prescribing of antibiotics? Should the choice of antibiotics be restricted, reserving some classes for human use? Are the appropriate antibiotics being used, or are antibiotics being used on resistant animals? Is there a need for tighter controls on the availability of antibiotics? Is there a need for tighter controls on the advertising of antibiotics?

Is there a need for legislation?

The European Food Safety Authority (EFSA) has concluded(3) that the use of antimicrobials in food-producing animals is a risk factor for the spread of bacterial strains that produce enzymes that makes them resistant to treatments with certain antibiotics including penicillin and cephalosporins.

They recommend that decreasing the overall use of antimicrobials in food-producing animals in the EU should be a priority in terms of limiting the risk to public health arising from resistance in the food chain, and that an effective option would be to restrict or stop the use of cephalosporins in the treatment of food-producing animals.

As what might turn out to be the first step towards increased legislation the European Medicines Agency has published (4) its first report on sales of veterinary antimicrobial agents. The report shows that tetracyclines, penicillins, and sulfonamides are the top three antimicrobial classes sold in tonnes, accounting for more than 80% of total sales.

Another finding is the substantial difference in the prescribing patterns of veterinary antimicrobial agents between countries. The European Medicines Agency concludes that data on the usage of antimicrobials in food-producing animals (and companion animals) are essential for identifying and quantifying the risk of developing and spreading antibiotic resistance in the food-chain.

What does the industry want in future?

We certainly want antibiotic usage in dairy cattle and the possible presence of residues in milk to disappear as a consumer issue. We want to be able to state with complete confidence that antibiotics are used responsibly, only when really necessary, and when used the antibiotics are those appropriate, and that residues do not get into milk. We need the evidence that human resistance to antibiotics is not a consequence of on-farm use of antibiotics in the dairy herd. We also want the approach to antibiotics to be global so that products meeting the regulatory requirements in one country can be freely traded in other countries. We have to accept that we can achieve this voluntarily through good practice, but if we delay we may be faced with additional legislation.

References

 "Meticillin-resistant Staphylococcus aureus with a novel mecA homologue in human and bovine populations in the UK and Denmark: a descriptive study". García-Álvarez L, Holden MT, Lindsay H, Webb CR, Brown DF, Curran MD, Walpole E, Brooks K, Pickard DJ, Teale C, Parkhill J, Bentley SD, Edwards GF, Girvan EK, Kearns AM, Pichon B, Hill RL, Larsen AR, Skov RL, Peacock SJ, Maskell DJ and Holmes MA, The Lancet infectious diseases 2011;11;8;595-603.

- 2. "The Independent", London, 17 June 2011.
- 3. "Scientific Opinion on the public health risks of bacterial strains producing extended-spectrum β -lactamases and/or AmpC β -lactamases in food and food-producing animals " EFSA Journal 2011;9(8):2322.
- 4. "Trends in the sales of veterinary antimicrobial agents in nine European countries", European Medicines Agency, 15th September 2011.

3. Antimicrobial use in the dairy industry in South Africa: sustainable food security requires the prudent use of antimicrobial agents

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Summary

In 2009, the Codex Alimentarius Commission (Codex) circulated a request for comments and information on veterinary drugs used in developing countries. South Africa can be considered a developing or transition country because of the dual nature of its dairy industry, with sophisticated dairy technology existing side by side with small scale and subsistence dairy farmers. Antimicrobials are important for treatment of tropical diseases in South Africa but can also, more controversially, be used to prevent mastitis in dry cows. From the point of view of human health, antimicrobial residues in milk can be toxic or cause allergies in consumers. Antimicrobial resistance (AMR) has emerged over the last 20 years as a consequence of the large scale use of antibiotics in both human and veterinary medicine. It can result in organisms, so-called "super-bugs", which are refractory to therapeutic doses and cause mortality in both humans and animals. Not only can AMR be transferred to human pathogens, but can also conceivably be transferred to bacteria used as cultures in dairy products, which could in turn transfer resistance to human enteric bacteria. The use and misuse of antimicrobials in the dairy industry in South Africa is reviewed. It is recommended that decision tree analysis and risk analysis be used to evaluate veterinary drugs for use in dairy animals. This is particularly appropriate in developing countries where a higher risk of tropical diseases could motivate in favour of using a wider spectrum of antimicrobials, to maintain health and welfare of dairy animals.

Introduction

South Africa is located at the most southern tip of the African continent and as it was on the sea route to the Far East and Australasia has a very cosmopolitan mix of cultures and farming systems. As Nelson Mandela said, a "Rainbow Nation". Dairy farming systems vary from the most modern technology for large scale production and processing to maintain food security at the national level, to small scale and subsistence systems. The climate is also diverse, Mediterranean along the southern and eastern seaboard, becoming arid further inland and rising to a savannah-like plateau, then dropping further north into subtropical and tropical areas. With the low proportion of arable land and the low rainfall, South Africa must prioritise food security for its population of nearly 50 million persons.

Food safety is an essential part of food security and South Africa is a signatory to the Codex Alimentarius Commission (Codex), where it is classified in the "developing or transition" sector. Antimicrobial resistance (AMR) has been recognised by Codex as a potential risk to the health of both livestock and humans. It has resulted from the escalation of the use of antibiotics in both human and veterinary medicine since the end of the Second World War (2,6,7,8,9). This can result in organisms, so-called "super-bugs" which are refractory to therapeutic doses. Staphylococcus aureus, Salmonella spp, Campylobacter jejuni, Enterobacter spp and Eschericia coli, among others, are bacteria found in dairy animals and dairy products that have been related to human disease and have shown AMR. Even non-pathogenic or spoilage bacteria in contact with drugs used to enhance growth of young livestock, prevent or treat disease, can develop

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AMR. If they enter the food chain, the genes enabling AMR can be passed across to pathogenic organisms at a later stage. This includes dairy products (4). Thus AMR surveillance is needed to identify and implement mitigation strategies to reduce the risks of transfer of AMR from animals to humans (2, 8,9). Resistant bacteria and resistance genes can also be transferred though the environment, particularly in water, by bacteria present in the excrement of humans and animals (7). It has been suggested that limiting the use of antimicrobials in livestock decreases the levels of AMR (1, 16,17).

In 2007, Codex suggested that it was important to find an appropriate balance between animal health needs and human public health and to reduce the use of any antimicrobials not absolutely essential for animal health (3). As a result, the World Organisation for Animal Health (OIE) has classified antimicrobials into three categories for animal use - critically important, highly important or important. The WHO has done the same for human drugs. In animals, the critically important antimicrobials are those essential for treatment of certain infections where there are no therapeutic alternatives. Although this proposed reduction in the use of antimicrobial drugs was in general supported by countries with highly intensive animal production systems, objections were received from countries where tropical diseases pose a serious risk to the health and welfare of animals as well as having negative effects on the socio-economics of the livestock sector and food security. As a result, in 2009, Codex circulated a request for comments and information on veterinary drugs used in developing and transitional countries.

Use of antimicrobial drugs in South Africa

In South Africa there are two main Acts under which veterinary drugs and stock remedies can be registered. These are Act 36 and Act 101. No drugs other than those registered under one of these two Acts may be manufactured, distributed, sold or used in either humans or animals. Animal feeds and feed additives are also registered under Act 36 and thus controlled in line with international norms (13). The overall proportion of drugs registered for use in animals (all species) is shown in order of magnitude, in Table 1 (12).

Table 1: Proportions of different groups of antimicrobials registered in South Africa, in order of magnitude (after Nel, 2002).

1	Tetracyclines
2	Penicillins
3	Sulphonamides
4	Macrolides
5	Lincosamides
6	Pleuromutalins

As a result of the emergence of AMR, the Joint Expert Committee for Food Additives and Contaminants (JECFA), which is a collaboration between OIE and WHO, has come into being. Its terms of reference are to :

- elaborate principles for safety evaluation of veterinary drugs;
- establish the acceptable daily intake (ADI) for chronic exposure to antibiotic residues in consumers;
- · recommend maximum residue levels in food of animal and plant origin; and
- determine the ideal methods of analysis for veterinary drugs in food.

AMR and the dairy sector in South Africa

In Africa many tropical diseases pose a threat to the income of dairy farmers and the health and welfare of dairy animals. Pests and parasites like Cullicoides midges, mosquitoes and ticks transmit life threatening diseases such as Blue Tongue, Rift Valley Fever and protozoal diseases like Heartwater. Regulations used in South Africa to control the use of antimicrobial substances used for animals fall under either the Department of Agriculture (registered stock remedies) or the Department of Health (scheduled animal medicines prescribed by veterinarians) (13).

Commercial dairy farms are usually intensive or semi-intensive and all dairy parlours and milking sheds must be registered under legislation that falls under the Department of Health. Registered dairy producers must involve registered veterinarians to maintain animal health and all milk or milk products sold must conform to stringent health and safety norms aligned to those specified by Codex and the OIE. Antimicrobial residues are not only routinely monitored to maintain human health but must comply with the even more stringent private standards of processors, as they interfere with starter cultures for yoghurt and cheese. The main scheduled antibiotics in the commercial dairy industry are penicillin and streptomycin used for prevention and treatment of mastitis. From Table 2 below, it can be seen that intramammary medications make up a very small fraction of the total use in animals (both livestock and pets) in South Africa.

Table 2: The proportional routes of administration for antimicrobials used in South Africa (from Nel, 2002).

%	Usage
68.5	feed
17.5	injectables
12	water
1.96	other
0.04	intramammary

Small scale or subsistence producers, who mainly farm extensively, have access to registered stock remedies. These are mainly used therapeutically for injuries, wounds and tropical diseases in livestock. Doses and withdrawal times must be stated on all labels. Fortunately, due to availability of these registered stock remedies, illegal and black market drugs are not a problem in South Africa (15). Livestock health in the small-scale and subsistence sector is a priority of state veterinary services and is available on a cost-recovery or totally subsidised basis to prevent transfer of transboundary and zoonotic diseases.

Challenges for the dairy industry

Recent research has shown that AMR genes are present in bacterial populations exposed to antimicrobials as a result of the well known "survival of the fittest" principle in genetics. Overuse of antimicrobials in both human and animals, is undesirable. However, human health demands for removing almost all veterinary antimicrobials are not realistic. It has been shown that the environment plays a role in dissemination of AMR (10,11).

However the health and welfare of production animals and the need for production levels to increase to meet food security needs of increasing human populations, requires that critically important antimicrobials should be used.

Human health demands the removal of all antimicrobials and this is reflected in several Codex and WHO published documents. In contrast, work done in South Africa by Mariano et al., 2008,

showed that impala (wild ungulates) in the Kruger National Park, that had never had any veterinary treatment, could have intestinal bacteria resistant to tetracycline if they drank polluted water. Impala drinking water that had not passed though human settlements, in contrast, had a significantly lower level of tetracycline resistance in their intestinal bacteria. It is postulated that the resistance resulted from tetracycline from human patients being treated with tetracycline for malaria possibly passing infected bacterial flora into surface water as sewage plants were not working well (10).

Tetracycline residues can be found in animal-derived foods. The challenge for the dairy industry in South Africa is the removal of tetracycline from the list of registered antibiotics that can be used for treating rickettsial diseases of cattle, as these tick-borne diseases are fatal. Unfortunately high producing dairy cow breeds such as the Holstein are particularly susceptible to bacterial and protozoal diseases in tropical climates, particularly those owned by subsistence or small-holder dairy farmers. This has a further effect on the welfare of dairy cattle as it makes treatment inaccessible and thus increases suffering.

Conclusions

It is concluded that although a reduction in AMR is desirable for both human and animal health, this should be approached with due care and less reliance on rigid legislation. It is recommended that decision tree analysis and risk analysis be used to evaluate veterinary drugs for use in dairy animals (14). This is particularly appropriate in developing countries where a higher risk of tropical diseases could motivate in favour of using a wider spectrum of antimicrobials to maintain health and welfare of dairy animals. Dairy cattle, particularly in Africa, need to have access to treatment with effective antimicrobials in the light of the high prevalence of tick borne diseases. In particular, the tetracyclines are effective against a wide range of parasitic diseases as well as common conditions such as hoof, udder and eye infections. There are already suitable control measures in place to reduce unnecessary use as milk with antimicrobial residues is discarded and processors (probably mainly because it affects cheese and yoghurt production) are very strict in this regard, often removing suppliers entirely from their list for varying lengths of time. Processors are advised to seek veterinary advice and use only registered antimicrobials, with strict adherence to withdrawal times. Fortunately, antimicrobials are not routinely used as growth promoters in the dairy industry in South Africa. It is suggested that researchers give priority to investigating alternatives for mastitis treatment and dry cow therapy, such ass the following:

- Informed and responsible use of registered drugs for therapeutic purposes
- Minimising the use of antibiotics as growth promoters
- New / alternative medications for dry cow therapy.

References

- 1. Aarestrup F M, Seyforth A M, Emborg H D, Pederson K, Hendriksen R, Bager F, 2001 Effect of abolishment of the use of antimicrobial agents for growth promotion on occurrence of antimicrobial resistance in faecal enterococci from food animals in Denmark. *Antimicrobial Agents and Chemotherapy* 45: 2054-2059.
- 2. Anderson A D , Nelson J M , Rossiter S, Angulo F J, 2003 Public Health consequences of antimicrobial agents in food animals in the United States. Microbial Drug Resistance 9 (4): 373-379.
- 3. Bonfiglio G, Simpore J, Pignatelli S, Musumeci S, Solinas M L, 2002 Epidemiology of bacterial resistance in gastro-intestinal pathogens in a tropical area. *International Journal of Antimicrobial Agents* 20: 387-389.
- 4. Cenci-Goga B, Crotti S, Costarelli S, Rondini C, Karanma M, Bennet P, 2004 Detection of Tetm Gene from raw milk by rapid DNA extraction followed by a two step PCR with nested primers. Journal of Food Protection: 2833-2838.

- 5. Chopra I, Roberts M, 2001 Tetracycline antibiotics: mode of action, applications, molecular biology and epidemiology of bacterial resistance. Microbiology and Molecular Biology Reviews 65: 232-260.
- 6. FAO/WHO/OIE, 2008. Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials. Report of a meeting held in FAO, Rome, Italy, 26–30 November 2007. FAO, Rome, Italy, and WHO, Geneva, Switzerland.
- 7. Davidson J, 1998 Genetic exchange between bacteria in the environment. *Plasmid* 42: 73-91
- 8. Florea N F, Nightingale CH, 2004 Review of the pharmacodynamics of antimicrobial use in food animal production. Diagnostic Microbiology and Infectious Diseases 49: 105-108.
- 9. Lees P, Aliabadi F S, 2002 Rational dosing of antimicrobial drugs: animals versus humans. *International Journal of Antimicrobial Agents* 19: 269-284.
- 10. Mariano V 2008, A study of tetracycline resistant *Escherichia coli* in impala (*Aepyceros melampus*) and their water sources . MSc thesis, University of Pretoria, South Africa.
- 11. McCrindle CME, Cenci-Goga B, 2008 Could the transfer of antimicrobial resistance be considered a new form of zoonosis? Proceedings of the SASVPM Conference, South Africa, 2008.
- 12. Nel H, 2002 The establishment and standardisation of a veterinary antimicrobial resistance program in South Africa. MSc thesis, University of Pretoria, South Africa.
- 13. Ogutto J W, 2007 Occurrence of antimicrobial drug resistance among broiler isolates fed antimicrobial growth promoters and exposed poultry abattoir workers. MSc thesis, University of Pretoria.
- 14. Salisbury J G, Nicholls TJ, Lammerding AM, Turnidge J, Nunn M J, 2002 A risk analysis framework for the long term management of antimicrobial resistance in food producing animals. *International Journal of Antimicrobial Agents* 20 (3): 153-164.
- 15. SANVAD, 2007 South African National Veterinary Surveillance and Monitoring Programme for Resistance to Antimicrobial Drugs ISBN: 978-1-86854-673.
- 16. Ungemach F R, Muller-Bahrdt D, Abraham G, 2006 Guidelines for prudent use of antimicrobials and their implications on antimicrobial usage in veterinary medicine. *International Journal of Medical Microbiology* 276 (S2): 33-38.
- 17. Vander Bogaard A E, Stobberingh E E, 2000 Epidemiology of resistance to antimicrobials: link between animals and humans. *International Journal of Antimicrobial Agents* 14: 327-335.

Nutrition

1. The role of dairy calcium in tooth and bone health through life stages

William R. Aimutis, Ph.D1

Abstract

Milk and dairy products are an important biological source of energy and nutrition for humans throughout their life stages. There is increasing evidence that nutrients, particularly minerals, also influence fetal development and metabolic imprinting in utero. Calcium is an essential mineral for skeletal development during pregnancy, and has continued importance to the infant and adolescent during their rapid growth phases through their first two decades of life. It is during this period that humans can prevent problems in later life through reasonable dairy consumption. In particular, dairy consumption reduces the risk for osteoporosis in later life if a dietary intake of 0.5-0.6 liters of fat-free or low-fat milk or other dairy products per day is accomplished as recommended by the Dietary Guidelines for Americans. The calcium contained in these dairy products significantly contributes to daily levels recommended for adults and children. Dairy calcium's importance through adulthood is further evidenced by reduced fracture risk and lower propensity to dental caries. Dental caries are caused by salivary organic acids demineralizing the calcium-enriched hydroxyapatite enamel coating teeth. Embedded within milk casein proteins are motifs of phosphopeptides that sequester calcium and other minerals to mineralize bones and teeth. Caseinophosphopeptide binds amorphous calcium phosphate as a nanocomplex to serve as a nucleating site for both bone and tooth mineralization. As humans enter their geriatric years calcium ingestion assists in maintaining bone mineral density, and reducing the likelihood of vertebral fractures. However, let us not confuse dairy product consumption in later life as important for preventing or reversing the debilitating effects of osteoporosis. These effects are imprinted during the first 20 years of life, and indicate the need for adequate dairy consumption throughout life.

1. Role of milk

1.1. Milk as a food for all ages

Our mothers began encouraging us to "drink our milk" at an age when we did not understand the ramifications of not consuming this nutritional beverage. Mammalian evolution developed a consumable fluid containing not only an assemblage of essential and non-essential amino acids, but also components impacting numerous physiological processes throughout our body to optimize skeletal development, enable us to chew food with healthy teeth, and protect us from a multitude of hazardous substances meant to harm our well-being. Unfortunately, genetics and our own lack of knowledge about the importance of continuing to meet daily nutritional needs through milk and other dairy products predisposes us to serious medical issues in later life. If we had continued to "drink our milk" as we went through adolescence, puberty, and into adulthood many of the health problems observed in this century may have been somewhat mitigated.

Milk is recognized by nutritionists and medical professionals worldwide to be associated with several health benefits after humans reach adulthood. Numerous studies have now shown

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consuming 3 recommended portions of dairy each day, along with 5 portions of fruits and vegetables as part of a low salt diet can reduce high blood pressure. Milk and dairy consumption are also linked to a reduced risk for cardiovascular disease. Several studies report people consuming dairy regularly in their diets have fewer heart attacks. Those individuals also have normal blood lipid levels and better blood sugar control. Furthermore, routine dairy consumption is usually associated with individuals of normal body weight. But perhaps the most striking benefit derived from milk is prevention of osteoporosis and joint problems in later life. Individuals consuming the recommended daily intake of dairy products tend to have better bone density, less likelihood of bone fractures, and be in better physical condition when they reach later life.

1.2. Health and aging related issues

Physiological aging refers to changes in structure and functioning of the body that occur over a lifespan. Most of these changes are involuntary and occur as we advance in age having been genetically programmed into humans while still in the womb. Most changes begin manifesting themselves when humans are approaching fifty years of age (Figure 1).

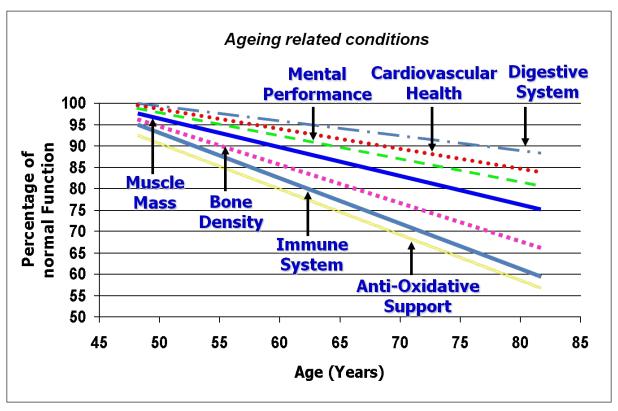


Figure 1. Major healthcare issues in the 21st century. These are the major health issues facing the world in the 21st century. The graph illustrates the age of onset and gradual disease progression.

Our muscle mass, immune system, bone density, and antioxidative support are changing most rapidly at this age. The immune system is one of the first physiological systems to deteriorate with advancing age, and this leaves us more susceptible to heart disease, arthritis, cancer, and pneumonia. Much of the aging process is controlled by genetics, and a weakening immune system is part of the deteriorating process by which our body begins attacking itself to lower our immune competency. Muscle tone and mass begin to be replaced by soft and/or fatty tissue, and our endurance and/or strength to undertake certain tasks may decrease. The loss

of muscle protein (sarcopenia) through aging can eventually lead to disability and a propensity to falling (1). Our skeletal system begins losing calcium as age advances until the bones are porous and brittle. This demineralization is especially apparent in women, but men are also affected by weakened bones. Consuming a diet high in calcium and vitamin D throughout our lives impacts our bone mineral density, and ultimately slows debilitation of the body. Healthy diets and maintaining an active lifestyle can help slow all these processes somewhat. It is also very important to maintain an exercise program after fifty years old to help maintain muscle tone that protects us from breaking bones if we fall. Additionally, intensive physical training improves circulatory function and blood pressure, especially in women, by improving peripheral vascular function (2).

1.3. Role of milk in mitigating health problems

The organic and inorganic composition of milk and dairy products play an important role in protecting humans from maladies described above. Milk as a biological fluid provides humans of all ages with significant nutrients, immunological protection, and biologically active peptides (3). Milk proteins, peptides, oligosaccharides, and other micronutrients have a key role in regulating three main biological functions in an infant or newborn animal, namely nutrient transport/lipid metabolism, establishment of the immune system response, and cellular proliferation processes (4). As humans age, milk continues to influence multiple physiological processes including those maintaining muscle mass, immune-stimulation, mineral metabolism, bacterial inhibition, cell proliferation, blood clotting, and antioxidation, to name a few.

Perhaps the most celebrated role for milk is as a carrier of minerals and vitamins to the body. Dairy foods in a healthy American diet contribute 70.3% of the calcium, 16% of the magnesium, 18.2% vitamin B12, 25% riboflavin, and 15% zinc (5) requirements. Additionally, many dairy foods are now fortified with vitamin D and they serve as an excellent dietary source for this vitamin. However, milk is not perfect, especially as individuals' age, as it is not a good source of fiber and iron. Just the same, three daily servings of milk and dairy products are recommended as part of a healthy diet.

Despite promotions and advertising by governmental and non-governmental organizations in the Western world about the need to consume recommended daily servings of dairy products, the population masses continue to refrain from meeting the guidelines. Unfortunately this is especially true with children and adolescents aged 2 to 19 years old. The United States Center for Health Statistics reported approximately 10% of this age group never consumed milk in the 30 days preceding their survey (6). Nearly 60% did not consume 3 or more servings per day, and girls were twice as unlikely to consume milk. Furthermore, earlier studies found adolescents not consuming milk or dairy products will not substitute other foods to compensate for the loss of nutrients, especially calcium and vitamin D (7; 8). This is especially troubling given the importance of dairy products in skeletal health.

1.4. Role of calcium as it pertains to bone and tooth health

Humans require 20 essential minerals for a healthy well-being. Calcium is one of the most important, and most people recognize calcium as a milk mineral needed for good bone development and homeostasis (9). However, calcium has other important roles in the human body including complexation of digestive byproducts to prevent kidney stones and colon cancer (10). Additionally, calcium is important as a cofactor for certain hormones involved in controlling hypertension, pre-eclampsia, cellular insulin uptake, and preventing obesity.

The majority (\sim 99%) of calcium in the human body is found in teeth and bones (11). The total calcium in a human's bones and teeth is approximately 1200 g, and exists in an inorganic crystalline structure, hydroxyapatite, in cooperation with phosphorus. Teeth and bones originate as a protein that becomes mineralized as a complex matrix with hydroxyapatite crystals in bones and teeth to provide rigidity to said structures (12). Bone also contains carbonate, citrate, sodium, magnesium, and fluoride (9).

2. Bone Health

2.1. Bone formation and remodeling

Our skeleton maintains structural support for our bodies, but is also a large mineral cache. Approximately 25 to 30 g of calcium is accumulated by the human fetus in a normal pregnancy that goes to term (13). The calcium accretion rate increases from 50 mg/day in week 20 to 330 mg/day in week 35. Bones begin as collagen protein that becomes encased by minerals. By the time the infant is delivered a sufficient quantity of minerals will have been delivered to the developing fetus to fully mineralize the skeleton. Bones continue to mineralize and grow until a human is 25 to 30 years old as long as there are no metabolic disorders and they continue with a good nutritional program ingesting the recommended daily nutrients especially calcium and vitamin D for healthy bone development. Although calcium needs can be met through supplementation, no other food group offers calcium concentrations at the density observed in milk and dairy products (14). Additionally, dairy products contain appreciable levels of phosphate, magnesium, protein, vitamin D, and potassium. Calcium from milk and dairy products seems to be protective of bone for a longer period than calcium supplements when tested in intervention studies (15).

Two types of bone compose our skeleton – cortical (compact bone) and trabecular (cancellous) bone. The cortical bone is located on the outer layer of long bones, and comprises about 80% of the skeletal mass (Figure 2). This bone has a very low turnover rate of approximately 3% annually. Trabecular bone is less dense and is the remaining 20% of skeletal mass. This bone region is especially metabolically active serving as a calcium reservoir for physiological needs and as such is located mainly in the axial skeleton and at the end of long bones. In developing children, a growth plate is present between the epiphysial and metaphyseal regions (Figure 2).

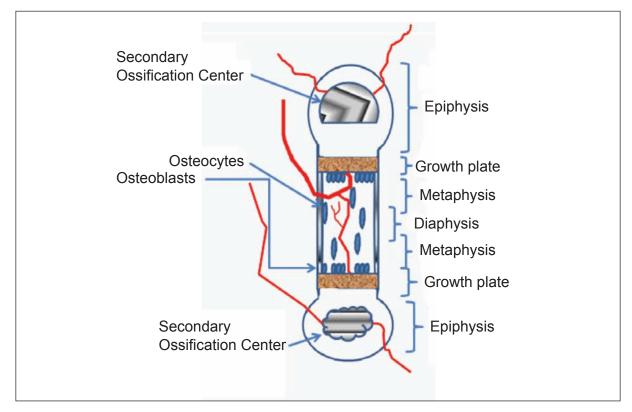


Figure 2a. Long bone anatomy. This bone type is part of the skeleton for structural architecture, and is usually composed mostly of compact (cortical) bone.

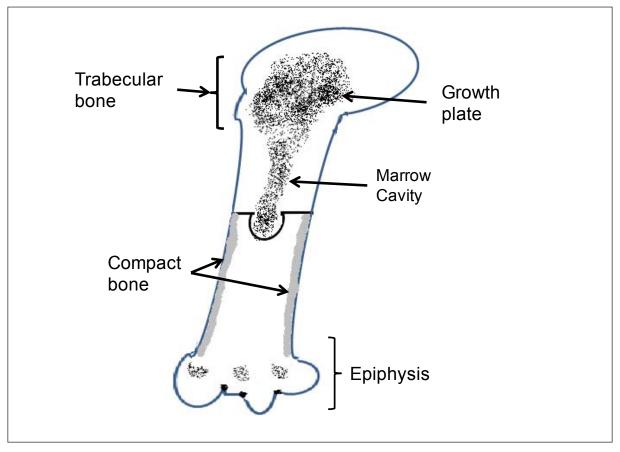


Figure 2b. Trabecular bone anatomy. This type of bone has a sponge like appearance, and is made up of a mesh network of trabeculae. It is usually found in active joints such as the shoulder, spine vertebrae, pelvis, and inner parts of long bones. Approximately 80% of bone is compact bone and the remainder is trabecular.

This is the site for ossification and cell hypertrophy to allow cartilage (collagen) to be transformed to growing mineralized bone. The skeleton will continue to grow in length, breadth, and mass until peak bone mass is attained as mentioned earlier. Maximum peak bone mass is important in later life to protect us from fractures in the event of falling. Maximum bone mass can only be achieved by good genetics, proper nutrition, healthy lifestyle, and exercise from the time our embryo began developing in the womb until we are in the middle decade of life (16). Any deviations along the way predispose us to osteopenia and potentially osteoporosis.

Even after peak bone mass is reached, our bones undergo constant remodeling to maintain bone integrity, repair minute fractures, and accommodate changing mechanical loads in our skeleton (Figure 3). Bone remodeling is a multi-cellular units process beginning with an influx of osteoclasts derived from circulatory monocytes and macrophage (17). Their role is to resorb the bone surface by removing mineralized bone matrix by acidification and proteolysis. Osteoclasts leave the resorption site when finished in the demineralization process. After a short resting session, osteoblasts migrate into the excavated area. Osteoblasts are specialized fibroblasts originating in the bone marrow that utilize calcium from resorption to remineralize the bone matrix by secreting osteoid which later mineralizes. Often osteoblasts must re-shape, or remodel, the bone to improve skeletal integrity or strength. The entire process can take 6 to 9 months to accomplish, but osteoclasts and osteoblasts are continuously infiltrating the points of remodeling during this time period. Bone remodeling is a well-choreographed event controlled by the parathyroid hormone, vitamin D, growth hormone, sex steroids, cytokines, and calcitonin. A human turns over approximately 10% of the skeleton annually.

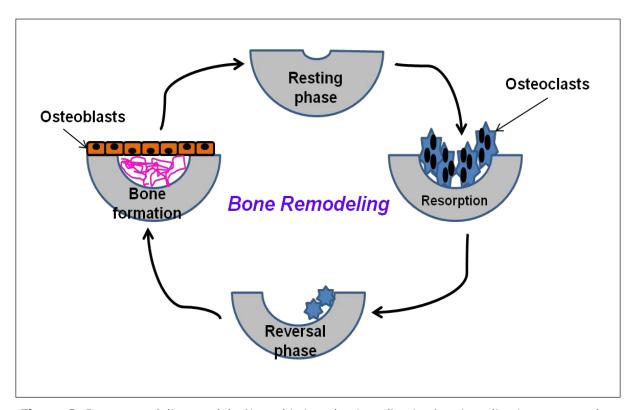


Figure 3. Bone remodeling model. Note this is a demineralization/remineralization process that relies on calcium from the diet and bone demineralization to rebuild bone demineralized by osteoclasts. This process accelerates during osteoporosis, but demineralization is metabolically faster than remineralization. The next result is deterioration of the bone network causing bone fragility.

The commonly used method for assessing bone health at all ages is dual energy x-ray absorptiometry (DXA). This instrument allows clinicians to measure bone mineral content (BMC) and bone mineral density (BMD). The BMC value is a measure of bone mass during growth, and is a more important measurement in children and adolescents frequently cited until peak bone mass is achieved (18). More information can be derived from the BMD value in older individuals; BMD is a measure of the amount of matter per cubic centimeter of bone and the values are interpretive of osteoporosis and fracture risk. Bone mass is also used as an indicator of healthy bone - this is a composite measure of bone size and mineral density. This value is a determinant of bone strength dependent upon the mass acquired during skeletal growth and development (19). The World Health Organization definition for osteoporosis is based on a T score which is a comparison of a DXA BMD result with the average BMD in young adults at the time of peak bone mass. This measure works well for adults, but is inappropriate to assess skeletal health of children using values from adult peak bone mass. Therefore, clinicians use a Z value for children to account for bone health relative to age and bone size (20). In addition, there are limitations with using DXA in infants and children. The issues include difficulties in scan acquisition due to inability to detect bone edges with existing software, and interpretation of the results in children with variable body size, body composition, and skeletal maturity (21).

Osteopenia is a precursor to osteoporosis, and is diagnosed when BMD is lower than normal peak BMD, but not low enough to be classified as osteoporosis. Younger people diagnosed with osteopenia have a greater risk of developing osteoporosis. Osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue leading to enhanced bone fragility and a consequent increase in fracture risk. The pathogenesis of both diseases is related to bone remodeling. An overabundance of osteoclasts

or osteoblasts activity begins affecting the fine structure of bones leading to loss of BMD and eventually bone fragility.

Osteoporosis pathogenesis begins rapidly progressing after the concentration of sex hormones begins decreasing with the onset of the menopause. Bone remodeling rate increases with elevated levels of osteoclasts and osteoblasts in the bone marrow, but less bone is replaced at each resorption site accelerating architectural decay (22). Men do not experience a midlife increase in bone remodeling, but as hypogonadism progresses they also experience bone deterioration. Calcium malabsorption and secondary hyperparathyroidism increases bone remodeling in both sexes. The result is more bone is removed from the bone mass than is being replaced. Several good reviews have been written on osteoporosis pathogenesis (17; 22).

Osteoporosis is a crippling disease causing infirmity in patients and making them more susceptible to falls that result in fractures of the hip and wrist. Hip fractures are more common in women whereas wrist fractures are more common in men. Recovery from these falls is seldom satisfactory, and in a third of the cases patients are left with a disability limiting them from doing ordinary tasks. Twenty percent of all patients with a hip fracture pass away within a year.

Osteoporosis affects approximately 12 million Americans; 80% of those are women. Numbers for Europe and Asia are more difficult to quantify because the disease is under diagnosed and under treated (23). Osteoporosis is responsible for more than 1.5 million fractures/year in the United States, and over 4 million in Europe. After age 50 years, 1 in 3 women and 1 in 5 men will sustain a fracture. The global economic impact is in excess of \$17-20 billion in the United States, and \in 25 billion in Europe. The increasing aged population is a huge global societal burden. By the year 2050, the number of hip fractures globally could increase to over 21 million and represent \in 50 billion in medical costs.

3. Dental Health

3.1. Morbidity of oral health issues specifically dental caries

Good oral health is essential for communication, smiling, chewing, and eating. Inability to do any of these leads to lowered self-esteem or could ultimately lead to death by malnutrition. A significant proportion of the world's population is infected with oral diseases that are costly to the human race in terms of morbidity and mortality (24). Oral diseases include dental caries, periodontal diseases, dental erosion, tooth loss, dental fluorosis, oral mucosal lesions and cancers, and noma. Oral diseases are expensive ailments to treat in industrialized nations, and cost unspecified amounts for lost time at school and work. Oral disease is likely to increase in developing countries as they transition to unhealthy diets high in sugars and begin using more tobacco. Furthermore as the global population ages, older people have very different oral health needs compared with children and young adults. The implications for dental costs of this particular population shift are not estimated.

Dental caries and periodontal disease are the dominant global oral health problems. Despite major investments in preventative procedures and educational activities by oral health professionals the problems continue to persist with nearly 100% of the global adult population and 60-90% of school-aged children affected by dental caries (25). Overall, improvements in developed countries have reduced incidence of dental caries and periodontal disease, but lower income and socially disadvantaged groups experience a disproportionately higher level of these diseases than others. For example, although overall severity of dental caries in Europe is fairly low, Eastern Europe has a much higher severity rate than the average.

3.2 Role of dairy in preventing dental caries and other oral health issues

Milk is a biological fluid now recognized as having more importance than just as a nutritive source. Milk has an effect on numerous physiological processes. Proteins, peptides, and other milk components have bioactivities that influence multiple physiological processes throughout the body, and in particular the oral cavity, including mineral metabolism, bacterial inhibition,

cell proliferation, blood clotting, and antioxidation. The incidence and severity of some oral health problems are reduced by milk and dairy products (26). Fluid milk, cheese, casein, and whey products prevent dental caries formation by contributing calcium and phosphate for tooth remineralization. Caseinophosphopeptides participate in the remineralization process by controlling crystal nucleation and growth of hydroxyapatite in the tooth microenvironment (27). Other bioactive components are bacteriostatic or bactericidal to odontopathogenic bacteria (28).

4. Role of dairy calcium on bone and tooth health through life stages

4.1. In utero

From the point of conception, a human begins undergoing rapid stages of physiological development lasting well into the prime of life. Our genome contains a prescribed developmental program defining our ultimate appearance. The human skeletal system develops in utero in two phases. The first phase, termed skeletal patterning, is formation of bones as soft tissue templates (29) during which the basic shape of all bones is preformed and completed by the end of embryonic development. In the second phase, soft tissue is calcified and begins growing in length and mass. Very little change in shape occurs during this phase. This second phase lasts until we reach adulthood and peak bone mass. Maternal nutrition at these stages of development must be optimized to allow proper expression of the fetal genome (30). Any errors by the mother during pregnancy, especially in the first two trimesters, will have lifelong consequences for her child.

Tooth development begins by the tenth day of embryogenesis after craniofacial formation. The mandibular cartilage and bone formation precedes tooth formation just under the differentiating gum epithelial cells (31). Further cell differentiation and specialization occurs throughout fetal development with the ultimate shape and positioning of primary teeth including dentine and enamel formation being completed while the fetus is in the womb. Within 6 months after birth, the genome completes tooth root formation including the circulatory and neural systems preceding tooth eruption.

Both tooth and bone developments require appreciable amounts of calcium from the pregnant mother. If her calcium and vitamin intake are inadequate, there could be damage to both the mother and fetus. Intrauterine programming appears to be a major contributor to the risk of osteoporosis in later life (32). Positive correlations indicate weight at birth and one year are related to adult bone mass, size, and density. Birth weight is significantly correlated with spinal and femoral BMC in adult men and women (33; 34). Further analysis of these data showed lifestyle and other factors (e.g. age, tobacco smoking and alcohol consumption, social class, physical activity, hormone replacement therapy, or years since menopause) had little effect in this correlation. However, genetic influences on bone size and density can be modified by undernutrition *in utero* (33).

The impact of maternal nutrition on intrauterine programming and ultimately an offspring's susceptibility to bone and tooth issues after birth should not be underestimated. A diet rich in dairy products will supply nutrients needed by both the mother and her fetus. Dairy foods are rich sources of protein, calcium, vitamins, phosphorus, magnesium, zinc, and bioactive components that will contribute to bone and tooth health. Pregnant teenagers compete with their developing fetuses for nutrients, especially calcium and vitamin D, required for developing bone mineralization (35). Pregnant women past peak bone mass accretion are less prone to this. When compared to offspring from mothers who followed a good nutritional program that included adequate dairy intake during pregnancy, children born to dairy-deficient mothers had lower birth weights (36), shorter femoral lengths (35), and lower BMC (37).

4.2. Birth (0-1 year old)

The average human body length at birth is 35.5 to 51 cm. Although all elements of the skeleton are present at birth, several major bones have not mineralized including the cranium and pelvis. Most infants are born edentulous, but often teeth are beginning to form under the infant's

gums. Their senses (hearing, sight, feeling, and smell) begin functioning immediately after birth though their acuity will not be as competent as what they will be after several months in normal development. The first year marks very rapid skeletal development as an infant will increase its height by 50%, and triple its weight.

Human milk is recommended as the only nutritional source during the first six months of life. However, numerous mothers tend to feed their infants infant formula because of convenience or a physical reason for not being able to breast feed. Bone accretion is more rapid in formula-fed infants than breast-fed. Human breast milk is lower in vitamin D and phosphate concentration decreases with increasing length of lactation (38). Many children are weaned from breast milk at 4 to 6 months of age, and with introduction of phosphate containing foods a breast fed infant total body BMC quickly equalizes formula-fed infants. Children breast fed for longer than 3 months have higher BMD values at 8 years of age than formula-fed children (39). Bone formation and growth in infants is stimulated by exercising the infant. Simple exercises, such as having the infant stand with assistance, will influence forces in large muscle groups to exert pressure on long bones in turn stimulating bone cell activity (38). Exclusively breast-fed infants should be supplemented with vitamin D to prevent rickets (osteomalacia), and improve calcium accretion prior to weaning.

Primary teeth begin erupting through the gums around 6 months of age, and the process continues through the child's first 2 years of life. Method of feeding seems to have little to no effect on the potential for tooth decay in infants (40). However, mothers should use caution when bottle feeding to not allow the infant to sleep with a bottle as carbohydrates (usually lactose and/or sucrose) in formula may lower pH in the oral environment and encourage growth of cariogenic bacteria. Infants ingesting foods, especially milk and other dairy products, high in calcium and phosphate will promote tooth mineralization which will lead to stronger primary teeth.

4.3. Childhood (1-10 years old)

Children 1 to 10 years old become very active, and are rapidly developing social skills important for later life. Boys and girls are growing at nearly equal rates at this point although boys later in this life stage will have greater bone mass than girls (Figure 4). At 2 years of age a child will weigh 4 times its birth weight if given adequate nutrition since birth; during the next 7 years children will gain weight at a rate of 1.8 to 2.3 kg/year. Their height correlates well with weight gain – a child will grow about 12.7 cm between 1 and 2 years, from 2 to 3 years about 3.5 cm/year, and from 3 years to puberty will grow another 5.1 cm/year. Much of a child's growth, height and weight, is encoded from their genetics and metabolic programming, but nutrition and exercise can also be major contributors.

Usually by 6 years of age children have a full set of primary teeth. Proper nutrition and oral hygiene protect these teeth from dental caries and decay. The "window of infectivity" for cariogenic bacteria begins when a child is around 2.5 years old. Parents should teach their children proper dental hygiene. Habits started in this age group usually persist throughout a lifetime. Primary teeth are replaced late in this life stage by permanent teeth.

The recommended daily calcium intake for children at this age is 700 to 1300 mg with higher levels being important as they near puberty later in this life stage. Inadequate nutrient intake (especially calcium and vitamin D) can contribute to bone accretion (38). Vitamin D deficiency will result in children developing rickets (osteomalacia).

More adolescents are being diagnosed with low BMD and osteoporosis than in previous generations of children. Those children diagnosed with osteoporosis had rare inherited conditions, but secondary forms of osteoporosis are becoming more common in recent years (41). There appear to be more societal issues with this than clinical. For example, current generations of young parents are not influencing their children to consume milk and dairy products because they themselves are not avid consumers. Childhood obesity is becoming a serious issue. However, it is not obesity implicated in lower bone mass in this age group, it is onset of Type II insulin dependent diabetes mellitus (T2DM) that impacts BMC (42). Few studies have addressed the impact of T2DM on bone health and later life development of osteoporosis. Studies with adults

inflicted with T2DM indicate accumulation of advanced glycation end products within the bone collagen may increase cortical porosity (42). This will ultimately interfere with bone remodeling. This is also seen in Type I diabetic patients after puberty (43; 44). This is certainly an emerging area for research.

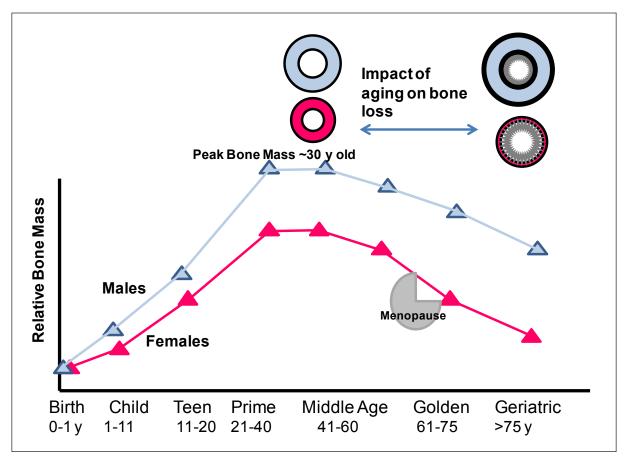


Figure 4. This graphic demonstrates peak bone mass development in boys and girls maturing through their life stages. The inset above demonstrates the absolute amount of endosteal bone loss is similar through aging in both men and women. However, the absolute amount of periosteal bone gained in less in women than men. Aging causes a greater net bone loss in women than men because of sex differences in absolute bone gain, not loss.

In studies with children that have been long term milk avoiders, it has been observed they tend to be more obese, shorter in height, had lower BMC, and lower BMD at several body locations (45). This group of children also had a greater number of fractures than children consuming milk consistently. Studies indicate the majority of girls 9 to 11 years old are not meeting their daily calcium requirements (46). This resulted in lower total body BMC. This study also reported young girls are receiving 70% of their calcium intake by consuming dairy products. The authors suggested increasing dairy intake among girls this age could be an effective strategy to increase calcium intake that will be important as they enter puberty.

Yogurt is an effective dairy product to prevent dental caries in primary teeth during this life stage (47). Japanese children 3 years old consuming yogurt (>4 servings per week) were 33% less likely to have dental caries than lower consuming groups. Yogurt has appreciable levels of calcium and phosphate to contribute to enamel remineralization. Protein hydrolysis by the starter cultures may also have liberated caseinophosphopeptides to promote tooth remineralization (28; 48). Another study in 3 to 5 year old children reported similar results (49).

4.4. Teenage (11-20 years old)

Puberty usually begins in girls around 9 to 10 years old, and boys begin around 12 years old. Girls usually have completed puberty by 15 to 17 years of age, and boys are completed around 16 to 18 years old. Puberty has a major role in bone development with skeletal mass doubling by the end of adolescence (50). The sex steroids (estrogen and testosterone, for girls and boys respectively), growth hormone, and insulin-like growth factors are determinants for pubertal bone mass increases. Proper nutrition, especially vitamin D, calcium, and phosphorus intakes, are critical for optimized bone mass accretion. Peak calcium-accretion rate is attained in this life stage. Girls peak at an average age of 12.9 years, but boys do not peak until 14.0 years old (51). Forty percent of the total lifetime bone mass is acquired during this period of life. Unfortunately this is also the age span teenagers begin consuming larger amounts of carbonated soft drinks instead of milk and other dairy products (Figure 5). Many teenagers, especially females, will experiment with fad diets or claim they are lactose intolerant to avoid drinking milk. Primary lactase deficiency does affect 70% of the world's population (52), but usually is not severe enough in teenagers of any race or ethnicity to justify not consuming the daily recommended levels of dairy products. Lactose can be tolerated in this age group by ingesting their 3 to 4 servings per day in smaller volumes more frequently throughout the day. As mentioned earlier, it is difficult to consume other food products to match the quantity of calcium derived from dairy during this rapid bone growth life stage. This is also a life stage when bone fractures begin increasing as children become more active in contact sports, vigorous exercise, or rough housing with each other. A fracture during this life stage will not properly heal if nutrition is inadequate, and will cause problems in later life.

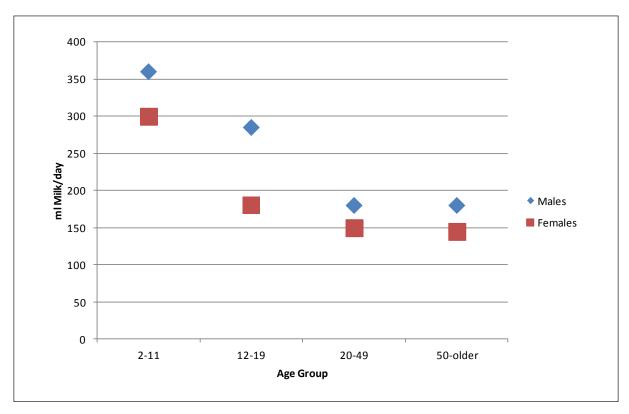


Figure 5. Although children drink the recommended daily amounts of milk while younger, as they enter teenage years they consume less for a variety of reasons. Neither sex consumes the recommended amounts as they age further, and need to ingest calcium from other food sources or supplements to supply the body with the required amounts of calcium for metabolism and to maintain skeletal integrity as they age.

Anorexia nervosa onset is usually during adolescence at a time when peak bone mass is accruing, and particularly impacts women. The disease is associated with reduced bone mass and bone fragility (53). Low bone mass in these patients seems to occur as a result of accelerated bone resorption and reduced bone formation. Clinical treatment of these patients is necessary because they often suffer from sex hormone deficiencies, hypercortisolism, low body weight, and poor nutrition that offer other complications such as multiple vitamin and mineral deficiencies. These individuals have increased incidences of bone fractures while they are anorexic, and most likely as they age will be more prone to fractures because of poor bone architecture.

Primary teeth have been replaced by permanent teeth. Teeth during this life stage continue to undergo rapid mineralization similar to bones to increase in mineral density. Dental hygiene becomes more critical as these teeth should literally last a lifetime. However, males tend to pay less attention to oral hygiene and often gingivitis begins during the teenage years. Also at the onset of puberty, hormonal imbalances seem to have a negative impact on tooth remineralization. Increased consumption of soft drinks in lieu of milk creates an unhealthy environment at the tooth's surface. Soft drinks are high in phosphoric acid causing tooth demineralization. Pit and fissure formation on the tooth's surface creates an environment which gives cariogenic bacteria an advantage to cause tooth decay (28).

This life stage is the most critical time in a human's life to follow a diet high in dairy products to meet the needs of a rapidly growing skeletal system. The recommended daily calcium intake for this life stage is 1300 mg which is approximately 1 liter milk per day or 750 ml of yogurt. Most older teenage, American adolescents do not achieve the recommended daily calcium intake (54). Higher milk intake during adolescence sets a pattern for good milk consumption in later life (55). High dairy intake during adolescence has a protective effect against fractures in boys and girls (56; 57). Young adolescent women who are good milk consumers have higher BMD and BMC than their negative cohort. This carries over into the period of life where peak bone mass is accumulating. Milk consumption frequency and intake levels were a good predictor of overall height in 12 to 18 year olds (58; 59). Epidemiological data indicates meeting the recommended daily intake of dairy during adolescence will achieve optimal bone mass accretion and reduce the degree of osteoporosis in adulthood (54). In pre-pubertal adolescents who are high consumers of dairy products normally, there is no increased benefit to bone health (60). Therefore, we cannot makeour children grow larger (height or BMD) by feeding them more milk! Adolescents meeting the daily recommended intake for dairy products showed no impact on overall body weight or body composition (61).

The role of calcium supplements to meet recommended daily nutritional needs by this age group has also been studied. In a group of 10-12 year old girls, cheese consumption (1000 mg Ca/d) was more beneficial to increasing cortical bone mass than similar amounts of calcium ingested as supplements (62). In a rodent model, non-fat dry milk was reported to be more effective than calcium carbonate supplements in improving BMD, BMC, cortical bone thickness, and improving bone strength (63).

Adolescents avoiding milk have lower BMC and sustain more forearm fractures (64). In a group of adolescents with low BMC that increased their milk consumption for 2 years after diagnosis, BMC and bone mass were found to recover but BMD levels were still lower than the earlier dairy consuming cohort (65). Height reduction and osteopenia also persisted in the dairy adverse group even after moderately increasing their milk consumption.

Dairy intake during adolescence is vitally important for BMC and BMD in later life, which will somewhat mitigate osteoporosis progression. Women aged 20 to 49 years old had lower BMC (5.6%) if they consumed less than 1 serving of dairy per week than children consuming more dairy products (66). Low milk intake in adolescence also impacted hip bone BMC and BMD. Women older than 50 years of age had a non-linear impact on hip bone BMC and BMD. However, women with low milk intake during childhood years had a greater than 2-fold risk of bone fractures.

4.5. Prime of life (21-40 years old)

Early in this life stage young human adults are at their "prime of life" in terms of physical growth and development. All of our internal organs, immune system, and other bodily systems have reached full development and are functioning at their peak in terms of strength and efficiency. This is the period of our life we are healthiest and sick the least amount of time. Our full height potential is usually reached by our mid-twenties. Our skeletal bones have reached their maximum bone mineral concentration, and stop growing in length and mass. After we peak in our mid twenties, our osteoblasts become less efficient at synthesizing new bone, and our BMD begins decreasing in our mid-30's. However, we still regenerate 3% new compact bone every year. Many become parents during this life stage which leads to bodily changes in the female as a result of pregnancy and possibly breast feeding. Although this life stage seems to be an age where we will be "at our peak" until we reach 40 years old, in reality the process of senescence begins during young adulthood and we begin declining in our physical development with decreases in the efficiency of our internal organs and bodily systems. It is also a stage of life when we are apt to experience high levels of stress often leading to substance abuse or poor nutritional habits. A result is establishment of negative habits that will impact us severely over the next couple of decades. It is extremely important during this life stage to eat correctly and include vigorous exercise in our weekly routines.

Oral health issues begin surfacing in this age group, and by the time most of us turn 30 years old we have had at least one tooth cavity (Figure 6). Humans during this life stage are susceptible to oral diseases for a number of reasons including genetics, poor hygiene, poor nutrition, alcohol and tobacco use, drug abuse (67), and complications from other diseases such as diabetes (68; 69), cancer (70), obesity (71), and osteoporosis (72). Oral infections themselves may play a role in progressing pathogenesis of many systemic diseases in healthy individuals, ill patients, and those immune-compromised (73).

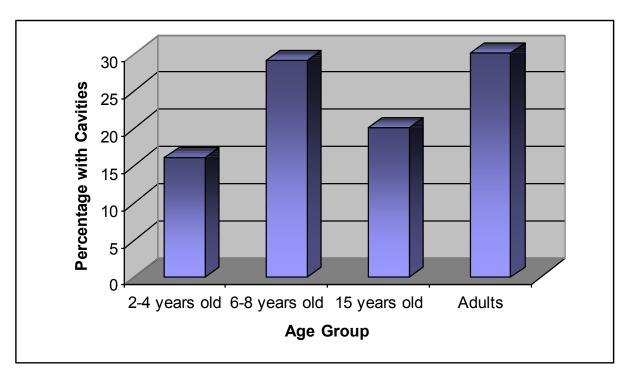


Figure 6. Dental caries are prevalent in all of the American population by adulthood. Similar trends are reported from other developed countries.

The recommended daily calcium intake for this life stage is 1000 mg for both men and women. Although this is typically the child-bearing life stage for many women, there is not a separate recommended daily intake for pregnant and lactating women. Many obstetricians are recommending that pregnant women consume 1200 mg calcium per day especially in the last trimester. Theoretically, women not meeting the body's calcium requirements during pregnancy could experience bone loss, impaired breast milk concentration, pre-eclampsia, or impaired fetal bone development. This could also put the mother at risk for osteoporosis in later life, however intestinal absorption of dietary calcium increases during pregnancy to compensate for the fetus' need (74). Calcium needed for breast milk is met by renal calcium conservation and by mobilization of calcium from the maternal skeleton. The body quickly replaces calcium after a woman resumes her menstrual cycle. Pregnancy and lactation does not seem to put women at an increased risk of osteoporotic fractures in later life.

Calcium intake through dairy products in this life stage is more about maintaining bones and teeth, which hopefully had a healthy start during adolescence. Peak bone mass is achieved between our 25th and 30th birthday. Dairy products need to be consumed in order to maintain a sufficient calcium pool for final bone development and tooth mineralization. The recommendation of three dairy servings per day will supply nearly all of the calcium required for this age group so long as a healthy life style is maintained, the individual does not smoke, suffer from substance abuse, or is a diabetic. Under any of these negative circumstances calcium/dairy intake will need to be increased.

4.6. Middle age (41-60 years old)

Numerous physiological changes begin occurring in this life stage. Both sexes begin developing skin wrinkles, loss of muscle tone, inefficiencies in organ function, fine motor skills begin deteriorating, reaction time increases, and our senses further lose their acuity. Our vision and hearing are especially impacted as many of us become far-sighted in our early 40's. Taste begins diminishing because we have lost 50% of the fungiform papillae on our tongues by the time we turn 50 years old. We notice ourselves slowing down as our heart and lung capacities are not as great as they once were earlier in our lives. At this life stage we also begin experiencing sleeping problems with sleep disordered breathing (SDB) being common in a third of us (75). A small percentage of men (6.8%) are prone to a more severe sleep disorder, sleep apnea disorder, at this age. Men with sleep apnea are more prone to hypertension, cardiovascular disease, stroke, daytime sleepiness, motor vehicle accidents, and a diminished quality of life (76).

Women especially undergo major physiological changes as estrogen levels begin decreasing and they generally enter menopause early in this life stage. Menopause has several symptoms that make women uncomfortable such as irritability, hot flushes, sweats, headaches, and swelling in different bodily regions. However, none of these symptoms are as serious as the decreases in BMD (osteopenia) that begins occurring at this age. Although genetics is a major contributor to a human developing osteoporosis, women who did not consume enough calcium through dairy or supplementation earlier in their lives will experience accelerated bone mineral loss, and minute fractures will begin developing in the spinal processes. As estrogen levels further decrease BMD loses continue, the bones begin structural deterioration and become more fragile. At that stage women (and men) have osteoporosis. The first visible signs of bone degeneration are noticed as we move from the correct upright posture we had in our late twenties toward a slumping appearance first noticed in the upper cervical vertebrae regions. As we age, our susceptibility to falls increases and usually results in fractures especially in people with osteoporosis. The results are frequently debilitating and crippling, with an increased risk of morbidity within a year after hip fractures.

Women can reduce the morbidity and eventually mortality associated with osteoporosis in this life stage by making some life style changes before menopause. These changes include making changes to healthier diets that include three dairy servings a day, stopping smoking, confirming adequate daily intake of vitamin D along with some sun exposure (15 to 20 minutes), and consistent weight-bearing exercise regimes (77). Life style changes such as this will ensure proper calcium is being ingested and absorbed for bone remodeling, and exercise will provide better

mobility as a woman continues to age. In the event she does fall, muscle mass surrounding the bones will be a better protective agent than fat or soft tissue.

Men also undergo male climacteric (male menopause) at this age as testosterone levels decrease. This causes physical symptoms such as poor appetite, lower libido, weakness, and inability to focus on tasks. None of these symptoms are as severe as those of female menopause. At this age, men only have a 30 to 45% likelihood of having osteoporosis compared to women at 50%. Early signs of cardiovascular disease, such as hypertension and dyslipidemia, become more common at this life stage. The prevalence of CVD steadily increases as we age in this life stage.

After decades of chewing food, potential nocturnal grinding, and inadequate nutrition our teeth begin showing combinations of erosion, attrition, and abrasion (78). Attrition usually occurs on the incisional and occlusal tooth surfaces as a result of tooth meeting tooth contact during improper chewing, grinding of the teeth, or clenching the jaw. These actions wear through the enamel and can eventually penetrate to the dentine areas. Teeth erode from dietary and gastric acids in contact with our tooth enamel, and when combined with attrition or abrasion there is a rapid rate of enamel wear on the tooth. This gives rise to the yellowing of teeth late in this life stage and into proceeding life stages. Inadequate oral hygiene in earlier life stages begins to cause complications in our oral health with periodontitis becoming common in this life stage. Oral inflammatory processes in vicinity of the skeleton can induce osteolysis where the amount of bone being resorbed exceeds that being formed. As time passes, the bone structure exhibits all the symptoms of osteoporosis (79). As osteoporosis proceeds, loss of mandibular tissue may cause a loosening of teeth in the jaw sockets that become more infected by periodontal pathogens potentially causing tooth loss. However, studies have been unsuccessful in demonstrating a consistent relationship between periodontal disease and tooth loss (80). Periodontitis diagnosed with radiologic evaluation may be an early warning sign of osteoporosis, and dentists are advised to suggest to these patients to visit an orthopedist.

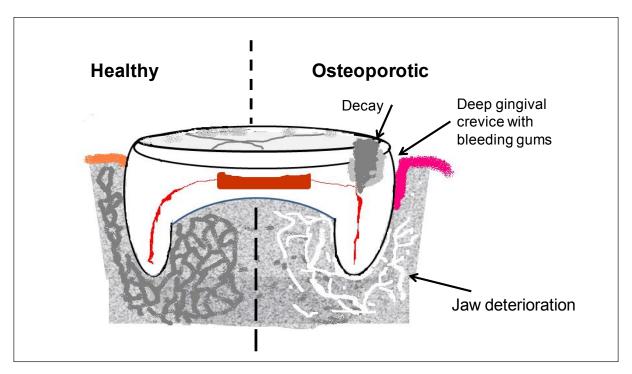


Figure 7. The left side of this drawing shows normal tooth anatomy in a healthy individual, whereas the right side shows the effects of osteoporosis. Teeth and affected by osteoporosis by an increase in dental caries, gingivitis, periodontitis, and eventually tooth loss as the jaw mandible deteriorates past a point teeth can be retained in the jaw socket.

It is important for this age group to maintain a diet consuming 1000 mg of calcium daily or the equivalent of 3 dairy or milk servings. Both sexes should strive to meet these dietary requirements although women are far more susceptible to osteoporosis at this age. Cross-sectional nutrition studies indicate both men and women were protected from bone loss in an intervention trial (81). There is also some indication calcium intake may reduce fracture risk if older women fall (82).

Oral health also benefits from dairy consumption in this life stage. Calcium is available to interact with fluorine from oral hygiene products to promote remineralization of teeth, and reducing dental caries. Furthermore, it appears dairy calcium has a role in preventing and treating periodontitis (83). Elderly adults often suffer from hyposalivation caused by numerous medications and this could compound the potential for dental caries. This condition is called xerostomia, and patients are often recommended to consume more milk because it has physical properties similar to saliva (84).

4.7. Golden years (61-75 years old)

The "golden years" are not really too precious. By the time we reach this life stage we are seeing an acceleration of the aging process affecting nearly every bodily system. We have increased losses in circulatory capacity that results in less blood flow to our kidneys and brain. Our nerves are less capable to transmit impulses to the brain. Our brain by this time has lost as much as 45% of the cells in the cerebral cortex, and weighs 7% less than in the prime of our lives. Renal function has decreased by 50% at age 70 causing us problems with dehydration and urinary tract infections. Soft tissues in our body, including skeletal connective tissue, eyes, ears, and circulatory system are less flexible and become rigid or hard as we age further. A third of all people over 65 have suffered hearing loss, and this percentage increases as we progress later in this life stage. Our sense of taste and smell have deteriorated to the point where it is difficult to distinguish saltiness and sweetness. We may not taste when a food is spoiled. Bone loss is more rapid in this age group regardless of the presence of osteoporosis. We begin looking and moving as frail individuals with poor stability, balance, and a propensity to falls. If we have osteoporosis, fractures are more frequent and crippling. However, a study of men and women >60 years old indicated dairy consumption at this age maintained a higher hip BMD in men than women (81).

T2DM is prevalent in developed countries and the aging population causing an increased risk of falling and vascular problems (85). This disease does not affect BMD in this age group. However, hip fracture risk increases in elderly people with T2DM 1.4 to 1.7 fold; vertebral fracture risk also increases. It is thought both these risks are associated with bone quality deterioration rather than bone mass reduction.

The situation for our teeth is just as grim – if we are lucky enough to still have teeth. All of the issues mentioned in the earlier life stages continue to further reduce our ability to keep our teeth at this age. Nearly 25% of all people over 65 have lost all of their teeth; periodontal disease affects over 50% of this age group. The remaining teeth are very brittle, yellowing, usually loose in the jaw socket, and very susceptible to breaking. Gum disease can lead to more serious problems such as endocarditis. Proper nutrition and a healthy life style (including not drinking, smoking, or taking prescription drugs) may prolong the time a person has before there are problems with their teeth.

The recommended daily Ca intake level for this life stage is 1200 mg - an increase over earlier life stages. The recommended increase is to compensate for the rapid bone remodeling in progress with this age group either by decreasing bone resorption rate or by providing a pool of calcium for remineralization. Milk and dairy products can be developed for elderly people by fortifying with vitamin D, calcium, and protein to provide a nutritional supplement that influences bone remodeling. Parathyroid hormone activity is reduced in older women consuming fortified milk for 16 weeks (86). In addition, lower levels of serum cross-linked telopeptide of type I collagen, propeptide of type I procollagen, and osteocalcin were reported. These results would be compatible with reduced bone turnover, and offers a nutritional approach to controlling osteoporosis in

1000

post-menopausal women. An increase in yogurt consumption (3 servings per day) by post-menopausal women, lowered urinary excretion of N-telepeptide a biomarker of bone resorption within 7 days of beginning the diet (87). Reduced bone resorption was observed in a similar study with older women consuming a cheese product fortified with vitamin D, calcium, and protein (88; 89). Dairy protein (whey protein isolate) ingestion in addition to calcium and vitamin D can be important in the elderly to maintaining bone health. Protein ingestion improves calcium absorption, elevates insulin-like growth factor I (IGF-1), and increases muscle mass and strength (90). Improvement in muscle mass could prevent fractures in the event of falling.

Lifestage	Calcium (mg/day)¹	Milk Equivalent (ml/day)
Infant (0-1 y)		Breast milk only
Childhood (1-11 y)	700-1100	585-920
Teen (11-20 y)	1100	920
Prime (21-40 y)	800	670
Pregnant and Lactating Women	1300	1085
Middle Age (41-60 y)	800-1000	670-835
Golden (61-75 v)	1200	1000

1200

Table 1: Recommended Daily Intake of Calcium Through Life Stages.

4.8. Geriatric (>75 years old)

Geriatric (> 75 y)

Better nutrition and health care than in past generations has enabled more people to live past 75 years old. If we are fortunate enough to have combined this with very good genetics and a healthy life style our entire lives we will make it to this point in life. However, our bodies are really beginning to struggle for survival. There are exceptions, but this age group has greatly reduced mobility, mental capacity, and their quality of life is greatly diminished compared to the prime of their lives. The United States has the largest numbers of individuals that have made it to be 100 years old (centenarians). There is quite a bit of contradictory information why these individuals live so long. Most of the research findings continue to indicate genetics, nutrition, and life style as the positive effectors. Those who consumed diets high in fiber, antioxidants, dairy, and low in fat, red meat, and carbohydrate tend to live longer and healthier. Life style habits to minimize detrimental aging effects included minimal alcohol consumption, low stress lives, frequent exercise (including at this particular age), no smoking, and spirituality. Nearly all women in this age group suffer from osteoporosis which results in relatively poor teeth and bones. In addition, osteoporosis in males rises exponentially in this life stage (91). The disease goes undiagnosed unless the man falls and fractures a bone. Minute fractures in the spine do not become as apparent in males at this age as they do in post menopausal women. Estrogen formation by aromatization of androgens triggers male osteoporosis (92). Enzymatic conversion of androstenedione to estrone and conversion of testosterone to estradiol causes suppression of osteoclasts generation and activation (93). This results in bone remodeling being shifted towards resorption similar to post menopausal hormone deficiency resulting in changes to bone microarchitecture. However, a complete model to explain male osteoporosis pathogenesis is still not completed. When men fall at this age it can be as devastating to them as women experience earlier in life with near certainty they will fracture a bone.

The role of dairy in this life stage is to provide a continual supply of calcium to the body for metabolic purposes including bone and tooth remodeling. The challenge aged individuals endure is consuming enough sustenance to maintain daily recommended levels of calories and

¹ Amounts recommended by the United States Department of Agriculture in Dietary Guidelines for Americans, 2010 (Reference: 5).

nutrients for survival (94). Consequences of malnourishment include inadequate micronutrient intake predisposing individuals to increased morbidities. Diets for this age group should include heavily fortified foodstuffs especially vitamins and minerals. Postmenopausal women showed improved bone metabolism benefits from a dietary intervention of dairy products fortified with elevated levels of calcium and vitamin D compared to simple calcium supplementation alone (95). Furthermore, elderly patients (> 60 years old) should be taking supplements to supply the recommended daily levels of vitamin D in conjunction with daily exposure to sunlight for optimal bone and muscle health (96).

5. Future Research and Conclusions

The impact of dairy products on improving bone and oral health is substantiated by considerable scientific evidence. Undoubtedly, milk's overall composition contributes to the nutritional impact, but key components exemplify an ability to provide nutrients needed for bones and teeth. Calcium and vitamin D are critical for well being throughout all stages of life. Additionally, there are several other vitamins, minerals, proteins, and peptides influencing bone and tooth metabolism. Prevention of later life bone and oral health morbidities is metabolically imprinted by human behavior during their adolescence. Insufficient intake of calcium during our pubertal years combined with our genetics could be establishing symptoms that will not manifest themselves until we reach our later years of life. Although there is a plethora of scientific data there remain numerous questions to the role of dairy, and specifically calcium, on bone and tooth health. For example, a potential research area is to investigate later life effects on osteoporosis in infants exclusively breastfed for extended periods of time (> 6 months). Male osteoporosis and pathogenesis is only beginning to be understood, and the role of dairy and calcium in middle and late life stages has not been addressed in preventing this disease. What is the exact role of dairy calcium in geriatrics greater than 75 years old? Finally, life style and genetics may influence bone and oral health disease progression, but dairy products provide a nutrient dense food that contains readily bioavailable calcium to reduce or mitigate morbidity. We should continue listening to our mothers as we age - "drink your milk!"

6. References

- Pennings, B., Boirie, Y., Senden, J. M. G., Gijsen, A. P., Kuipers, H. & Van Loon, L. J. C. Whey
 protein stimulates postprandial muscle protein accretion more effectively than do casein
 and casein hydrolysate in older men. American Journal of Clinical Nutrition. 93:997-1005
 (2011).
- 2. Martin III, W. H., Ogawa, T., Kohrt, W. M., Malley, M. T., Korte, E., Kieffer, P. S. & Schechtman, K. B. Effects of aging, gender, and physical training on peripheral vascular function. Circulation. 84:654-664 (1991).
- 3. Clare, D. A. & Swaisgood, H. E. Bioactive milk peptides: A prospectus. Journal of Dairy Science. 83:1187-1195 (2000).
- 4. D'Alessandro, A., Scaloni, A. & Zolla, L. Human milk proteins: An interactomics and updated functional overview. Journal of Proteome Research. 9:3339-3373 (2010).
- 5. United States Department of Agriculture and United States Department of Health and Human Services. Dietary guidelines for Americans, 7th edition. U.S. Government Printing Office, Washington D.C. (2010).
- 6. Kit, B. K., Carroll, M.D. & Ogden, C.L. . Low-fat milk consumption among children and adolescents in the United States, 2007-2008. United States Department of Health and Human Services, National Center for Health Statistics, No. 75 (2011).
- 7. Fulgoni III, V., Nicholls, J., Reed, A., Buckley, R., Kafer, K., Huth, P., Dirienzo, D. & Miller, G. D. Dairy Consumption and Related Nutrient Intake in African-American Adults and Children in the United States: Continuing Survey of Food Intakes by Individuals 1994-1996, 1998, and the National Health and Nutrition Examination Survey 1999-2000. Journal of the American Dietetic Association. 107:256-264 (2007).

- 8. Gao, X., Wilde, P. E., Lichtenstein, A. H. & Tucker, K. L. Meeting Adequate Intake for Dietary Calcium without Dairy Foods in Adolescents Aged 9 to 18 Years (National Health and Nutrition Examination Survey 2001-2002). Journal of the American Dietetic Association. 106:1759-1765 (2006).
- 9. Cashman, K. D. Milk minerals (including trace elements) and bone health. International Dairy Journal. 16:1389-1398 (2006).
- 10. Heaney, R. P. Calcium intake and disease prevention. Arquivos Brasileiros de Endocrinologia e Metabologia. 50:685-693 (2006).
- 11. Theobald, H. Dietary calcium and health. Nutrition Bulletin. 30:237-277 (2005).
- 12. Miyamoto, Y. & Kamijo, R. Overview: Molecular regulation of mineralization and its failure. Journal of Oral Biosciences. 52:1-5 (2010).
- 13. Teti, A. Bone development: overview of bone cells and signalling. Current Osteoporosis Reports. *In press. Online September 27*, 2011.
- 14. Heaney, R. P. Calcium, dairy products and osteoporosis. Journal of the American College of Nutrition. 19:83S-99S (2000).
- 15. Cheng, S., Lyytikäinen, A., Kröger, H., Lamberg-Allardt, C., Alén, M., Koistinen, A., Wang, Q. J., Suuriniemi, M., Suominen, H., Mahonen, A., et al. Effects of calcium, dairy product, and vitamin D supplementation on bone mass accrual and body composition in 10-12-y-old girls: A 2-y randomized trial. American Journal of Clinical Nutrition. 82:1115-1126 (2005).
- 16. Heaney, R. P., Abrams, S., Dawson-Hughes, B., Looker, A., Marcus, R., Matkovic, V. & Weaver, C. Peak bone mass. Osteoporosis International. 11:985-1009 (2000).
- 17. Manolagas, S. C. Birth and death of bone cells: Basic regulatory mechanisms and implications for the pathogenesis and treatment of osteoporosis. Endocrine Reviews. 21:115-137 (2000).
- 18. Heaney, R. P. How should we evaluate bone mass in children? Journal of Bone and Mineral Research. 22:1313 (2007).
- 19. Bishop, N., Braillon, P., Burnham, J., Cimaz, R., Davies, J., Fewtrell, M., Hogler, W., Kennedy, K., Mäkitie, O., Mughal, Z., et al. Dual-Energy X-ray Aborptiometry Assessment in Children and Adolescents with Diseases that May Affect the Skeleton: The 2007 ISCD Pediatric Official Positions. Journal of Clinical Densitometry. 11:29-42 (2008).
- 20. Tuchman, S., Thayu, M., Shults, J., Zemel, B. S., Burnham, J. M. & Leonard, M. B. Interpretation of Biomarkers of Bone Metabolism in Children: Impact of Growth Velocity and Body Size in Healthy Children and Chronic Disease. Journal of Pediatrics. 153:484-490.e482 (2008).
- 21. Gafni, R. I. & Baron, J. Overdiagnosis of osteoporosis in children due to misinterpretation of Dual-energy x-ray absorptiometry (DEXA). Journal of Pediatrics. 144:253-257 (2004).
- 22. Seeman, E. Invited Review: Pathogenesis of osteoporosis. Journal of Applied Physiology. 95:2142-2151 (2003).
- 23. International Osteoporosis Foundation: www.iofbone health.org/patients-public/osteoporosis-socieites-worldwide.htm (2011).
- 24. Petersen, P. E. The World Oral Health Report 2003: Continuous improvement of oral health in the 21st century The approach of the WHO Global Oral Health Programme. Community Dentistry and Oral Epidemiology. 31:3-24 (2003).
- 25. Petersen, P. E., Bourgeois, D., Ogawa, H., Estupinan-Day, S. & Ndiaye, C. The global burden of oral diseases and risks to oral health. Bulletin of the World Health Organization. 83:661-669 (2005).
- 26. Erlebacher, A., Filvaroff, E.H., Gitelman, S.E. & Derynck, R. Toward a molecular understanding of skeletal development. Cell. 80:371-378 (1995).

- 27. Stayton, P. S., Drobny, G. P., Shaw, W. J., Long, J. R. & Gilbert, M. Molecular recognition at the protein-hydroxyapatite interface. Critical Reviews in Oral Biology and Medicine. 14:370-376 (2003).
- 28. Aimutis, W. R. Bioactive Properties of Milk Proteins with Particular Focus on Anticariogenesis. Journal of Nutrition. 134:989S-995S (2004).
- 29. Erlebacher, A., Filvaroff, E. H., Gitelman, S. E. & Derynck, R. Toward a molecular understanding of skeletal development. Cell. 80:371-378 (1995).
- 30. Wu, G., Bazer, F. W., Cudd, T. A., Meininger, C. J. & Spencer, T. E. Maternal Nutrition and Fetal Development. The Journal of Nutrition. 134:2169-2172 (2004).
- 31. Slavkin, H. C. Molecular determinants of tooth development: A review. Critical Reviews in Oral Biology and Medicine. 1:1-16 (1990).
- 32. Gale, C. R., Martyn, C. N., Kellingray, S., Eastell, R. & Cooper, C. Intrauterine programming of adult body composition. Journal of Clinical Endocrinology and Metabolism. 86:267-272 (2001).
- 33. Dennison, E. M., Arden, N. K., Keen, R. W., Syddall, H., Day, I. N. M., Spector, T. D. & Cooper, C. Birthweight, vitamin D receptor genotype and the programming of osteoporosis. Paediatric and Perinatal Epidemiology. 15:211-219 (2001).
- 34. Baird, J., Kurshid, M. A., Kim, M., Harvey, N., Dennison, E. & Cooper, C. Does birthweight predict bone mass in adulthood? A systematic review and meta-analysis. Osteoporosis International. 22:1323-1334 (2011).
- 35. Chang, S. C., O'Brien, K. O., Nathanson, M. S., Caulfield, L. E., Mancini, J. & Witter, F. R. Fetal femur length is influenced by maternal dairy intake in pregnant African American adolescents. American Journal of Clinical Nutrition. 77:1248-1254 (2003).
- 36. Mannion, C. A., Gray-Donald, K. & Koski, K. G. Association of low intake of milk and vitamin D during pregnancy with decreased birth weight. Canadian Medical Association Journal. 174:1273-1277 (2006).
- 37. Javaid, M. K., Crozier, S. R., Harvey, N. C., Gale, C. R., Dennison, E. M., Boucher, B. J., Arden, N. K., Godfrey, K. M. & Cooper, C. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: A longitudinal study. Lancet. 367:36-43 (2006).
- 38. McDevitt, H. & Ahmed, S. F. Establishing good bone health in children. Paediatrics and Child Health. 20:83-87 (2010).
- 39. Jones, G., Riley, M. & Dwyer, T. Breastfeeding in early life and bone mass in prepubertal children: A longitudinal study. Osteoporosis International. 11:146-152 (2000).
- 40. Aimutis, W. R. Lactose cariogenicity with an emphasis on childhood dental caries. International Dairy Journal. *In press*: (2012).
- 41. Da Fonseca, M. A. Osteoporosis: An increasing concern in pediatric dentistry. Pediatric Dentistry. 33:241-245 (2011).
- 42. Valkusz, Z. Diabetes and osteoporosis. Diabetes és osteoporosis. 152:1161-1166 (2011).
- 43. Abd El Dayem, S. M., El-Shehaby, A. M., Abd El Gafar, A., Fawzy, A. & Salama, H. Bone density, body composition, and markers of bone remodeling in type 1 diabetic patients. Scandinavian Journal of Clinical and Laboratory Investigation. 71:387-393 (2011).
- 44. Maggio, A. B. R., Ferrari, S., Kraenzlin, M., Marchand, L. M., Schwitzgebel, V., Beghetti, M., Rizzoli, R. & Farpour-Lambert, N. J. Decreased bone turnover in children and adolescents with well controlled type 1 diabetes. Journal of Pediatric Endocrinology and Metabolism. 23:697-707 (2010).
- 45. Black, R. E., Williams, S. M., Jones, L. E. & Goulding, A. Children who avoid drinking cow milk have low dietary calcium intakes and poor bone health. American Journal of Clinical Nutrition. 76:675-680 (2002).
- 46. Fiorito, L. M., Mitchell, D. C., Smiciklas-Wright, H. & Birch, L. L. Girls' Calcium Intake Is Associated with Bone Mineral Content During Middle Childhood. The Journal of Nutrition. 136:1281-1286 (2006).

- 47. Tanaka, K., Miyake, Y. & Sasaki, S. Intake of dairy products and the prevalence of dental caries in young children. Journal of dentistry. 38:579-583 (2010).
- 48. Cross, K. J., Huq, N. L. & Reynolds, E. C. Casein phosphopeptides in oral health Chemistry and clinical applications. Current Pharmaceutical Design. 13:793-800 (2007).
- 49. Petti, S., Cairella, G. & Tarsitani, G. Rampant early childhood dental decay: An example from Italy. Journal of Public Health Dentistry. 60:159-166 (2000).
- 50. Saggese, G., Baroncelli, G. I. & Bertelloni, S. Puberty and bone development. Best Practice and Research: Clinical Endocrinology and Metabolism. 16:53-64 (2002).
- 51. Bailey, D. A., Martin, A. D., McKay, H. A., Whiting, S. & Mirwald, R. Calcium accretion in girls and boys during puberty: A longitudinal analysis. Journal of Bone and Mineral Research. 15:2245-2250 (2000).
- 52. Heyman, M. B. Lactose intolerance in infants, children, and adolescents. Pediatrics. 118:1279-1286 (2006).
- 53. Golden, N. H. Osteoporosis in anorexia nervosa. Expert Review of Endocrinology and Metabolism. 5:723-732 (2010).
- 54. Greer, F. R., Krebs, N. F., Baker Jr, R. D., Bhatia, J. J. S., Heyman, M. B., Lifshitz, F., Blum-Kemelor, D., Boland, M. P., Dietz, W., Hubbard, V. S., et al. Optimizing bone health and calcium intakes of infants, children, and adolescents. Pediatrics. 117:578-585 (2006).
- 55. Teegarden, D., Lyle, R. M., Proulx, W. R., Johnston, C. C. & Weaver, C. M. Previous milk consumption is associated with greater bone density in young women. American Journal of Clinical Nutrition. 69:1014-1017 (1999).
- 56. Goulding, A., Cannan, R., Williams, S. M., Gold, E. J., Taylor, R. W. & Lewis-Barned, N. J. Bone mineral density in girls with forearm fractures. Journal of Bone and Mineral Research. 13:143-148 (1998).
- 57. Goulding, A., Jones, I. E., Taylor, R. W., Williams, S. M. & Manning, P. J. Bone mineral density and body composition in boys with distal forearm fractures: A dual-energy x-ray absorptiometry study. Journal of Pediatrics. 139:509-515 (2001).
- 58. Wiley, A. S. Does milk make children grow? Relationships between milk consumption and height in NHANES 1999-2002. American Journal of Human Biology. 17:425-441 (2005).
- 59. Wiley, A. S. Consumption of milk, but not other dairy products, is associated with height among US preschool children in NHANES 1999-2002. Annals of Human Biology. 36:125-138 (2009).
- 60. Gibbons, M. J., Gilchrist, N. L., Frampton, C., Maguire, P., Reilly, P. H., March, R. L. & Wall, C. R. The effects of a high calcium dairy food on bone health in pre-pubertal children in New Zealand. Asia Pacific Journal of Clinical Nutrition. 13:341-347 (2004).
- 61. Spence, L. A., Cifelli, C. J. & Miller, G. D. The role of dairy products in healthy weight and body composition in children and adolescents. Current Nutrition and Food Science. 7:40-49 (2011).
- 62. Cheng, S., Lyytikäinen, A., Kröger, H., Lamberg-Allardt, C., Alén, M., Koistinen, A., Wang, Q. J., Suuriniemi, M., Suominen, H., Mahonen, A., et al. Effects of calcium, dairy product, and vitamin D supplementation on bone mass accrual and body composition in 10-12-y-old girls: a 2-y randomized trial. The American Journal of Clinical Nutrition. 82:1115-1126 (2005).
- 63. Weaver, C. M., Janle, E., Martin, B., Browne, S., Guiden, H., Lachcik, P. & Lee, W. H. Dairy versus calcium carbonate in promoting peak bone mass and bone maintenance during subsequent calcium deficiency. Journal of Bone and Mineral Research. 24:1411-1419 (2009).
- 64. Goulding, A., Rockell, J. E. P., Black, R. E., Grant, A. M., Jones, I. E. & Williams, S. M. Children who avoid drinking cow's milk are at increased risk for prepubertal bone fractures. Journal of the American Dietetic Association. 104:250-253 (2004).

- 65. Rockell, J. E. P., Williams, S. M., Taylor, R. W., Grant, A. M., Jones, I. E. & Goulding, A. Two-year changes in bone and body composition in young children with a history of prolonged milk avoidance. Osteoporosis International. 16:1016-1023 (2005).
- 66. Kalkwarf, H. J., Khoury, J. C. & Lanphear, B. P. Milk intake during childhood and adolescence, adult bone density, and osteoporotic fractures in US women. American Journal of Clinical Nutrition. 77:257-265 (2003).
- 67. Shaner, J. W., Kimmes, N., Saini, T. & Edwards, P. "Meth mouth": Rampant caries in methamphetamine abusers. AIDS Patient Care and STDs. 20:146-150 (2006).
- 68. Sandberg, G. E., Sundberg, H. E., Fjellstrom, C. A. & Wikblad, K. F. Type 2 diabetes and oral health: A comparison between diabetic and non- diabetic subjects. Diabetes Research and Clinical Practice. 50:27-34 (2000).
- 69. Twetman, S., Johansson, I., Birkhed, D. & Nederfors, T. Caries incidence in young type 1 diabetes mellitus patients in relation to metabolic control and caries-associated risk factors. Caries Research. 36:31-35 (2002).
- 70. Woo, S. B., Sonis, S. T., Monopoli, M. M. & Sonis, A. L. A longitudinal study of oral ulcerative mucositis in bone marrow transplant recipients. Cancer. 72:1612-1617 (1993).
- 71. Ritchie, C. S. & Kinane, D. F. Nutrition, inflammation, and periodontal disease. Nutrition. 19:475-476 (2003).
- 72. Norlén, P., Steen, B., Birkhed, D. & Björn, A. L. On the relations between dietary habits, nutrients, and oral health in women at the age of retirement. Acta Odontologica Scandinavica. 51:277-284 (1993).
- 73. Ridker, P. M. & Haughie, P. Prospective studies of C-reactive protein as a risk factor for cardiovascular disease. Journal of Investigative Medicine. 46:391-395 (1998).
- 74. Kalkwarf, H. J. & Specker, B. L. Bone mineral changes during pregnancy and lactation. Endocrine. 17:49-53 (2002).
- 75. Zamarrón Sanz, C., Gude, F., Otero, Y., Alvarez, J. M., Golpe, A. & Rodriguez, J. R. Prevalence of sleep disordered breathing and sleep apnea in 50- to 70-year-old individuals. Respiration. 66:317-322 (1999).
- 76. Young, T., Peppard, P. E. & Gottlieb, D. J. Epidemiology of obstructive sleep apnea: A population health perspective. American Journal of Respiratory and Critical Care Medicine. 165:1217-1239 (2002).
- 77. Cuzick, J., Glasier, A., La Vecchia, C., Maraganore, D. M., Negri, E., Rossi, M., Spector, T., Trichopoulos, D., van Baak, M. A., Zocchetti, C., et al. Perimenopausal risk factors and future health. Human Reproduction Update. 17:706-717 (2011).
- 78. Bartlett, D. W. The role of erosion in tooth wear: aetiology, prevention and management. International Dental Journal. 55:277-284 (2005).
- 79. Lerner, U. H. Inflammation-induced bone remodeling in periodontal disease and the influence of post-menopausal osteoporosis. Journal of Dental Research. 85:596-607 (2006).
- 80. Martínez-Maestre, M. A., González-Cejudo, C., MacHuca, G., Torrejón, R. & Castelo-Branco, C. Periodontitis and osteoporosis: A systematic review. Climacteric. 13:523-529 (2010).
- 81. McCabe, L. D., Martin, B. R., McCabe, G. P., Johnston, C. C., Weaver, C. M. & Peacock, M. Dairy intakes affect bone density in the elderly. The American Journal of Clinical Nutrition. 80:1066-1074 (2004).
- 82. Spangler, M., Phillips, B. B., Ross, M. B. & Moores, K. G. Calcium supplementation in postmenopausal women to reduce the risk of osteoporotic fractures. American Journal of Health-System Pharmacy. 68:309-318 (2011).
- 83. Al-Zahrani, M. S. Increased intake of dairy products is related to lower periodontitis prevalence. Journal of Periodontology. 77:289-294 (2006).
- 84. Herod, E. L. The use of milk as a saliva substitute. Journal of Public Health Dentistry. 54:184-189 (1994).

- 85. Yamaguchi, T. & Sugimoto, T. Bone metabolism and fracture risk in type 2 diabetes mellitus. Endocrine Journal. 58:613-624 (2011).
- 86. Bonjour, J. P., Brandolini-Bunlon, M., Boirie, Y., Morel-Laporte, F., Braesco, V., Bertière, M. C. & Souberbielle, J. C. Inhibition of bone turnover by milk intake in postmenopausal women. British Journal of Nutrition. 100:866-874 (2008).
- 87. Heaney, R. P., Rafferty, K. & Dowell, M. S. Effect of yogurt on a urinary marker of bone resorption in postmenopausal women. Journal of the American Dietetic Association. 102:1672-1674 (2002).
- 88. Bonjour, J. P., Benoit, V., Pourchaire, O., Ferry, M., Rousseau, B. & Souberbielle, J. C. Inhibition of markers of bone resorption by consumption of vitamin D and calcium-fortified soft plain cheese by institutionalised elderly women. British Journal of Nutrition. 102:962-966 (2009).
- 89. Bonjour, J. P., Benoit, V., Pourchaire, O., Rousseau, B. & Souberbielle, J. C. Nutritional approach for inhibiting bone resorption in institutionalized elderly women with vitamin D insufficiency and high prevalence of fracture. Journal of Nutrition, Health and Aging. 15:404-409 (2011).
- 90. Surdykowski, A. K., Kenny, A. M., Insogna, K. L. & Kerstetter, J. E. Optimizing bone health in older adults: The importance of dietary protein. Aging Health. 6:345-357 (2010).
- 91. Nabipour, I., Ebeling, P. R. & Seibel, M. J. Osteoporosis in older men. Expert Review of Endocrinology and Metabolism. 6:629-645 (2011).
- 92. Patsch, J., Muschitz, C., Resch, H. & Pietschmann, P. Of mice and men: pathophysiology of male osteoporosis. Journal of Men's Health and Gender. 4:87-93 (2007).
- 93. Schiller, C., Gruber, R., Redlich, K., Ho, G. M., Katzgraber, F., Willheim, M., Pietschmann, P. & Peterlik, M. 17β-estradiol antagonizes effects of 1α,25-dihydroxyvitamin D3 on interleukin-6 production and osteoclast-like cell formation in mouse bone marrow primary cultures. Endocrinology. 138:4567-4571 (1997).
- 94. Lesourd, B. & Soulier, K. Nutrition in aged persons and handicap prevention. Alimentation du sujet âgé et prévention du handicap. 59:69-73 (2009).
- 95. Manios, Y., Moschonis, G., Trovas, G. & Lyritis, G. P. Changes in biochemical indexes of bone metabolism and bone mineral density after a 12-mo dietary intervention program: The Postmenopausal Health Study. American Journal of Clinical Nutrition. 86:781-789 (2007).
- 96. Bischoff-Ferrari, H. A. & Staehelin, H. B. Importance of vitamin D and calcium at older age. International Journal for Vitamin and Nutrition Research. 78:286-292 (2008).

2. Traditional Dairy Products in Developing Countries

Jashbhai B. Prajapati¹

Abstract

Dairying is one of the prime sectors for socio-economic development in most developing countries. Current statistics reveal that the dairy sector is growing at a faster rate in developing countries. Furthermore, dairy sector development is identified as 'a powerful tool for reducing poverty' in developing countries. Apart from liquid milk, the real strength of the dairy sector in developing countries lies in traditional dairy products. It is estimated that about 50-55% of the milk produced in developing countries is utilized for making traditional dairy products and most of these are still in the unorganized sector. The art and science of manufacture of such products is age old. These products have been developed not only for diversification, but for many other purposes, viz; preservation of milk, meeting requirements of tastes and textures in different regions, enhancing nutritional value, catering to the needs of different groups of people, improving health properties and of course for improving trade. Traditional dairy products can be categorized on the basis of principle of manufacture. The principal products in developing countries are fermented milk products (yoghurt, dahi, curd, lassi, buttermilk, kadam, irgo, laban, shrikhand, chhash, etc.); cheese and coagulated milk products (ayib, farm chanco, goat cheese, queso crillo, prato, mozzarella, cuartirolo, paneer, channa, etc.); heat desiccated products (khoa, peda, rabri, kheer, etc.); frozen desserts (kulfi, ice cream, mouhalayeh, etc.) and fat rich products (butter, makhan, ghee, etc.). Several countries are working hard on standardization of traditional technologies and equipment for large scale commercial manufacture of certain products which have export potential beyond catering to domestic needs. A significant increase in value added functional dairy products is seen and the market for probiotic dahi, lassi and buttermilk is increasing. These products have the potential to give better returns to the producers and could also help in tackling the problem of nutritional security in the developing world.

Historical perspective

Traditional dairy products are intimately connected with society and culture in developing countries since ancient times and this relationship continues. These products were indicators of wealth and status of the people. Apart from the routine use, traditional products were commonly used to honour the guests and also as special item of diet in several social functions. Their use in rituals and for medicinal purposes is also well known. In some parts of Indian sub-continent, sale of milk, fermented milk, butter milk, etc was considered unethical. Religious beliefs indicated that they were meant for free distribution in the society and not for sale. Ancient Indian literature depicts Lord Krishna's act of stopping milk maids from selling the milk products and retaining them in villages and distributing them partly to those who need them. It is easy to understand now that this might be with an intention to give such nutritious foods to all those members of the society who cannot afford to buy. Probably this was the first step taken by our ancestors to tackle the problem of food and nutrition security.

In the modern days also the traditional dairy products are most important to all the developing countries, irrespective of whether they are made by empirical methods in rural or semi-urban areas or by improved industrial processes by the organized dairy sector. Traditional dairy products take care of dietary requirements of the masses of national population and have the potential to serve as an engine for meeting requirements of food and nutritional security.

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Significance of Traditional Dairy Products

Current statistics reveal that dairy sector is growing at a faster rate in developing countries. Figure 1 shows the milk production growth in various parts of the world.

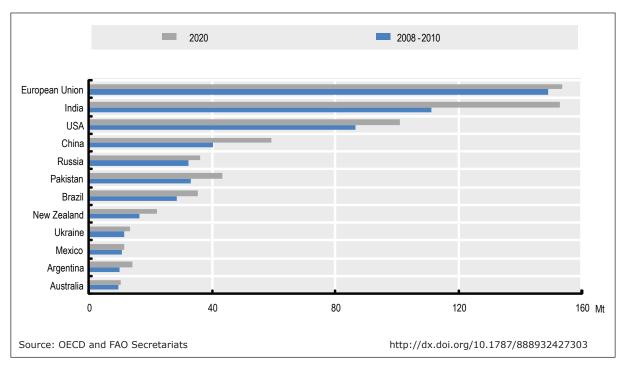


Figure 1. Milk production growth in different regions of the world.

According to one of the statements by FAO's Director, "Global milk demand is growing by 15 million tons per year, mostly in developing countries. Production of this increased volume of milk by small scale dairy farmers would create approximately 3 million jobs per year in primary production alone". Hence it can be a powerful tool for reducing poverty in developing countries. Apart from liquid milk, the real strength of the dairy sector in developing countries lies in traditional dairy products. It is estimated that about 50-55% of the milk produced in developing countries is utilized for making traditional dairy products (Table 1) and most of these is still in the unorganized sector.

Table 1: Utilization pattern of milk and milk products in India.

Sr. No.	Milk product	Percent of total
1	Fluid milk	46.0
2	Butter	06.5
3	Milk powders	03.5
4	Ghee	27.5
5	Curd	07.0
6	Khoa	06.5
7	Paneer & Chhanna	02.0
8	Others, including cream , ice cream	01.0

Source: <u>business@mapsofindia.com</u>

The art and science of manufacture of the traditional dairy products (TDP) have been developed to produce variety of products not only for taste and textures, but with different nutritional values. Apart from diversification, TDP have been developed for many other purposes, *viz*; preservation of milk, meeting requirements of tastes and textures in different regions, enhancing nutritional value, catering to the needs of different groups of people, improving health properties and of course for making better trade.

Types of Traditional Dairy Products

Hundreds of traditional dairy products have evolved in various countries. These can be best classified based on the principle of their method of production (Table 2). The varieties of traditional products indicate that they were developed to satisfy the needs of taste and aroma of the consumers, nutritional needs of the society and take advantage of health benefits of the processes, products and ingredients.

Table 2: Classification of traditional dairy products of the developing countries.

Sr. No.	Category	Examples	Principle of manufacture
1	Fermented	Sour milk, sour cream, Dahi, Yo- ghurt, Lassi, Chhash, Shrikhand, Cheese	Fermentation of milk with or without partial removal of moisture.
2	Cheeses	Cottage cheeses, soft, pickled, brined, hard and dry varieties.	Coagulation by enzyme or acid followed by removal of moisture.
3	Acid coagulated	Paneer, Channa, Sandesh, Rasogolla	Coagulation of hot milk by addition of acid and drainage of whey.
4	Heat Desiccated	Khoa, peda, burfi, basundi, kheer, puddings	Partial removal of water by evaporation followed by blending with sugar and other ingredients.
5	Fat rich	Butter, makhan, ghee	Separation of fat by churning. Clarification by heat treatment for making ghee.
6	Frozen	Kulfi, Ice-cream	Freezing of concentrated milk with sugar and other ingredients.

The art and science of product manufacture

The word 'traditional' prefixed to the name of the dairy products suggests that these are the products that have emerged out of tradition. This means that the process of their manufacture has been learnt by mankind by experience and inherited by the successive generations. When these products are analysed and evaluated in the present context, it reminds us that our ancestors were not only good technologists or artists but were very good food scientists too! The majority of the traditional dairy products are so developed that they not only satisfy the organoleptic requirements of the consumers, but preserve or improve their nutritional and heath attributes.

Preparation of traditional products was only a household activity earlier. But now it has become a commercially attractive business. However, the level of processing of milk for manufacturing of these products varies in different countries. In India, mainly Dairy Cooperatives and few private companies collect milk and process to indigenous products. Attempts are being made to organize milk producers cooperatives in some parts of Africa and elsewhere. The proportion of milk retained on individual farms in the South Cone countries of Latin America ranges from ten per cent in the case of Argentina to eighty per cent in the case of Paraguay (FAO, 2002).

Traditional milk products produced on a small scale are in most cases capable of being adapted to medium and large-scale methods. A brief description of art of making TDP is given below.

Fermented Milks

The fermentation is one of the oldest methods of food preservation learnt by mankind. The fermented milk products like dahi in India, Laban in Syria or Irgo in Ethiopia and other soured milk in southern and eastern Africa are made at home by taking a portion of good quality milk, boiling it, cooling to lukewarm state and then adding (inoculating) a small quantity of previous day's good quality curd. This is mixed and kept (usually overnight) till it sets at room temperature. This curd is consumed fresh or stored under refrigeration for future use. Using this curd or dahi, other traditional fermented milks are produced in India and neighbouring countries, which are depicted in Figure 2.

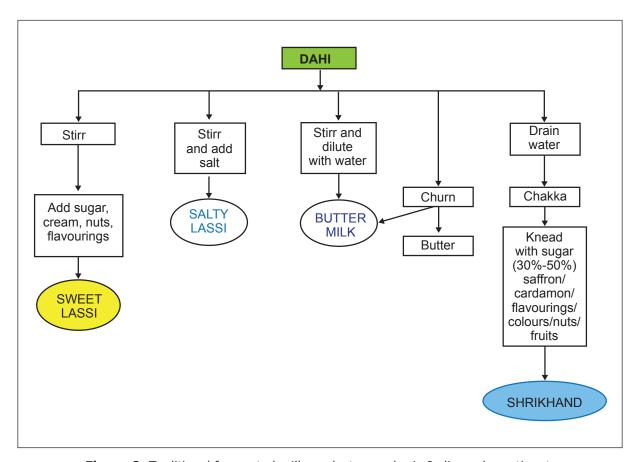


Figure 2. Traditional fermented milk products popular in Indian sub-continent.

Most of these products have travelled from household preparation to industrial manufacture now. Industrial manufacturers use well characterized starter cultures, in liquid or direct vat set (DVS) form, to have better uniformity and consistency in the product.

In most African countries, naturally fermented sour milk is the most common traditional milk product. In several cases, the traditional people have developed an art of application of wood smoke, which results in unique flavor and enhanced shelf-life of the product.

An insight in to African food products indicates that fermented milks are the major source of animal proteins in the diet of the people (Table 3).

Table 3: Fermented animal proteins of Africa.

Product	Area of Production	Substrate	Microorganisms Involved
Maziwa Lala	East Africa	Milk	Streptococcus lactis
Traziwa Lara	East / iiiica	Tillix	S. thermophilus
Nono (Milk curd)	Northern part of West Africa	Milk	Lactic acid bacteria
Guedi	Senegal	Fish	Not known
Bonone (Stink fish)	Ghana	Fish	Not known
			Lactic streptococci
Leban (Sour milk)	Morocco	Milk	Leuconostoc lactis
			L. cremoris
Wara	West Africa	Milk	Lactococcus lactis
vvara	West Affica		Lactobacillus sp
Exac	Ethiopia	Milk	Lactobacillus sp
Ergo	Ethiopia		Lactococcus sp

Source: Odunfa et al, 1985; Olasupo et al, 2001.

Cheeses and coagulated products

Almost every country of the world has its own traditional cheese. The basic process of cheese making involves coagulation of milk by enzymes or acid and partly removes the water from coagulated mass. Much of Africa has no tradition of cheese making based on coagulation of casein. In the Indian sub-continent, organic acids are used to precipitate milk proteins. In the South Cone countries of Latin America cheese making is an important sector of the dairy industry and traditional cheese types based on rennet coagulation of milk, and in most cases bearing a similarity to European varieties, are made on a small-scale in farms and by modern methods in dairy factories.

Paneer is a classical example of acid and heat coagulated milk from which moisture is removed by draining and with pressure. It is present in small blocks. Paneer can be eaten fresh, it can be deep fried in ghee/oil and eaten and can be used in several culinary preparations. Chhana is made with almost similar process of heat and acid coagulation but pressure is not applied to drain the whey. It remains as a soft ball and serves as base for making several sweets like rasogolla, sandesh, ras-malai and so on. These sweets are very popular in west Bengal, eastern part of India, and Bangladesh.

Most of the traditional cheeses are fresh type cottage cheeses. However, several regions have developed the arts of brining, ripening, salting and drying too. It goes without saying that these products are nutrient dense and can satisfy the nutritional requirements of a person even in small quantity.

Heat desiccated products

Partial dehydration of milk by open evaporation is the first step of production for many traditional dairy products in India and Latin America. Khoa is a semi solid product prepared in Indian subcontinent by partial dehydration of milk in an open pan with continuous stirring. It is dehydrated till the product becomes brown and comes to pat formation stage and makes a uniform lump. The khoa is a base material for making several kind of sweetmeats. The state, type and extent of sugar mixing results into variety of sweets like *peda*, *burfi*, *gulab-jamun*, *laddo*, etc.

Several other traditional products with other ingredients are also prepared by this method. A product resembling sweetened condensed milk is called as *Basundi* or *Rabri*. This is usually garnished by dry fruits. A product called Kheer can be prepared by simmering rice in condensed milk

Frozen desserts

Ice cream is the most popular dairy product all over the world. Traditional ice cream known as *kulfi* is prepared by freezing a concentrated mix of milk, powder, cream, sugar and condiments in an ice bath with common salt to reduce the temperature below 0°C. It is a very common scene in many developing countries where streets are flooded with vendors of ice cream and kulfi. Traditionally such ice cream is made in small ice cream freezers developed by artisans by putting a hand churn in a box of salt mixed with ice.

Fat rich products

Fat is considered as most valuable component of milk in many countries. Milk prices are still decided on the basis of fat content in several developing countries. The traditional technologies involved separation of fat from milk and selling it at higher prices. *Ghee* (clarified butter) and *makhan* (traditional butter) are the major traditional fat-rich products. The traditional art of making makhan and ghee in the household involved collecting surplus milk in containers and allowing it to ferment. Once a sufficient quantity is gathered (usually once in week in a small household with 2-3 animals), the housewife churns it in a big earthen butter churn with a wooden hand-operated stirrer. The churning was to remove makhan and the remaining liquid with most milk solids was distributed as *chhash* (buttermilk). The makhan was then slowly boiled over wood fired *chulah* to clarify it and make *ghee*.

Ghee is most precious product which is used to prepare several sweets and many other nutritious food products. It is also used in several rituals and for performing *yagna/homa* (holy firing) in Hindu tradition.

Probiotics, prebiotics, synbiotics

Traditional fermented milks may carry several probiotic bacteria and hence these products are one of the important sources for isolation of probiotics. As described in the Veda and Hindu tradition, one of the most common product used in rituals is *Panchmruta* (means five nectars), which contained fermented milk and honey as major ingredients. It was known by sages that fermented milk can be a good source of probiotic bacteria and honey is a good source of prebiotics and thus *panchamruta* was probably the first synbiotic product scientifically designed by our ancestors and to ensure that such healthy product is consumed by everybody regularly, it was incorporated as part of the rituals.

Asia, Africa, Latin America have a rich bio-diversity of microflora. Many can be isolated and scientifically tested. Similarly there are several plants and herbs which can serve as excellent prebiotic ingredients. There is a tradition of preparing products known as "Raita", which are made in the home by blending curd with shreds/pieces of fruits and vegetables like onions, tomato, carrot, mango, cucumber, pineapple, banana, etc. These blends make simpler synbiotic products, because most of the supplement fruits and vegetables used in these preparations are excellent sources of prebiotics - mainly oligosaccharides, inulin and so on.

The food and health industry have identified huge business potential in probiotics, prebiotics and synbiotics in developing countries, especially in the Indian sub-continent and hence many such products are on the market now. The Indian Council of Agricultural Research has recognized SMC College of Dairy Science, Anand, India as Niche Area of Excellence in fermented dairy products with synbiotics. Some of the products developed using indigenous probiotic cultures by this centre are given in Table 4.

Table 4: Probiotic and synbiotic products developed at Anand, India.

Sr. No.	Product	Ingredients	Remarks
1	Synbiotic dahi	Milk, Inulin, Sugar	Set coagulated product with 10 ⁸ viable cells of probiotic lactobacilli per gram.
2	Synbiotic raita	Milk, Inulin, Fructooligosachharide, Tomato, Cucumber, Onion, Banana, Sapota, sugar	Stirred yoghurt type products fermented by probiotic lactobacilli and garnished with fruits and vegetables.
3	Synbiotic lassi	Milk, Oat, fructo-oligosaccharides (FOS), Carrot, Mango, sugar	Thick liquid with probiotics and shelf life of 3 weeks at 5C.
4	Whey drink	Whey, Sugar, Pineapple	Beverage with fruit pieces and 10 ⁸ cells/ml of probiotic lactobacilli.
5	Herbal probiotic lassi	Milk, Safed musli, sugar, honey	Milk fermented by probiotic lactobacilli and supplemented with herbs.
6	Protein rich lassi	Milk, Spirulina, sugar	Fermented milk enriched in protein by spirulina.
7	Acidophilus banana powder	Acidophilus milk, banana, sugar, elachi	Dried product with 10 million/g viable cells of <i>Lb. acidophilus</i> .
8	Acidophilus wheat malt powder	Acidophilus milk, wheat malt, sugar, cocoa powder	Dried product with 10 million/g viable cells of <i>Lb. acidophilus</i> .
9	Milk-Rice probiotic food	Milk, Rice, Freeze dried probiotic culture	Milk and rice were fermented and spray dried and blended with freeze dried probiotic lactobacillus cells.

Nutritional Value of Traditional Dairy Products (TDP)

Most of the traditional dairy products are nutrient dense, hence their consumption in small amounts also contributes significantly to the nutritional requirements of a person.

The nutritional value of TDP depends on many factors starting from the standardization of milk, processing steps for manufacture, storage conditions and so on. Gross composition of some TDP is given in Tables 5 to 10. It can be seen that most of the products are good sources of fat, protein and carbohydrates.

Table 5: Gross composition of fat rich products.

Product	Makkhan	Tunisian Butter	Butter	Ghee	Ghee residue
Moisture %	20	0.79 (aw)	16	<0.5	13.4
Fat (%).	80	65.7	81	99.5	33.4
Saturated fat (%)	-		51	46	-
Monounsaturated fat (%)	-	-	21	37	-
Polyunsaturated fat (%)	-	-	3	54.5-56	-
Cholesterol (mg)	-	-	215	275-330	-
Protein (%)	-	1.10	1 .0	0	32.8
Total carbohydrates (%)	-	1.01	0	0	12.3-15.4
Ash (%)	-	1.80	-	-	5.2
Calories (kcal)	-	-	717	120	-

Table 6: Composition of traditional fermented milks.

Product	Yoghurt	Labenah	Dahi	Lassi	Chhash	Mattha	Zabady
Moisture (%)	85.4	77.0	85-92	80	88-92	92.44	86.48
Fat (%)	3.9	2.0 g	0.1-8.0	5.0	0.5	0.85	3.16
Protein (%)	4.3	2.0 g	3.5-4.0	4.5	4.4	3.7	3.81
Total carbohydrates (%)	5.5	2.0 g	3.8-5.3	15-20	6.0.	2.5	3.85
Ash (%)	0.9	0.1 g	0.64-0.72	0.8	0.5	0.73	0.72
Calories (kcal)	74	40.0	-	-	98	-	-
Acidity%	10-1.5	1.5	0.5-1.1	1.0	-	1.5	1.09

Table 7: Composition of traditional fermented milk products.

Product	Gariss	Rob	Nono	Wara	Kishk	Shrikhand
Moisture (%)	91.7 - 92.65	92.8	86.03	55.68	6.48	30-40
Fat (%)	2.15-2.9	0.16	3.68	18.55	7.00	3-8
Protein (%)	3.4-3.85	3.3	6.40	23.0	15.39	5-9
Total carbohydrates (%)	1.4-1.35	2.0	2.90	1.00	68.53	40-55
Ash (%)	0.75-0.8	-	0.97	1.50	2.60	0.8-1.5
Acidity (%)	1.0-1.8	1.9	1.37	0.48	-	1.4

Table 8: Composition of heat desiccated products.

Product	Khoa	Kheer	Rabri	Basundi	Rice pudding
Moisture (%)	20-40	65-75	45.0-59.30	52.6	-
Fat (%)	22-39	3.0	10.0-19.80	11.6	1.3
Protein (%)	16-26	6.0	9.5	9.9	3.3
Total carbohydrates (%)	17-33	34.0	10.15-14.00	11.5-12.7	16.1
Ash (%)	3-5	0.8	1.99	1.7	-
Calories (kcal)	206-421	182	-	-	85

Table 9: Composition of milk sweets.

Product	Burfi	Rasogolla	Gulab Jamun	Kalakand	Peda	Sandesh
Moisture (%)	20.5	41.80-54.86	25-30	20.0	13.5	24.11
Fat (%)	26.8	4.90-7.90	8.5-10	23.2	20.0	18.67
Protein (%)	20.3	5.05-5.58	6-7.6	17.1	19.5	16.10
Total carbohydrates (%)	59.7	34.35-43.83	8.5-52	37.5	16.31-31.8	38.61
Ash (%)	3.2	0.84-0.91	0.9-1.0	2.2	-	1.71
Calories (kcal)	74	235	-	-	-	-

Table 10: Composition of cheese type of products.

Product	Paneer	Channa	Karish Cheese	Mish Cheese	Chhurpi	Ayib
Moisture (%)	50-54	70.0	70.23	55-74	14.5	79.5
Fat (%)	24-30	53.61.0	4.26	3.3-18.0	ND	1.8
Protein (%)	13-19	30-3	17.74	1.6-2.9	56.9	14.7
Total carbohydrates (%)	2.0-2.4	4.6-4.8	-	-	-	-
Ash (%)	-	4.1	6.00	-	-	0.9
Calories (kcal)	265-292	-	-	-	-	-

It is clear from above tables that TDP are great source of major nutrients required for the body. However, apart from that, these products are capable of providing various vitamins also (Table 11). The main fat rich product called ghee has several essential micro elements (Table 12). As milk is rich in minerals, the products prepared out of it are also rich in minerals Tables 13 and 14 reveals the significance of mineral status in TDPs.

Table 11: Vitamin content of some traditional dairy products.

Vitamins	Yoghurt (100g)	Dahi (100g)	Ghee (per tbsp)	Chhana (100g)	Rice pudding (100g)
Vitamin A (IU)	70-140	102.0	393	366	16 µg
Thiamine (B1)	30-42 μg	49 μg	105 µg	73 µg	10 µg
Riboflavin (B2)	190-200 µg	157 µg	Trace	15 µg	130 µg
Pyridoxine (B6)	46	-	-	-	10 μg
Cyanocobalamine	0.23 μg	-	-	-	Trace
Vitamin C	0.7 mg	1.3 mg	-	2.8 mg	0
Vitamin E	Trace		36 mg	-	0.16 mg
Folic Acid	4.1	178	-	-	0
Nicotin acid (Niacin)	125 µg	86 µg	-	-	0.2 mg
Pantothenic acid	380 µg	183 μg	Trace	-	0.30 μg
Biotin	2.6 μg	3.2 µg	-	-	2.0 μg
Choline	0.6 μg	-	-	-	
Carotene	-	-	25 mg	-	10 μg

Table 12: Minor Constituents of Ghee.

Produc	t	Ghee
Saponi	fiable constituents	
Tr	iglycerides %	
	Short chain	41.45
	Long Chain	52.55
	Trisaturated	39.85
	High melting	6.8
Pa	artial glycerides %	
	Diglycerides	4.4
Monoglycerides		0.65
Phospholipids (mg%)		40.25
Unsapo	onifiable constituents	
	Total Cholesterol (mg %)	302.5
	Lanosterol (mg %)	8.795
	Lutein (µg/g)	3.65
	Squalene (µg/g)	60.8
	Carotene (µg/g)	7.2
	Vitamin A (μg/g)	9.35
Vitamin E (µg/g)		28.45
Ubiquinone (µg/g)		5.75
Flavou	r Components (μM/g)	
	Total carbonyls	7.92
	Volatile carbonyls	0.28
	Head space carbonyls	0.031

Source: Sharma, 1981

Table 13: Mineral content of some fermented dairy products.

Product	Yoghurt	Labenah	Dahi	Robe	Zabady	Kishk
Sodium (mg%)	80	143	-	52.6	-	1360
Potassium (mg%)	280	96	-	211.2	-	740-760
Calcium (mg%)	200	147	149	279.0	129.1	439-485
Magnesium (mg%)	19	15.3	-	36.8	12.58	104-137
Phosphorus (mg%)	170	141	93.0	166.8	99.6	544-644
Iron (mg%)	0.10	0.2	-	0.16	0.059	6.53-9.20
Copper (mg%)	Trace	0.02	-	-	0.012	0.18-0.42
Zinc (mg%)	0.7	0.6	-	1.0	0.383	2.86-4.14
Manganese (mg%)	Trace	0.02	-	0.16	0.002	-

Table 14: Mineral content of some TDP.

Product	Kheer	Rasogolla	Gulabjamun	Pedha	Paneer	Chhana
Sodium (mg)	29	7	0.2	-	10	26-30.13
Potassium (mg)		12	43	-	16	12.50-62.08
Calcium (mg)	338	47	128	708	138	475-655
Magnesium (mg)	-	-	-	-	-	26.26-32.20
Phosphorus (mg)	237	6	177	221.4	102	250-347.50
Iron (mg)	-	-	0.1	14.3	1.0	0.36-0.53
Copper (mg)	-	-	-	-	-	0.13-0.14
Zinc (mg)	-	-	-	-	-	2.26-2.46
Chloride (mg)	-	-	-	-	-	54.52-77.39

The process of fermentation is known to make protein more digestible. This is mainly due to soft curd formation in presence of lactic acid produced by the cultures. Further, some lactic acid bacteria are able to slowly breakdown the protein and release free essential amino acids. The status of amino acids in Mish cheese, Kishk and Robe is shown in Table 15. It could be seen that these products are an excellent source of almost all essential amino acids. Similarly the nutritive value of dairy products as affected efficiency of protein digestion is indicated in Tables 16 and 17.

Table 15: Amino acid prolife of Kishk and mish Cheese.

Amino acid content	Mish Cheese (mg/g)	Kishk (mg/g)	Robe (mg/100g)
Aspartic acid	0.219	6.60	0.56
Threonine	0.812	3.37	1.80
Serine	0.976	3.37	2.30
Glutamic acid	0.570	34.43	3.00
Proline	0.865	11.99	0.80
Glycine	0.662	3.95	0.60
Alanine	1.679	4.02	-
Cystine	0.319	3.97	0.16
Valine	1.137	6.81	1.07
Methionine	0.475	4.01	0.12
Isoleucine	1.047	5.36	0.10
Leucine	1.312	9.42	2.30
Tyrosine	0.317	3.82	4.60
Phenylalanine	1.022	6.19	0.73
γ-Aminobutyric acid	4.709	ND	ND
Ornithine	0.418	ND	ND
Lysine	2.235	4.67	0.60
Histidine	0.165	2.95	-
Tryptophan	Traces	ND	ND
Arginine	-	1.64	0.20
Ref.	Shaker (1983)	Prajapati et al (2005)	Sulieman (2009)

ND = Not done

Table 16: Nutritive value indicators of some TDPs.

Parameter	Milk	Dhap Khoa	Pindi Khoa	Chhana	Paneer
Biological Value (%)	98.88	99.22	99.2	88	86.5
Digestibility coefficient (%)	99.12	97.7	96.34	92	97.3
Protein Efficiency Ratio Value	3.61	3.83	3.61	3.1	2.5
Net Protein Utilization (%)	82.03	84.98	85.93	71.5	82.1
Net Protein Ratio	2.33	3.96	4.12	5.25	-
Calorific value (kcal)	-	-	-	1300-1700	-
References	Aneja et al, 2002	Aneja et al, 2002	Aneja et al, 2002	Aneja et al, 2002	Soni, 1979

Table 17: Biological value and digestibility of milk and milk products.

Product	Biological Value	Digestibility %
Milk	76	95
Dahi	66	98
Khoa	69	90
Kheer	76	97
Channa	67	97

Source : Mahadevan (1991)

Health Benefits of TDP

The habit of consuming nutrient dense traditional products like khoa based sweets, ghee, butter, etc by elites has started giving negative effects in terms of obesity, diabetes and hypertension. However, this will not qualify traditional products as unhealthy. These products are good source of energy in working class people and are good source of nutrients.

Most healthy products among TDP are fermented milks and cheeses. Further, to add value to this, several probiotic products are emerging.

Ghee has been recognized as a therapeutic agent in the Ayurvedic system of medicine. It has been found that ghee has fully digestible class of fats putting relatively less strain on the body. It can therefore be an important dietary constituent for patients having diseases of the stomach, intestinal tract, liver, kidney and gall bladder. Cholesterol content of milk fat is very low (2.8 mg/g for cow and 1.9 mg/g for buffalo milk) and is not a problem for coronary heart diseases. (Pandya & Sharma, 2002) Ghee is also rich in CLA (6-28 μ /g of fat) which give anticarcinogenic activity. Ghee also is a good vehicle for fat soluble vitamins A , D , E and all of them are essential for the body.

Ghee residues, which are residual solids after straining the hot liquid fat is a rich source of natural antioxidants and are rich in milk proteins, fat and minerals and can be used as nutritional supplement (Galhotra and Wadhwa, 1993).

There are several reports on therapeutic value of **fermented milk products**. Ancient literature indicates that fermented milks like dahi and buttermilk are important in alleviating gastro-intestinal disorder. Several therapeutic uses of chhash have been depicted in the Ayurvedic system of medicine. Modern science has now proved that lactic acid bacteria present in such fermented milks possess antimicrobial activity towards food borne pathogens and thereby reduce the possibilities of diseases caused by them.

Some clinical trials on Indian dahi and indigenous probiotic fermented milk have demonstrated beneficial effects. In a study conducted by Khedkar et al. (2003), 135 children of 2-5 years of age were recruited and fed either dahi, a probiotic fermented milk or buffalo milk for one month. The results indicated that probiotic bacteria implanted in the intestinal tract of the subjects prevented gastrointestinal ailments during the feeding trials and 90 days after termination.

A community-based randomized controlled double blind study was carried out by Aggarwal and Bhasin (2002) at the University College of Medical Sciences, Delhi, to control acute diarrhea in children (n=150) of 6 months to 5 years of age. Seventy five subjects in each, hospital and slum cluster, were randomized into 3 groups and administered with (1) commercial fermented milk Actimel (10^8 organisms/g), (2) Indian dahi (10^8 organisms/g) and (3) ultra-heat-treated yoghurt (without live bacterial cells) till the diarrhea was cured. Mean curing time was superior for Actimel (1.7 d) followed by Indian dahi (2.0 d) and UHT yoghurt (2.25 d) in the control of acute diarrhea.

A randomized feeding trial on 27 human volunteers of normal as well as hyperlipemia groups was conducted by Ashar and Prajapati (2001). All the subjects were fed 200 ml of stirred acidophilus milk (containing 5×10^8 live lactobacilli per ml) for 20 days. The results showed wide variations among the volunteers. However, a significant reduction of 7.6% in total cholesterol and 15.7% in LDL cholesterol was noticed in the volunteers during the study.

A study was conducted at tertiary care hospital in east Delhi during September 2003 to August 2004 to assess the impact of supplementation of curd (dahi) and micronutrient-rich leaf protein concentrate (LPC) on nutritional status, and immunity in children suffering from protein energy malnutrition (PEM) (Dewan et al., 2006). Eighty moderate to severely malnourished children (1-5 y) were randomized to receive either curd (Group A, n=32) or LPC (Group B, n=36) in addition to WHO recommended two-step diet over 15 days. The results indicated that the change in weight, haemoglobin level and CD4:CD8 T-cell subpopulation were significantly higher in both the groups after supplementation.

Rajpal and Kansal (2009) observed that feeding probiotic dahi containing L. acidophilus and B.bifidum increased β -glucuronidase, β -glucosidease and phagocytic activities as compared to feeding only buffalo milk in mice model. Pawan and Bhatia (2007) also reported that feeding lassi and dahi reduced cholesterol level and increased immune activity in humans.

Socio-economic Dimensions of TDP

Traditional dairy products have significant role to play in the economies of milk producers. TDPs are most important farm commodities in several developing countries and have direct relevance with the livelihood of millions of people. In some developing countries, where fresh milk marketing is still not possible due to poor shelf-life, TDPs like sour milk, cheese, ghee are major items for trade. TDPs also provide good outlet for milk from other species; for example, indigenous cheeses from goat and sheep milk in the Middle East and yak cheese in the Himalayan region. In certain areas of the developing world, TDPs are the only products for trade and people barter these products to purchase grains and other items for living.

The OECD-FAO (2011) report states that in developing regions, the consumption of all dairy products is increasing vigorously at around 30%, which is mainly driven by increasing population, increasing purchasing power and increased awareness about health properties of certain dairy products. Traditional dairy products are major contributors to the dairy sector in developing countries. However, the probiotics sector is among the fastest growing parts of the dairy business.

TDP are among the most value added dairy products. One report states that Indian traditional dairy products market is estimated at US\$3 billion in India and US\$1 billion overseas. Promotion of trade of selected TDPs, especially typical cheeses, sweetmeats, lassi, etc can be used to earn more revenue for the milk producers and help sustain their business in a better way. Expanding the trade of TDPs can also generate more jobs.

As per the statement of Director of FAO's Animal Production and Health Division, judicious development of dairy sector could make substantial contribution to achieving the millennium development goal of eradicating hunger and poverty.

In some parts of India, buttermilk is provided to school children in the midday meal program, which serves as cheaper source of valuable nutrients to children. There are several religious centres, where cool buttermilk is freely distributed. The advantage of such arrangements is usually taken by poor and that helps to reduce the gap of their nutritional deficiency.

The need

Immediate attention of all the stakeholders and policy makers is required on following points to promote traditional dairy products as domestic and international level.

- 1. Improving shelf life
- 2. Improvement in hygienic quality
- 3. Developing packaging technology
- 4. Organized marketing
- 5. Systematic survey and documentation
- 6. Increasing awareness outside region or traditional society
- 7. Systematic research and development work
- 8. Promotion of TDPs by national governments and NGOs.

Epilogue

The traditional dairy products of developing countries have the potential to create extra jobs. They are the means of food security for millions of people. The proven nutritional value of milk and TDPs is also a boon to at least partly cater to the nutritional requirements of masses. Many products can be industrialized and marketed outside their traditional regions to earn more revenue for the milk producers. Similarly, several products, especially fermented milks, can be promoted as heath products, which can facilitate nutritional security at relatively lower cost for the masses in developing countries.

References

- Aggarwal KN and Bhasin SK (2002). Feasibility studies to control acute diarrhea in children by feeding fermented milk preparations Actimel and Indian dahi. Eur J Clin Nutr, 56: 556-559.
- 2. Aneja RP, Mathur BN, Chandan RC and Banerjee AK (2002). Technology of Indian milk products. ISBN 81-901603-0-3, A Dairy India Publication, Delhi, India.
- 3. Ashar MN and Prajapati JB (2001). Serum cholesterol level in humans fed with acidophilus milk. Indian J. Microbiol. 41: 257-263.
- 4. Dewan P, Kaur, I., Chattopadhya, D, Faridi MMA and Agarwal, KN (2007). A pilot study on the effects of curd (dahi) and leaf protein concentrate in children with protein energy malnutrition (PEM). Indian J Med Res, 126: 199-203.
- 5. FAO (1990). The technology of traditional milk products in developing countries. FAO Animal production and health paper No. 85. Food and Agriculture Organization of the United Nations, Rome.
- 6. Galhotra KK and Wadhwa BK (1993). Chemistry of ghee residues, its significance and utilization- a review. Indian J Dairy Sci., 46(4):142-146.

- 7. Khedkar CD, Patil MR, Gyananath G, Bajad DN and Sarode AR (2003). Studies on implantationability of a probiotic culture of *Lactobacillus acidophilus* in gastrointestinal tract of tribal children. Proceedings of the International Seminar and Workshop on Fermented Foods, Health Status and Social Well being, organized by Gujarat Agricultural University, SASNET-Fermented Foods and Department of Applied Nutrition Lund University, Sweden at Anand, India, Nov 13-14, 2003, pp 62-63.
- 8. Mahadevan AP (1991), Nutritional Value of Traditional Milk Products of India, Indian Dairyman, 43(2): 95-101.
- 9. OECD-FAO (2011). OECD-FAO Agricultural Outlook 2011-2020, Chapter 9; Dairy, pp 159-173.
- 10. Ounfa, S.A. African fermented foods. In: Microbiology of fermented foods. Wood, B.J., ed., London and New York: Elsevier Applied Science Publishers, 1985, pp151–191.
- 11. Olasupo, N.A., U. Schillinger, W.H. Holzapfel. Studies of some properties of predominant lactic acid bacteria isolated from Nigerian fermented foods. Food Biotech. 15:157–161, 2001.
- 12. Pandya AJ and Sharma RS (2002). Ghee its chemistry, technology and nutrition: an overview. Proceedings of National Seminar on role of pure ghee in health and nutrition-exploding myths, 13-14 June 2002 organized by Indian Dairy Association, Gujarat Chapter at Anand, pp. 1-14.
- 13. Pawan R and Bhatia A (2007). Systematic immunomodulation and hypocholesterolemia by dietary probiotics: A clinical study. J.Clin.Diagno. Res. 6:467-475.
- 14. Prajapati, Neha; Rema Subhash and Prajapati JB (2005). Manufacture of Indian Kishk and a study of its nutritional properties. Poster presented at Second International Conference on "Fermented Foods, Health Status and Social Well-being" organized by SASNET-FF, AAU, Lund University and IRMA, December 17-18, 2005 at AAU, Anand, pp 82-84.
- 15. Rajpal S and Kansal VK (2009). Probiotic dahi containing *Lb. acidophilus* and *B. bifidum* stimulates immune system in mice. Milchwissenschaft, 67:147-150.
- 16. Shaker M. El. Gendy (1993). Fermented Foods of Egypt and the Middle East. J. Food Prot. 46(4):358-367.
- 17. Sharma RS (1981). Ghee: A Resume of Recent Researches, J Food Sci & Technol, 18:70-77.
- 18. Soni N (1979). Nutritive value of paneer. M.Sc. Thesis, Kurukshetra University, Kurkshetra, India; as cited by Rao KVSS, Zanjad PN, Mathur BN (1992). Paneer Technology- A Review, Indian .J. Dairy Sci. 45(6)281-291.
- 19. Sulieman, AME, Dirar HA, Elkhalifa EA and Ali AO (2009). Effect of fermentation on some chemical components of Sudanese fermented buttermilk-robe. J Sci. Technol. 10 (1):1-10.

3. The anti-infective potential of milk products: Positive effects of milk to prevent gastrointestinal infection and inflammation

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Abstract

Milk and its constituents exert bioactivities that promote gut health. Bioactivity of milk includes antimicrobial activity, balancing gut microbiota composition, improving the gut barrier function, and immune modulation. Therefore, milk or its constituents may improve the defense towards gut infection and may reduce gastrointestinal inflammation. This paper summarizes the effect of milk and milk constituents on gut infections and inflammation. There is overwhelming evidence that dairy products promote gut health, which fits with the biological role of milk. However, in many studies, the anti-infective potential of single milk ingredients is tested rather than their contribution in the complete dairy matrix. In addition, most data are obtained from *in vitro* or animal studies only. Therefore, the question whether high dairy consumption is beneficial for human gut health is still unanswered. Well designed intervention trials are needed to establish the role of milk and milk products in improving human resistance to gastrointestinal infection and inflammation.

1.1. Introduction

Gastroenteritis, an inflammation of the gastrointestinal tract, involves both the stomach and the intestine and may result in acute diarrhea. It is one of the most common diseases in the world. Diarrhea is one of the leading causes of death in children under 5 years of age. The WHO estimates 10.6 million deaths worldwide in this age group each year. Diarrhea accounts for 18% of these deaths (approximately 2 million diarrheal deaths; [1]). Multiple episodes of acute diarrhea and persistent diarrhea can seriously affect growth, nutritional status, and cognition. In industrialized countries, the associated death rate is low, but the incidence of illness remains high. Death due to diarrheal disease in high income countries is predominantly observed in the elderly, with 9.7 deaths per 100,000 inhabitants for subjects aged >80 years [2]. Moreover, an estimated 10 million people—20% to 50% of international travelers—develop travelers' diarrhea annually.

Gastrointestinal inflammation is most often caused by infection by certain viruses, bacteria or parasites, or an adverse reaction to something in the diet or to medication. Norovirus and rotavirus are the most common causes of viral diarrhea [3, 4]. Whereas rotavirus is usally restricted to infection in infants, norovirus is a common cause of diarrhea in both children and adults, since no lifetime immunity towards this virus can be obtained. Gastroenteritis is also induced by different species of bacteria, including *Salmonella, Campylobacter jejuni, Escherichia coli Clostridium, Shigella, Staphylococcus,* and *Yersinia*. Because of the increasing resistance of pathogens to antibiotics and antiviral drugs, food or food components that prevent gastrointestinal infections by improving gastrointestinal host resistance may form an attractive approach.

Another type of gastrointestinal inflammation, chronic inflammatory bowel disease (IBD), a multifactorial disease with unknown etiology, is a growing disease in Western societies [5]. The incidence in Europe is 5.6 new cases per 100,000 per year for Crohn's disease and 10.4 per 100,000 per year for colitis ulcerosa, the two main types of IBD [6]. In the USA, incidence rates are 7.9 and 8.8 per 100,000 per year for Crohn's disease and colitis ulcerosa, respectively [7]. Several factors are involved in the development of the disease, such as genetic susceptibility, immunological malfunction, the intestinal microbiota, gut barrier dysfunction, and environmental

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factors [5, 8]. The prevalence of IBD increased rapidly in Europe and North America in the second half of the twentieth century and IBD is becoming more common in the rest of the world when various countries adopt a Western lifestyle [5]. This indicates a role for lifestyle and diet. In addition, the factors identified to be involved in the development of IBD are known to be sensitive to dietary modulation. It is therefore quite surprising that the potential of food interventions as adjuvant therapy to prevent or ameliorate IBD is only beginning to be explored. Several of the above-mentioned factors related to IBD development are also important for host defense against intestinal infections. So, despite the different nature of gut infections and IBD, there are generic mechanisms involved. This also implies that food components, e.g. from dairy, shown to be effective against gut infection may also have beneficial effects in IBD amelioration.

Milk is a natural carrier of components that enhance host defense, which may have effects on gastrointestinal inflammation. The main biological functions of milk are provision of a balanced mixture of nutrients to the newborn, and protecting the newborn from infectious diseases. There are good indications that the action of these compounds in cow's milk may have a beneficial effect on the human defense system too. With respect to milk constituents, the focus of this paper is on intact components rather than hydrolysed products (e.g. antimicrobial peptides).

1.2. single milk constituents and potential protection against gut infection

Milk components have multiple protective actions on gut infection. This section focuses on mechanistic aspects of milk components and on evidence obtained from single milk constituents, since most studies have been performed with isolated dairy components rather than the whole milk matrix. Table 1 summarizes the action of several dairy components. Milk fat, the milk fat globule membrane, whey proteins, and calcium have been best studied, and are therefore discussed in more detail.

Table 1: Overview of the effects of various milk components on gastrointestinal infections.

	In vitro studies	Animal studies	Human studies
	as2-, β-, and κ-casein did not inhibit HIV-1 replication [55]	NIA1	NIA
Dairy component Casein(s)	Human but not bovine kappa-casein inhibited H. pylori adhesion to human gastric mucosa; role of fucose moiety [56].		
	Several casein-derived peptides displayed antibacterial activity towards relevant human pathogens.		
Whey proteins			
	A high molecular weight fraction inhibited replication of rotavirus [57].	Shortened period of severe diarrhea in rotavirus-infected suckling BALB/c mice [20] and rats [21].	NIA
Whey protein concentrate		Modulated the immune response and ameliorates rat rotavirus-induced diarrhea [21].	
		Enhanced fecal mucin in rats [18], whereas intestinal mucins inhibited murine rotavirus infection [58].	

Table 1: Overview of the effects of various milk components on gastrointestinal infections. (Continued)

	In vitro studies	Animal studies	Human studies
β-lactoglobulin	Inhibition of rotavirus replication in human cell line [59] No effect on adenovirus infectivity [60]	NIA	NIA
a-lactalbumin	No effect on rotavirus entry and replication [59] and on adenovirus infectivity [60].	a-lactalbumin-enriched infant food reduced enteropathogenic E. coli- induced diarrhea in rhesus monkeys [61]	NIA
	Inhibited rotavirus infectivity in cell lines [35].	Affected the shedding of rotavirus in the stools of experimentally infected mice [35]	NIA
Immunoglobulin G (non-specific)		Limited effects were seen for colostrum preparations rich in immunoglobulins. More effects are to be expected from colostrum obtained after immunization.	
Lactoperoxidase	Direct antimicrobial activity [11]	Mice showed a significantly lower lung consolidation score, serum IL-6 and lung infiltrated leukocytes after infection with influenza virus [62].	NIA
GMP	Inhibition of hemagglutination of human influenza virus and prevention of Epstein-Barr virus-induced morphological transformation of peripheral blood lymphocytes [63].	GMP-enriched infant food reduced enteropathogenic E. coli-induced diarrhea in rhesus monkeys [61]	NIA
	GMP prevented binding of Salmonella and EHEC to Caco- 2 cells [10].		

Table 1: Overview of the effects of various milk components on gastrointestinal infections. (Continued)

	In vitro studies	Animal studies	Human studies
Lactoferrin	Inhibition of hepatitis B virus replication in human cell line [64]. Prevention of the entry and intercellular spread of herpes simplex virus [65]. Inhibition of echovirus [66]. Inhibition of HIV-1 replication [55]. Prevention of rotavirus binding and replication in human cell line [59], of adenovirus infectivity [60] and of feline calicivirus infectivity by inhibition of cell entry [24]. Direct antimicrobial activity [11]. Inhibition of Salmonella growth, adherence and invasion, prevention of adherence of enterotoxigenic E. coli, Shiga-like toxin producing E. coli and enteropathogenic E.coli adherence [27].	Intraperitoneally administered lactoferrin augmented NK cell activity and protected against cytomegalovirus [67]. Reduces viral titres of the polycythemia-inducing strain of the Friend virus complex in mice [68]. Mice showed a significantly lower lung consolidation score and lung-infiltrated leukocytes after infection with influenza virus [62]. Oral lactoferrin inhibited H. pylori infection [69] and clostridium infection [70] in mice. Oral intake suppressed translocation of enterobacteria in mice [71].	Improvement of blood markers in a subgroup of patients with hepatitis C during a pilot study [72], but not in randomized controlled trial [73]. Daily consumption of 100 mg of bovine-lactoferrin containing products for 3 months had no effect on rotavirus incidence in children below the age of 5 years, but reduced frequency and duration of vomiting and diarrhea [27]. Systematic review: Currently there is no evidence to recommend or refute the use of lactoferrin for the treatment of neonatal sepsis or necrotizing enterocolitis as an adjunct to antibiotic therapy [74]. No conclusive evidence on lactoferrin and H. pylori colonization. Suppression of colonization [75], vs no additive effect on H. pylori eradication by commonly used regimen [76].
Milk fat globular membrane	Bovine MFGM binds enterotoxigenic E. coli [77]	Sweet buttermilk powder protected rats against Listeria infection [78]. Butter prevented short term, but not long term colonization of H. pylori (Figure 2).	In one epidemiological study, whole milk was associated with less gastroenteritis in children than low fat milk [28].
Lactadherin	Inhibited rotavirus infections in MA104 and Caco-2 cell lines [9].	Suppressed fecal rotavirus shedding in low dose challenged mice but not in high dose challenged mice [35].	NIA

Table 1: Overview of the effects of various milk components on gastrointestinal infections. (Continued)

	In vitro studies	Animal studies	Human studies
Milk mucin (MUC1)	Inhibition of human immunodeficiency virus by human MUC1 [79] and certain rota virus strains [9]. Bovine MUC inhibited rotavirus infection of a human enterocyte cell line [59]. No effect on adenovirus infectivity [60].	Human milk mucin prevented experimental rotavirus in mice; effect is partly dependent on its sialic acid content [23]. Muc1-/- mice are more susceptible to C. jejuni infection than Muc1+/+ cells, indicating an important role for MUC1 in prevention of infection [80]. Suppressed fecal rotavirus shedding in low dose challenged mice but not in high dose challenged mice [35].	NIA
Sphingolipids	Glycosphingolipid binding to rotavirus with sialic acid/binding epitope [22]. Murine norovirus can bind to sialic acid moieties of gangliosides [25]. Digestion products are strongly bactericidal [30]. Glycosylated sphingolipids exhibited inhibition of pathogen binding (e.g. E. coli, H. pylori, Campylobacter, bacterial toxins) [78]. The glycolipids lactosylceramide, GD3 and GM3 bind to E. coli [77].		In one epidemiological study, whole milk was associated with less gastroenteritis in children than low fat milk [28].
Butyrophilin	NIA	NIA	NIA
Others			
Calcium	NIA	Dietary calcium prevented E. coli and salmonella infections [36, 37], but increases the colonization of Listeria [31].	Calcium in milk reduced diarrhea severity and duration due to E. coli infection in healthy subjects [38].
Milk fat triglycerides	Medium chain fatty acids possess antimicrobial activity against Listeria and Campylobacter [30].	Milk fat inhibited colonization of Listeria, but not of Salmonella [33]. Butter prevented short term, but not long term colonization of H. pylori in rats (Figure 2)	In one epidemiological study, whole milk was associated with less gastroenteritis in children than low fat milk [28].

Table 1: Overview of the effects of various milk components on gastrointestinal infections. (Continued)

	In vitro studies	Animal studies	Human studies
Sialyl lactose	Sialyl lactose may inhibit influenza virus [81]. Sialidase treatment decreased binding of GMP to Salmonella and enterohemorrhagic E. coli [10], indicating role of sialic acid as decoy. Sialylated oligosaccharides suppressed adhesion to gastric epithelial cells [82]. Sialyl lactose inhibited cholera toxin binding [83].	Sialyl lactose diminished H. pylori infection in rhesus monkeys [84].	Oral sialyl lactose was ineffective in reducing gastric mucosal H. pylori colonization in dyspeptic patients [85, 86].

¹ NIA: No information available.

1.2.1. Milk and protection against gastrointestinal infections: mechanisms

Milk contains several components that can affect the course of gastrointestinal infections at many levels. Figure 1 shows the course of infection and exemplifies dairy constituents with anti-infective potential. In order to be able to infect the intestinal tract and in the case of invasive pathogens translocate to extra-intestinal organs, pathogens must survive gastrointestinal conditions during their transit. Several milk constituents exert bactericidal activity [9-12]. These milk constituents may prevent gastrointestinal infection and its clinical consequences such as diarrhea and mucosal inflammation by reducing the number of viable pathogens in the lumen. Pathogens may not only survive but may also proliferate in the gastrointestinal tract. Bacteriostatic effects have been described for several milk constituents [9-11] which aid in the protection against gastrointestinal infection. Moreover, most pathogens require adherence to gastrointestinal cells to induce infection and diarrhea. Several milk constituents act as pathogen decoys. By functioning as luminal soluble receptors for pathogens, these milk components inhibit adhesion of pathogens to gastrointestinal cells [13]. Some invasive pathogens, such as Salmonella and Listeria, translocate from the intestine to other organs, such as mesenteric lymph nodes and spleen. By strengthening the gut barrier, milk constituents may prevent translocation. In addition, the immune response towards an infection is important in clearing pathogens. Milk constituents have also been shown to modify immune responses [14, 15]. Finally, the microbiota composition of the gastrointestinal tract can influence the course of infections by production of antimicrobial agents in the large intestine, by competition for nutrients for bacterial growth and mucosal adhesion sites, and by modifying the immune response [16]. Several milk constituents have been shown to modify the gut microbiota composition [17-19]. Together, these activities can result in a lower pathogenic load and diminished diarrhea.

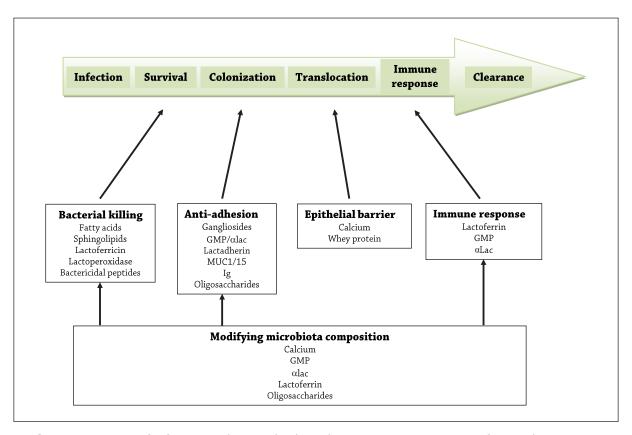


Figure 1. Course of infection and examples how dairy constituents can interfere in this process.

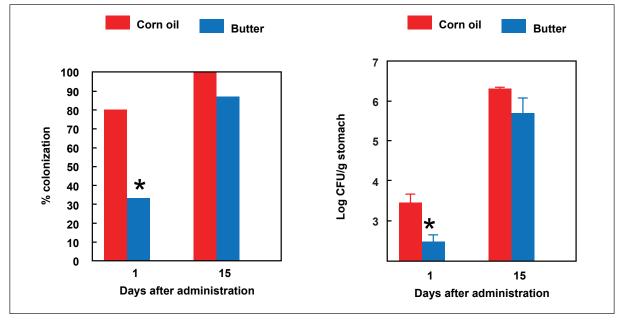


Figure 2. Effect van corn oil or butter (5% in feed) on percentage H. pylori colonization (left panel) and the number of pathogen adherent to the gastric mucosa (rigth panel) of rats infected with 10^9 CFU H. pylori. * P < 0.05 compared with corn oil.

1.2.2. Whey protein(s)

Whey proteins, and particularly the whey protein lactoferrin, are the best studied milk components. Bioactivity against both viral and bacterial gut pathogens has been shown. Whey protein components are good inhibitors of rotavirus (Table 1). In vitro efficacy has been demonstrated for a high molecular weight fraction (probably immunoglobulins), actual immunoglobulins, β-lactoglobulin and lactoferrin. In vivo evidence has been obtained for whey protein concentrate: suckling BALB/c mice were treated by daily gavage with whey protein concentrate or with bovine serum albumin as control protein from the age of 9 to 17 d, and were infected with murine rotavirus at the age of 11 d. Severe diarrhea occurred for a 4-d period in the control group but only for a 2-d period in the whey group [20]. In a later study, supplementing suckling rats with whey protein concentrate modulated the immune response and was also found to ameliorate rotavirus-induced diarrhea in rats [21]. A related intriguing mechanism needs further evaluation. We have shown that both cheese whey protein and acidic whey protein increase the amount of faecal mucin in rats [18]. Intestinal mucins have been shown to inhibit rotavirus infection in mice [22]. Thus, whey protein may stimulate the body's own defenses against rotavirus. Additional supportive evidence for a protective role of mucin in rotavirus infection comes from a study in suckling mice. Mice were supplemented with the acidic mucin fraction of human milk and rotavirus diarrhea was almost completely prevented [23].

With respect to norovirus, the antiviral efficacy of lactoferrin was screened *in vitro* using feline calicivirus as model of human norovirus [24]. Lactoferrin reduced infectivity of the feline calicivirus cells. No other evidence for milk constituents on norovirus infectivity is available. This is probably due to the relatively recent recognition of the relevance of norovirus (compared with rotavirus) for human gut infectious disease, difficulties of *in vitro* culturing of most noroviruses and the only recently available murine norovirus model. Since norovirus and rotavirus can bind sialic acid moieties [25, 26], one could speculate that glycosylated proteins, such as glycomacropeptide (GMP), may act as decoys, thus preventing adherence of virus to the intestinal epithelium.

As well as being widely investigated for its effects on viral pathogens, lactoferrin is also the whey protein constituent that has been best studied, both in vitro and *in vivo*, for its effect on a range of bacterial pathogens (Table 1).

Human evidence on the functionality of whey proteins against gut infections is scarce. An intervention in infants supplemented with 100 mg bovine lactoferrin for 3 months did not reduce rotavirus incidence, but the frequency and duration of vomiting and diarrhea were diminished [27]. However, lactoferrin supplementation (850 mg/L) for 12 months did not show any effect on non-specified diarrhea incidence or duration in bottle-fed infants [27]. Therefore, lactoferrin at a concentration naturally present in bovine milk will likely not be helpful in preventing non-rotaviral enteric infections in infants. This underlines the importance of well designed human trials for substantiation of health claims.

1.2.3. Milk fat and the milk fat globule membrane

Whole milk consumption in children is associated with fewer gastrointestinal infections than consumption of low fat milk [28], indicating that milk fat or its globule membrane may protect against gastroenteritis. Milk fat contains triglycerides which, upon digestion, can be converted to antimicrobial fatty acids and monoglycerides. These lipid components have surfactant activity and can disrupt the outer membrane of bacterial pathogens. Particularly $C_{10:0}$ and $C_{12:0}$ fatty acids and monoglycerides are bactericidal, killing a broad range of pathogens *in vitro*, including Salmonella, Escherichia coli, Campylobacter jejuni, Vibrio cholerae, Shigella, Helicobacter pylori and Listeria [29-31]. Generally, Gram-positive bacteria are more sensitive to the bactericidal effects of milk fatty acids and monoglycerides than Gram-negative bacteria, except for H. pylori and C. jejuni, which appear to be very sensitive Gram-negative bacteria. Although enveloped viruses are lipid-sensitive [32], the impact of milk fatty acids on viral gastroenteritis is likely insignificant, since most gastrointestinal viruses do not possess an envelope. Although the antimicrobial activity of fatty acids *in vitro* is well-established, *in vivo* evidence is scarce. Intake

of milk fat protected rats against infection with *Listeria monocytogenes*, but not against *Salmonella enteritidis* [33], which is in line with the proposal that Gram-positive bacteria (*Listeria*) are more sensitive than Gram-negatives (*Salmonella*). There is no published evidence from human intervention trials.

Besides milk fat triglycerides, a broad range of other antimicrobial agents is present in the bovine milk fat globule membrane ([34]; Table 1). Pathogen decoy activity is the predominantly mentioned bioactivity.

Constituents of the bovine milk fat globular membrane appear to be good inhibitors of rotavirus adhesion *in vitro*, but *in vivo* evidence is scarce, except for MUC1 and lactadherin [35]. Since norovirus and several bacterial pathogens can bind sialic acid [13, 25] and sugar moieties [13], bovine milk fat globule constituents containing sialic acid and sugar groups, such as milk gangliosides, mucin and other glycosylated proteins, theoretically may act as decoys, thus preventing adherence of these pathogens to the intestinal epithelium. However, this needs to be confirmed. Except for sphingolipids, the effect of the milk fat membrane constituents is less well studied for bacterial pathogens than for viral pathogens.

So far, evidence from the milk fat globule membrane has been mainly obtained from *in vitro* data, whereas data from animal models is limited and scattered over different pathogens (Table 1). Human evidence has not been published up to now.

1.2.4. Calcium

We have demonstrated a protective effect of milk calcium against Salmonella infection [36, 37]. Since Salmonella and E. coli are related Gram-negative bacterial pathogens (both belong to the Enterobacteriaceae) and both predominantly infect the small intestine, it was investigated whether calcium protected against E. coli infection as well. Indeed, calcium reduced infectious diarrhea caused by enterotoxigenic E. coli infection in rats and, more importantly, it had the same protective effects in healthy subjects [38]. The underlying protective mechanism is not completely clear but is likely multi-factorial. One of the factors relates to gut microbiota modulation. Milk calcium is dissolved in the acidic gastric juice but re-complexes with dietary phosphate in the upper small intestine because of the higher pH in this part of the intestinal tract. This freshly formed amorphous calcium phosphate precipitates luminal surfactants such as fatty acids and bile salts. These surfactants are especially bactericidal to Gram-positive bacteria, such as bifidobacteria and lactobacilli, of the endogenous microbiota and considered important for colonization resistance. By precipitating luminal surfactants, calcium enhanced intestinal numbers of these potentially beneficial bacteria [17]. Moreover, by precipitating luminal surfactants, calcium may protect the gut barrier itself. More recent studies have shown that calcium decreases intestinal permeability [39, 40]. This may also contribute to the inhibition of pathogen translocation from the gut lumen to extra-intestinal organs observed in several animal infection studies [36, 37]. Whether the protective calcium effects are specific for Gram-negative bacterial infections or also apply to viral enteric infections needs further investigation.

1.3. Milk, milk products and protection against gastrointestinal infections: evidence from animal and human studies

There is reason to assume that synergy in efficacy will be obtained when the complete milk matrix is used in intervention studies in comparison to interventions with individual milk components. However, few studies have addressed the effect of milk and milk products in reducing gastrointestinal infections. This section describes evidence from studies with milk and milk products.

Epidemiological data have shown that whole milk consumption is associated with fewer episodes of gastrointestinal infections in children than consumption of low fat milk: children over one year of age that were taking low fat milk as their only milk source in the three weeks prior to illness had five times the risk of a doctor's visit for acute gastrointestinal illness compared with children taking whole milk during the same period [28]. This points to a protective effect for

milk fat in humans. The risk did not differ for rotaviral or non-rotaviral illness, suggesting that milk fat is protective against both viral and non-viral causes of gastroenteritis.

Sweet buttermilk powder, which is rich in milk fat globule membrane components, protected rats against *Listeria* infection when compared to skim milk [31]. This effect can be explained by the bactericidal effect of digestion products of sphingolipids, i.e. lysosphingolipids and sphingosine, or by the presence of milk fat globule membrane constituents that act as pathogen decoys, such as gangliosides, MUC1 and lactadherin.

We have studied the effect of butter in a *Helicobacter. pylori* infection model in rats. H.pylori is the main cause of gastritis in humans and is sensitive to the bactericidal effects of $C_{10:0}$ and $C_{12:0}$ fatty acids *in vitro* [29]. Milk is rich is in these fatty acids, which are liberated in the gastric environment [33]. When rats were fed butter-containing diets, the initial gastric colonization of H.pylori (1 day after inoculation) was decreased compared with rats fed diets containing corn oil, which does not contain $C_{10:0}$ and $C_{12:0}$ fatty acids (Figure 2). However, when gastric mucosal samples were obtained 15 days after H.pylori inoculation, no differences in colonization between butter- and corn oil-containing diets were observed (Figure 2). This indicates that butter consumption may have an immediate effect, but does not prevent long term H.pylori colonization. With initial infections (i.e. freshly ingested H.pylori), the interaction between milk fatty acids and H.pylori in an acidic environment may be optimal, leading to an initial reduction of colonization. Once H.pylori has colonized, it adheres to the gastric epithelium, which is covered by a thick mucous layer. This may prevent a direct interaction with bactericidal fatty acids in the gastric lumen. In addition, Helicobacter's urease activity increases local pH, rendering fatty acids less effective since protonation is a prerequisite for bactericidal activity of fatty acids [30].

The above examples show that milk is not only a nutrient-dense food, but also contains several potentially antimicrobial components which can improve host resistance to gut infection. Up to now, studies into activities of individual milk components have been mainly limited to *in vitro* studies and animal infection models. Scattered evidence is present for multiple pathogens. Human confirmation is scarce, more difficult to obtain, but greatly needed. For evolutionary reasons, it can be expected that milk constituents act synergistically in protecting against gastrointestinal infections. The effect of the complete milk matrix is poorly studied so far, but is strongly recommended for future research.

1.4. Dairy, its constuents and protection against gastrointestinal inflammation

1.4.1. Whey protein(s)

Whey protein isolate has been shown to protect against chemically induced colitis in rats [18]. Reduction of diarrhea and rectal bleeding, two major clinical symptoms of colitis, coincided with diminished mucosal gene expression of inflammation markers. In the same experiment, another group of rats received a casein diet supplemented with threonine and cysteine. Comparable to the whey protein group, clinical symptoms and gene expression of inflammation markers were reduced by these amino acids. Threonine and cysteine are important building blocks of intestinal mucins, which are the major protein constituents of the mucous gel layer that lines the entire gastrointestinal tract and protects the delicate epithelium from irritating components in the gut lumen. The importance of mucin in protecting the gut epithelium is underlined by the observations that depletion of the secretory mucin MUC2 is observed in IBD patients [41] and that MUC2 knockout mice spontaneously develop colitis [42]. The essential amino acid threonine is highly utilized by the gut. Approximately 60% of dietary threonine is retained by the gut and is mainly used for mucin synthesis [43]. Supplementation of threonine, cysteine, serine, and proline above the recommended level improved mucin synthesis and prevented inflammation in animal models of IBD [44], indicating that requirements may increase under stress conditions. Fecal mucin excretion in a chemical model of colitis was increased in rats fed cheese whey protein, which is a rich source of threonine and cysteine [18]. This indicates that whey protein isolate, which is rich in threonine and cysteine, may be useful to stimulate mucin production and thus protection of the gut epithelium.

Moreover, whey protein isolate and α -lactalbumin have been shown to improve the mucous layer in the stomach [45, 46]. Whey protein isolate increased the thickness of the protective gastric mucous layer in rats and protected against ethanol-induced and stress-induced gastric mucosal injury. When individual whey proteins were dosed at levels present in whey protein isolate, only α -lactalbumin showed comparable effects whereas the other major whey proteins, β -lactoglobulin, bovine serum albumin, and immunoglobulins were not effective [45]. Interestingly, considering the amino acid composition of the administered oral loads [45], the effects cannot be attributed to their contents of sulfur amino acids or threonine, which were higher in the α -lactoglobulin load than in the β -lactalbumin load. This suggests that α -lactalbumin may directly stimulate the gastric protective mucous layer in an as yet unidentified way.

Whey proteins and whey-derived growth factors are also proposed to contribute to gut health by modifying the immune response and supporting mucosal wound healing. Oral administration of GMP and lactoferrin have been shown to protect against chemical-induced colitis in rats [47-49]. Protection against colitis coincided with an inhibition of immune cell activation [47] or by redirecting cytokines, which are important messengers in the immune response, into an anti-inflammatory mode [48, 49]. In addition, whey protein contains growth factors, which could help mucosal wound healing. A milk growth factor extract derived from cheese whey ameliorated intestinal damage and decreased gut permeability in rats receiving the chemotherapy drug methotrexate [50], and reduced experimental colitis in rats [51]. Whether whey proteins stimulate human gastrointestinal mucin secretion and subsequently benefit IBD patients needs verification.

Taken together, these results show that whey protein or its constituents can improve the mucous layer in the gastrointestinal tract and may function as anti-inflammatory ingredient. It is not clear, however, whether natural levels of whey protein(s) in milk are sufficient to exhibit these effects. Therefore, the efficacy of milk in preventing gut inflammation in humans still needs to be established in controlled intervention studies.

1.4.2. Calcium

Based on the anti-diarrheal and intestinal resistance-enhancing effects of dietary calcium in rat infection models and in a strictly-controlled human *E. coli* infection study, we speculated that calcium might be protective against gut inflammation as well. The above-mentioned beneficial effects of calcium on gut microbiota composition (stimulation of *Lactobacilli* and *Bifidobacteria*) and the decrease in non-specific intestinal permeability observed in several rat studies likely contribute to the enhanced resistance to infectious disease but are also relevant for gut inflammation. Microbial factors are crucial for induction of intestinal mucosal inflammation as inflammation cannot be induced in germ-free animals and antibiotic treatment can alleviate symptoms in IBD patients. In addition, increased intestinal permeability is observed in IBD patients, and interestingly, it seems to precede periods of increased inflammation [52]. Increased and uncontrolled leakage of immune-reactive bacteria or their components from the gut lumen into the gut mucosa triggers the inflammatory response.

To test the proposed beneficial effects of calcium against intestinal inflammation, dietary intervention studies were performed in transgenic HLA-B27 rats, which spontaneously develop colitis [40, 53]. The calcium diet significantly inhibited the chronic increase in intestinal permeability and inflammation-related diarrhea which is characteristic for this model and mimics human IBD. In support of this, mucosal levels of neutrophil myeloperoxidase and pro-inflammatory cytokines, and histological colitis scores, were also lower. Gene expression profiling showed that calcium prevented the colitis-induced increase in the expression of extracellular matrix remodeling genes (e.g. matrix metalloproteinases, procollagens, fibronectin), which was confirmed at the mucosal protein level [40, 53]. The effects of calcium were reproducible and far more powerful than those of antioxidant supplementation [54], which has been suggested as potential therapy in the literature. In summary, calcium ameliorates several clinically relevant aspects of colitis

severity, at least in a rat IBD model for spontaneous colitis. Reduction of mucosal irritation by luminal components, due to improved maintenance of gut barrier function, might be part of the protective mechanism.

To further substantiate these novel findings on calcium functionality in the gut, verification in human subjects is needed. A calcium intervention study in IBD or irritable bowel syndrome (IBS) patients is proposed. IBS patients suffer from milder mucosal inflammation together with variable intestinal discomfort. It should be noted that intestinal inflammation in IBD is mostly severe and will always need pharmacological treatment to relieve symptoms. Depending on the outcomes of human follow-up studies in the near future, the role of calcium as adjunct therapy besides drug treatment in IBD or as sole intervention in IBS should become clearer.

1.5. Conclusions

Milk is dense in potentially bioactive components which can improve host resistance to gut infection and inflammation. So far, bioactivities of individual milk components have been studied, rather than the complete milk matrix. However, there is good reason to assume that synergy in efficacy will be obtained if the complete milk matrix is used for milk is, among other functions, evolutionarily aimed to provide complete nutrition to the newborn and protect it from infections by enhancing the host defense. Up to now, most activities of individual milk components have only been tested *in vitro* and in various animal infection and inflammation models. So far, human evidence is still largely missing, but greatly needed to confirm the suggested beneficial effects on host resistance. Therefore, we strongly recommend well-designed human intervention trials, studying the anti-infective and anti-inflammatory potential of the milk matrix to follow-up the promising preclinical scientific evidence so far.

References

- 1. Bryce, J., C. Boschi-Pinto, K. Shibuya, and R.E. Black, WHO estimates of the causes of death in children. Lancet, 2005. 365(9465): p. 1147-52.
- 2. Mathers, C.D., A.D. Lopez, and C.J.L. Murray, The burden of Disease and mortality by condition: Data, methods, and results for 2001, in Global burden of disease and risk factors. 2006, Oxford University Press p. 45-93.
- 3. Grimwood, K., S.B. Lambert, and R.J. Milne, Rotavirus infections and vaccines: burden of illness and potential impact of vaccination. Paediatr Drugs, 2010. 12(4): p. 235-56.
- 4. Koo, H.L., N. Ajami, R.L. Atmar, and H.L. DuPont, Noroviruses: The leading cause of gastroenteritis worldwide. Discov Med, 2010. 10(50): p. 61-70.
- 5. Sartor, R.B., Mechanisms of disease: pathogenesis of Crohn's disease and ulcerative colitis. Nat Clin Pract Gastroenterol Hepatol, 2006. 3(7): p. 390-407.
- 6. Binder, V., Epidemiology of IBD during the twentieth century: an integrated view. Best Pract Res Clin Gastroenterol, 2004. 18(3): p. 463-79.
- 7. Loftus, C.G., E.V. Loftus, Jr., W.S. Harmsen, A.R. Zinsmeister, W.J. Tremaine, L.J. Melton, 3rd, and W.J. Sandborn, Update on the incidence and prevalence of Crohn's disease and ulcerative colitis in Olmsted County, Minnesota, 1940-2000. Inflamm Bowel Dis, 2007. 13(3): p. 254-61.
- 8. Fiocchi, C., Inflammatory bowel disease: etiology and pathogenesis. Gastroenterology, 1998. 115(1): p. 182-205.
- 9. Kvistgaard, A.S., L.T. Pallesen, C.F. Arias, S. Lopez, T.E. Petersen, C.W. Heegaard, and J.T. Rasmussen, Inhibitory effects of human and bovine milk constituents on rotavirus infections. J Dairy Sci, 2004. 87(12): p. 4088-96.
- 10. Nakajima, K., N. Tamura, K. Kobayashi-Hattori, T. Yoshida, Y. Hara-Kudo, M. Ikedo, Y. Sugita-Konishi, and M. Hattori, Prevention of intestinal infection by glycomacropeptide. Biosci Biotechnol Biochem, 2005. 69(12): p. 2294-301.

- 11. van Hooijdonk, A.C., K.D. Kussendrager, and J.M. Steijns, *In vivo* antimicrobial and antiviral activity of components in bovine milk and colostrum involved in non-specific defence. Br J Nutr, 2000. 84 Suppl 1: p. S127-34.
- 12. Moller, N.P., K.E. Scholz-Ahrens, N. Roos, and J. Schrezenmeir, Bioactive peptides and proteins from foods: indication for health effects. Eur J Nutr, 2008. 47(4): p. 171-82.
- 13. Bode, L., Human milk oligosaccharides: prebiotics and beyond. Nutr Rev, 2009. 67 Suppl 2: p. S183-91.
- 14. Cross, M.L. and H.S. Gill, Modulation of immune function by a modified bovine whey protein concentrate. Immunol Cell Biol, 1999. 77(4): p. 345-50.
- 15. Solomons, N.W., Modulation of the immune system and the response against pathogens with bovine colostrum concentrates. Eur J Clin Nutr, 2002. 56 Suppl 3: p. S24-8.
- 16. Snel, J., H.M. Timmerman, and M. Kleerebezem, The human intestine microbiome in health and disease. An emerging diagnostic and therapeutic target. Agro Food Industry Hi-Tech 2011. 22: p. S22-S24.
- 17. Bovee-Oudenhoven, I.M., M.L. Wissink, J.T. Wouters, and R. van der Meer, Dietary calcium phosphate stimulates intestinal *lactobacilli* and decreases the severity of a *salmonella* infection in rats. J Nutr, 1999. 129(3): p. 607-12.
- 18. Sprong, R.C., A.J. Schonewille, and R. van der Meer, Dietary cheese whey protein protects rats against mild dextran sulfate sodium-induced colitis: role of mucin and microbiota. J Dairy Sci, 2010. 93(4): p. 1364-71.
- 19. Coppa, G.V., L. Zampini, T. Galeazzi, and O. Gabrielli, Prebiotics in human milk: a review. Dig Liver Dis, 2006. 38 Suppl 2: p. S291-4.
- 20. Wolber, F.M., A.M. Broomfield, L. Fray, M.L. Cross, and D. Dey, Supplemental dietary whey protein concentrate reduces rotavirus-induced disease symptoms in suckling mice. J Nutr, 2005. 135(6): p. 1470-4.
- 21. Perez-Cano, F.J., S. Marin-Gallen, M. Castell, M. Rodriguez-Palmero, M. Rivero, C. Castellote, and A. Franch, Supplementing suckling rats with whey protein concentrate modulates the immune response and ameliorates rat rotavirus-induced diarrhea. J Nutr, 2008. 138(12): p. 2392-8.
- 22. Delorme, C., H. Brussow, J. Sidoti, N. Roche, K.A. Karlsson, J.R. Neeser, and S. Teneberg, Glycosphingolipid binding specificities of rotavirus: identification of a sialic acid-binding epitope. J Virol, 2001. 75(5): p. 2276-87.
- 23. Yolken, R.H., J.A. Peterson, S.L. Vonderfecht, E.T. Fouts, K. Midthun, and D.S. Newburg, Human milk mucin inhibits rotavirus replication and prevents experimental gastroenteritis. J Clin Invest, 1992. 90(5): p. 1984-91.
- 24. McCann, K.B., A. Lee, J. Wan, H. Roginski, and M.J. Coventry, The effect of bovine lactoferrin and lactoferricin B on the ability of feline calicivirus (a norovirus surrogate) and poliovirus to infect cell cultures. J Appl Microbiol, 2003. 95(5): p. 1026-33.
- 25. Taube, S., J.W. Perry, K. Yetming, S.P. Patel, H. Auble, L. Shu, H.F. Nawar, C.H. Lee, T.D. Connell, J.A. Shayman, and C.E. Wobus, Ganglioside-linked terminal sialic acid moieties on murine macrophages function as attachment receptors for murine noroviruses. J Virol, 2009. 83(9): p. 4092-101.
- 26. Baker, M. and B.V. Prasad, Rotavirus cell entry. Curr Top Microbiol Immunol, 2010. 343: p. 121-48.
- 27. Ochoa, T.J. and T.G. Cleary, Effect of lactoferrin on enteric pathogens. Biochimie, 2009. 91(1): p. 30-4.
- 28. Koopman, J.S., V.J. Turkisk, A.S. Monto, F.E. Thompson, and R.E. Isaacson, Milk fat and gastrointestinal illness. Am J Public Health, 1984. 74(12): p. 1371-3.
- 29. Petschow, B.W., R.P. Batema, and L.L. Ford, Susceptibility of *Helicobacter pylori* to bactericidal properties of medium-chain *monoglycerides* and free fatty acids. Antimicrob Agents Chemother, 1996. 40(2): p. 302-6.

- 30. Sprong, R.C., M.F. Hulstein, and R. Van der Meer, Bactericidal activities of milk lipids. Antimicrob Agents Chemother, 2001. 45(4): p. 1298-301.
- 31. Sprong, R.C., M.F. Hulstein, and R. van der Meer, Dietary calcium phosphate promotes *Listeria monocytogenes* colonization and translocation in rats fed diets containing corn oil but not milk fat. J Nutr, 2002. 132(6): p. 1269-74.
- 32. Thormar, H., C.E. Isaacs, H.R. Brown, M.R. Barshatzky, and T. Pessolano, Inactivation of enveloped viruses and killing of cells by fatty acids and monoglycerides. Antimicrob Agents Chemother, 1987. 31(1): p. 27-31.
- 33. Sprong, R.C., M.F. Hulstein, and R. van der Meer, High intake of milk fat inhibits intestinal colonization of *Listeria* but not of *Salmonella* in rats. J Nutr, 1999. 129(7): p. 1382-9.
- 34. Dewettinck, K., R. Rombauts, and N. Thienpont, Nutritional and technological aspects of milk fat globule membrane material. Int. Dairy J., 2008. 18: p. 436-457.
- 35. Bojsen, A., J. Buesa, R. Montava, A.S. Kvistgaard, M.B. Kongsbak, T.E. Petersen, C.W. Heegaard, and J.T. Rasmussen, Inhibitory activities of bovine macromolecular whey proteins on rotavirus infections *in vitro* and *in vivo*. J Dairy Sci, 2007. 90(1): p. 66-74.
- 36. Bovee-Oudenhoven, I., D. Termont, R. Dekker, and R. van der Meer, Calcium in milk and fermentation by yoghurt bacteria increase the resistance of rats to *Salmonella* infection. Gut, 1996. 38(1): p. 59-65.
- 37. Bovee-Oudenhoven, I.M., D.S. Termont, A.H. Weerkamp, M.A. Faassen-Peters, and R. Van der Meer, Dietary calcium inhibits the intestinal colonization and translocation of *Salmonella* in rats. Gastroenterology, 1997. 113(2): p. 550-7.
- 38. Bovee-Oudenhoven, I.M., M.L. Lettink-Wissink, W. Van Doesburg, B.J. Witteman, and R. Van Der Meer, Diarrhea caused by enterotoxigenic *Escherichia coli* infection of humans is inhibited by dietary calcium. Gastroenterology, 2003. 125(2): p. 469-76.
- 39. Schepens, M.A., A. Rijnierse, A.J. Schonewille, C. Vink, R.J. Brummer, L.E. Willemsen, R. van der Meer, and I.M. Bovee-Oudenhoven, Dietary calcium decreases but short-chain fructo-oligosaccharides increase colonic permeability in rats. Br J Nutr, 2010. 104(12): p. 1780-6.
- 40. Schepens, M.A., S.J. Ten Bruggencate, A.J. Schonewille, R.J. Brummer, R. van der Meer, and I.M. Bovee-Oudenhoven, The protective effect of supplemental calcium on colonic permeability depends on a calcium phosphate-induced increase in luminal buffering capacity. Br J Nutr, 2011: p. 1-7.
- 41. Tytgat, K.M., J.W. van der Wal, A.W. Einerhand, H.A. Buller, and J. Dekker, Quantitative analysis of MUC2 synthesis in ulcerative colitis. Biochem Biophys Res Commun, 1996. 224(2): p. 397-405.
- 42. Van der Sluis, M., B.A. De Koning, A.C. De Bruijn, A. Velcich, J.P. Meijerink, J.B. Van Goudoever, H.A. Buller, J. Dekker, I. Van Seuningen, I.B. Renes, and A.W. Einerhand, Muc2-deficient mice spontaneously develop colitis, indicating that MUC2 is critical for colonic protection. Gastroenterology, 2006. 131(1): p. 117-29.
- 43. Van Der Schoor, S.R., P.J. Reeds, B. Stoll, J.F. Henry, J.R. Rosenberger, D.G. Burrin, and J.B. Van Goudoever, The high metabolic cost of a functional gut. Gastroenterology, 2002. 123(6): p. 1931-40.
- 44. Faure, M., D. Moennoz, F. Montigon, C. Mettraux, D. Breuille, and O. Ballevre, Dietary threonine restriction specifically reduces intestinal mucin synthesis in rats. J Nutr, 2005. 135(3): p. 486-91.
- 45. Matsumoto, H., Y. Shimokawa, Y. Ushida, T. Toida, and H. Hayasawa, New biological function of bovine alpha-lactalbumin: protective effect against ethanol- and stress-induced gastric mucosal injury in rats. Biosci Biotechnol Biochem, 2001. 65(5): p. 1104-11.
- 46. Ushida, Y., Y. Shimokawa, T. Toida, H. Matsui, and M. Takase, Bovine alpha-lactalbumin stimulates mucus metabolism in gastric mucosa. J Dairy Sci, 2007. 90(2): p. 541-6.

- 47. Daddaoua, A., V. Puerta, A. Zarzuelo, M.D. Suarez, F. Sanchez de Medina, and O. Martinez-Augustin, Bovine glycomacropeptide is anti-inflammatory in rats with hapten-induced colitis. J Nutr, 2005. 135(5): p. 1164-70.
- 48. Togawa, J., H. Nagase, K. Tanaka, M. Inamori, A. Nakajima, N. Ueno, T. Saito, and H. Sekihara, Oral administration of lactoferrin reduces colitis in rats via modulation of the immune system and correction of cytokine imbalance. J Gastroenterol Hepatol, 2002. 17(12): p. 1291-8.
- 49. Togawa, J., H. Nagase, K. Tanaka, M. Inamori, T. Umezawa, A. Nakajima, M. Naito, S. Sato, T. Saito, and H. Sekihara, Lactoferrin reduces colitis in rats via modulation of the immune system and correction of cytokine imbalance. Am J Physiol Gastrointest Liver Physiol, 2002. 283(1): p. G187-95.
- 50. Tran, C.D., G.S. Howarth, P. Coyle, J.C. Philcox, A.M. Rofe, and R.N. Butler, Dietary supplementation with zinc and a growth factor extract derived from bovine cheese whey improves methotrexate-damaged rat intestine. Am J Clin Nutr, 2003. 77(5): p. 1296-303.
- 51. Porter, S.N., G.S. Howarth, and R.N. Butler, An orally administered growth factor extract derived from bovine whey suppresses breath ethane in colitic rats. Scand J. Gastroenterol, 1998. 33(9): p. 967-74.
- 52. Wyatt, J., H. Vogelsang, W. Hubl, T. Waldhoer, and H. Lochs, Intestinal permeability and the prediction of relapse in Crohn's disease. Lancet, 1993. 341(8858): p. 1437-9.
- 53. Schepens, M.A., A.J. Schonewille, C. Vink, E.M. van Schothorst, E. Kramer, T. Hendriks, R.J. Brummer, J. Keijer, R. van der Meer, and I.M. Bovee-Oudenhoven, Supplemental calcium attenuates the colitis-related increase in diarrhea, intestinal permeability, and extracellular matrix breakdown in HLA-B27 transgenic rats. J Nutr, 2009. 139(8): p. 1525-33.
- 54. Schepens, M.A., C. Vink, A.J. Schonewille, H.M. Roelofs, R.J. Brummer, R. van der Meer, and I.M. Bovee-Oudenhoven, Supplemental antioxidants do not ameliorate colitis development in HLA-B27 transgenic rats despite extremely low glutathione levels in colonic mucosa. Inflamm Bowel Dis, 2011. 17(10): p. 2065-75.
- 55. Berkhout, B., J.L. van Wamel, L. Beljaars, D.K. Meijer, S. Visser, and R. Floris, Characterization of the anti-HIV effects of native lactoferrin and other milk proteins and protein-derived peptides. Antiviral Res, 2002. 55(2): p. 341-55.
- 56. Stromqvist, M., P. Falk, S. Bergstrom, L. Hansson, B. Lonnerdal, S. Normark, and O. Hernell, Human milk kappa-casein and inhibition of *Helicobacter pylori* adhesion to human gastric mucosa. J Pediatr Gastroenterol Nutr, 1995. 21(3): p. 288-96.
- 57. Kanamaru, Y., M. Etoh, X.G. Song, T. Mikogami, H. Hayasawa, T. Ebina, and N. Minamoto, A high-Mr glycoprotein fraction from cow's milk potent in inhibiting replication of human rotavirus *in vitro*. Biosci Biotechnol Biochem, 1999. 63(1): p. 246-9.
- 58. Chen, C.C., M. Baylor, and D.M. Bass, Murine intestinal mucins inhibit rotavirus infection. Gastroenterology, 1993. 105(1): p. 84-92.
- 59. Superti, F., M.G. Ammendolia, P. Valenti, and L. Seganti, Antirotaviral activity of milk proteins: lactoferrin prevents rotavirus infection in the enterocyte-like cell line HT-29. Med Microbiol Immunol, 1997. 186(2-3): p. 83-91.
- 60. Arnold, D., A.M. Di Biase, M. Marchetti, A. Pietrantoni, P. Valenti, L. Seganti, and F. Superti, Antiadenovirus activity of milk proteins: lactoferrin prevents viral infection. Antiviral Res, 2002. 53(2): p. 153-8.
- 61. Bruck, W.M., S.L. Kelleher, G.R. Gibson, K.E. Nielsen, D.E. Chatterton, and B. Lonnerdal, rRNA probes used to quantify the effects of glycomacropeptide and alpha-lactalbumin supplementation on the predominant groups of intestinal bacteria of infant rhesus monkeys challenged with enteropathogenic *Escherichia coli*. J Pediatr Gastroenterol Nutr, 2003. 37(3): p. 273-80.
- 62. Shin, K., H. Wakabayashi, K. Yamauchi, S. Teraguchi, Y. Tamura, M. Kurokawa, and K. Shiraki, Effects of orally administered bovine lactoferrin and lactoperoxidase on influenza virus infection in mice. J Med Microbiol, 2005. 54(Pt 8): p. 717-23.

- 63. Brody, E.P., Biological activities of bovine glycomacropeptide. Br J Nutr, 2000. 84 Suppl 1: p. S39-46.
- 64. Li, S., H. Zhou, G. Huang, and N. Liu, Inhibition of HBV infection by bovine lactoferrin and iron-, zinc-saturated lactoferrin. Med Microbiol Immunol, 2009. 198(1): p. 19-25.
- 65. Ammendolia, M.G., M. Marchetti, and F. Superti, Bovine lactoferrin prevents the entry and intercellular spread of herpes simplex virus type 1 in Green Monkey Kidney cells. Antiviral Res, 2007. 76(3): p. 252-62.
- 66. Ammendolia, M.G., A. Pietrantoni, A. Tinari, P. Valenti, and F. Superti, Bovine lactoferrin inhibits echovirus endocytic pathway by interacting with viral structural polypeptides. Antiviral Res, 2007. 73(3): p. 151-60.
- 67. Shimizu, K., H. Matsuzawa, K. Okada, S. Tazume, S. Dosako, Y. Kawasaki, K. Hashimoto, and Y. Koga, Lactoferrin-mediated protection of the host from murine cytomegalovirus infection by a T-cell-dependent augmentation of natural killer cell activity. Arch Virol, 1996. 141(10): p. 1875-89.
- 68. Lu, L., G. Hangoc, A. Oliff, L.T. Chen, R.N. Shen, and H.E. Broxmeyer, Protective influence of lactoferrin on mice infected with the polycythemia-inducing strain of Friend virus complex. Cancer Res, 1987. 47(15): p. 4184-8.
- 69. Wang, X., S. Hirmo, R. Willen, and T. Wadstrom, Inhibition of *Helicobacter pylori* infection by bovine milk glycoconjugates in a BAlb/cA mouse model. J Med Microbiol, 2001. 50(5): p. 430-5.
- 70. Teraguchi, S., K. Shin, K. Ozawa, S. Nakamura, Y. Fukuwatari, S. Tsuyuki, H. Namihira, and S. Shimamura, Bacteriostatic effect of orally administered bovine lactoferrin on proliferation of Clostridium species in the gut of mice fed bovine milk. Appl Environ Microbiol, 1995. 61(2): p. 501-6.
- 71. Teraguchi, S., K. Shin, T. Ogata, M. Kingaku, A. Kaino, H. Miyauchi, Y. Fukuwatari, and S. Shimamura, Orally administered bovine lactoferrin inhibits bacterial translocation in mice fed bovine milk. Appl Environ Microbiol, 1995. 61(11): p. 4131-4.
- 72. Tanaka, K., M. Ikeda, A. Nozaki, N. Kato, H. Tsuda, S. Saito, and H. Sekihara, Lactoferrin inhibits hepatitis C virus viremia in patients with chronic hepatitis C: a pilot study. Jpn J Cancer Res, 1999. 90(4): p. 367-71.
- 73. Ueno, H., T. Sato, S. Yamamoto, K. Tanaka, S. Ohkawa, H. Takagi, O. Yokosuka, J. Furuse, H. Saito, A. Sawaki, H. Kasugai, Y. Osaki, S. Fujiyama, K. Sato, K. Wakabayashi, and T. Okusaka, Randomized, double-blind, placebo-controlled trial of bovine lactoferrin in patients with chronic hepatitis C. Cancer Sci, 2006. 97(10): p. 1105-10.
- 74. Mohan, P. and S.A. Abrams, Oral lactoferrin for the treatment of sepsis and necrotizing enterocolitis in neonates. Cochrane Database Syst Rev, 2009(1): p. CD007138.
- 75. Okuda, M., T. Nakazawa, K. Yamauchi, E. Miyashiro, R. Koizumi, M. Booka, S. Teraguchi, Y. Tamura, N. Yoshikawa, Y. Adachi, and I. Imoto, Bovine lactoferrin is effective to suppress *Helicobacter pylori* colonization in the human stomach: a randomized, double-blind, placebocontrolled study. J Infect Chemother, 2005. 11(6): p. 265-9.
- 76. Zullo, A., V. De Francesco, G. Scaccianoce, G. Manes, C. Efrati, C. Hassan, G. Maconi, D. Piglionica, C. Cannaviello, C. Panella, S. Morini, and E. Ierardi, *Helicobacter pylori* eradication with either quadruple regimen with lactoferrin or levofloxacin-based triple therapy: a multicentre study. Dig Liver Dis, 2007. 39(9): p. 806-10.
- 77. Sanchez-Juanes, F., J.M. Alonso, L. Zancada, and P. Hueso, Glycosphingolipids from bovine milk and milk fat globule membranes: a comparative study. Adhesion to enterotoxigenic *Escherichia coli* strains. Biol Chem, 2009. 390(1): p. 31-40.
- 78. Sprong, R.C., M.F. Hulstein, and R. Van Der Meer, Bovine milk fat components inhibit foodborne pathogens. Int Dairy J, 2002. 12: p. 209-215.
- 79. Habte, H.H., C. de Beer, Z.E. Lotz, M.G. Tyler, D. Kahn, and A.S. Mall, Inhibition of human immunodeficiency virus type 1 activity by purified human breast milk mucin (MUC1) in an inhibition assay. Neonatology, 2008. 93(3): p. 162-70.

- 80. McAuley, J.L., S.K. Linden, C.W. Png, R.M. King, H.L. Pennington, S.J. Gendler, T.H. Florin, G.R. Hill, V. Korolik, and M.A. McGuckin, MUC1 cell surface mucin is a critical element of the mucosal barrier to infection. J Clin Invest, 2007. 117(8): p. 2313-24.
- 81. Oka, H., T. Onaga, T. Koyama, C.T. Guo, Y. Suzuki, Y. Esumi, K. Hatano, D. Terunuma, and K. Matsuoka, Syntheses and biological evaluations of carbosilane dendrimers uniformly functionalized with sialyl alpha(2-->3) lactose moieties as inhibitors for human influenza viruses. Bioorg Med Chem, 2009. 17(15): p. 5465-75.
- 82. Simon, P.M., P.L. Goode, A. Mobasseri, and D. Zopf, Inhibition of *Helicobacter pylori* binding to gastrointestinal epithelial cells by sialic acid-containing oligosaccharides. Infect Immun, 1997. 65(2): p. 750-7.
- 83. Idota, T., H. Kawakami, Y. Murakami, and M. Sugawara, Inhibition of cholera toxin by human milk fractions and sialyllactose. Biosci Biotechnol Biochem, 1995. 59(3): p. 417-9.
- 84. Mysore, J.V., T. Wigginton, P.M. Simon, D. Zopf, L.M. Heman-Ackah, and A. Dubois, Treatment of *Helicobacter pylori* infection in rhesus monkeys using a novel antiadhesion compound. Gastroenterology, 1999. 117(6): p. 1316-25.
- 85. Opekun, A.R., H.M. El-Zaimaity, M.S. Osato, M.A. Gilger, H.M. Malaty, M. Terry, D.R. Headon, and D.Y. Graham, Novel therapies for *Helicobacter pylori* infection. Aliment Pharmacol Ther, 1999. 13(1): p. 35-42.
- 86. Parente, F., C. Cucino, A. Anderloni, G. Grandinetti, and G. Bianchi Porro, Treatment of *Helicobacter pylori* infection using a novel antiadhesion compound (3'sialyllactose sodium salt). A double blind, placebo-controlled clinical study. Helicobacter, 2003. 8(4): p. 252-6.

PROCEEDINGS OF THE IDF WORD DAIRY SUMMIT 2011 - PARMA, ITALY, 12-19 OCTOBER 2011

ABSTRACT

Collection of papers from conferences during the IDF World Dairy Summit in Parma, Italy, in October 2011

Animal Feeding

The link between feeding and welfare in dairy cattle - Cheryl M. E. McCrindle, South Africa, and Beniamino T. Cenci Goga, Italy

Animal welfare involves well-being, living in harmony with the environment, fulfilment of physical, health and behavioural needs and not being subjected to unreasonable pain or distress, protein-energy malnutrition, water deprivation, mineral deficiencies and imbalances, Feeding is described in relation to protein-energy malnutrition, water deprivation, mineral deficiencies and imbalances, fast fermenting sugars and starches, roughage and forage composition and feeding behaviour. Diseases linked to feeding include starvation resulting in suboptimal body condition score, laminitis, arthritis, acidosis, abomasal displacement, milk fever, calving difficulties and retained afterbirth. Feeding systems should be formulated tocontribute to well-being, and hence result in better productivity.

Keywords: animal welfare, feeding composition, iadequate feeding, dairy productivity.

Animal Health

The welfare of diary animals: the perspective of Mediterranean farmers - Paolo Ferrari, Italy

Animal welfare requirements of EU legislation represent progress, and are sufficient as they stand to achieve desired objectives. Further upgrading of animal welfare standards can be achieved by voluntary agreements between milk producers, milk processors, animal welfare groups and retailers. Higher standards involve a greater burden on producers, especially small producers who are numerous in the Mediterranean zone. Improvements are needed in producer education, equipment and organization of advice to farmers to achieve these levels. Stricter legislation brings the danger of more administrative demands on producers who are already heavily burdened. Enforcement of the rules should be uniform across Europe to avoid creating unfair competition.

Keywords: animal welfare legislation, voluntary agreements; administrative burdens, uniform enforcement

Lameness, Cow Welfare And Sustainable Farming ¬ H. Hogeveen, M.R.N. Bruijnis and E.N. Stassen, Netherlands

Sustainable dairy farming system can involves animal welfare, in combination with social responsibility and a decent profit. Diseases affect both welfare and profit. Foot disorders are an important health problem in current dairy farming. Costings are provided for the different type of foot disorder. Studying foot disease and its effects results in improved advice on animal care and improved profitability.

Keywords: sustainable dairy farming, animal welfare, foot disorders, lameness, profitability

Dairy Policies

Protected Designation of Origin - Italian model - Leo Bertozzi, Italy

Protected designation of origin for traditional cheeses from dairy animals of commercially available species covers 51% of all milk produced in Italy. PDO products, currently 42 different types in Italy, enjoy market growth, their qualities being appreciated by consumers. Production statistics are provided. Traditional production techniques represent the sum of long experience and relevant modern developments. The internationally recognized Stresa Convention on Cheeses (1951) recognized the distinction between generic and authentic names, a distinction necessary to avoid misleading consumers. Signatories undertook to ptrotect authentic names and ban their misuse in their territories. These principles of protection of geographical designations are now applied Europe-wide. A table shows the number of such products per EU country.

Keywords: protected designation of origin, traditional products, Stresa Convention, Europe

Global milk production - Torsten Hemme, Germany

IFCN has analysed milk production trends and the factors that determine them since the year 2000. Milk production creates the greatest proportion of costs, resources used, emissions created and political challenges in the dairy chain. Milk prices have shown considerable volatility in the last six years. Production costs, on the other hand, relate largely to the situation in the area of production and the management systems used. Feed prices have risen inexorably in recent years. Farm structure affects the suitability of systems to farm size and location. A table shows the top 21 milk processors in the world. Criteria are identified for the factors putting ptressure on milk production.

Keywords: milk production, farm size, production costs, milk prices, feed prices

World dairy companies: restructuring & investments - B. Rouyer, France

Leading dairy companies dominate the world market, but the geographical spread of countries involved in the top 24 has grown in the past twelve years. Many mergers and acquisitions have ocurred in established firms and in new growing markets (Asia) firms have grown to join the top 24. Another trend is the increase in international operations of many companies hitherto limited to one country or one continent.

Keywords: World dairy markets, mergers and acquisitions, internationalization

Environment

Towards a partnership on benchmarking and monitoring the environmental performance of livestock food chains - Michael MacLeod and Pierre Gerber, Food and Agriculture Organization of the United Nations (FAO), Rome

The livestock sector should improve its environmental performance, while meeting increasing demand for its products. FAO is setting up a global Partnership to aid improving the environmental performance of livestock supply chains. Involving stakeholders from different sectors is a key feature. The Partnership is open to members from the private sector, NGOs, governments, international organizations and technical experts. The Partnership will pursue the following activities:

- 1. sector-specific guidelines for the assessment of greenhouse gas (GHG) emissions.
- 2. analytical tools for the assessment of GHG emissions associated with feed ingredients.
- 3. indicators of the wider environmental performance of livestock supply chains.
- 4. transparent and balanced communication of the findings.

Keywords: livestock sector, environmental performance, greenhouse gases, global partnership

Food Safety

The Biology of Antimicrobial Resistance - Where Does It Come From and How Does It Spread? Glenn F. Browning, Australia

Prudent use of antimicrobials is a cornerstone of modern animal welfare. Reduction of antimicrobial resistance must be based on this fact. The success of antibiotics in disease control has resulting in extensive use and increased exposure of the microorganisms they attack. Natural selection ensures that microorganisms with resistant genes will tend to survive. But, the rate of discovery of new classes of antibiotics has slowed.

Use of the same drugs for treatment human and veterinary medicine has lead to accusations that veterinary use is less rigorously controlled but there is no reason to assume this. Multiple resistance means resistance by one organism to a multiplicity of drugs. The origin of much microbial resistance appears to lie in organisms in the environment. Control of resistance requires recognition of the fact that resistance genes have been in some organisms long before medical and veterinary use of antibiotics was started. These organisms needed them to survive in the natural environment where antibiotics are also found. Options for control of resistance are discussed in relation to specific organisms as examples of possible approaches. Limiting usage, application of biosecurity measures, using antimicrobials targeted to the microorganism causing the problem.

Keywords: resistance control, prudent use, alternative strategies, biosecurity

The concerns of the dairy industry in relation to public health and market access - Dr E.S. Komorowski, United Kingdom

Although the use of antibiotics is strictly controlled and monitored by the dairy industry there is a need to continue to challenge existing practices, to ensure a robust defence against ill-informed attacks.

Reactions in the media tend to sensationalism. The reality is that the use of veterinary drugs is subject to controls and these controls are enforced to eliminate antibiotic residues from milk and combat the evolution of resistant bacterial strains. Mistakes can be made, of course, and these have to be minimized by farm management and veterinary practice. Certain antibiotics have to be excluded from veterinary use. It is desirable for the prescribing of antibiotics to be uniform between countries to minimize difficulties of trade. Voluntarily agreed good practice can achieve these aims, but legislation may be introduced if this is not done.

Keywords: antibiotic use, dairy industry, farm management, veterinary practice

Antimicrobial use in the dairy industry in South Africa: sustainable food security requires the prudent use of antimicrobial agents, - CME McCrindle, South Africa, Cenci Goga B T, Italy, Botha C, South Africa, Naidoo V, South Africa

In South Africa sophisticated dairying exists alongside small scale and subsistence dairy farms. Antimicrobials are use to treat tropical diseases in animals as well as mastitis. Antimicrobial residues can create problems. Antimicrobial resistance must be avoided. Use and misuse of antimicrobials in South Africa is reviewed. A decision-tree approach and risk analysis are recommended.

Keywords: antimicrobials, tropical disease, antibiotic residues, antibiotic resistance, decision-trees

Nutrition

The Role Of Dairy Calcium In Tooth And Bone Health Through Life Stages - William R. Aimutis, USA

Nutrients influence fetal development. Calcium is an essential mineral for skeletal development. dairy consumption reduces the risk for osteoporosis in later life. Calcium consumption in the first 30 years of life means reduced bone fracture risk and lower propensity to dental caries. But calcium consumption should be continued to reduce loss in bone mass. Physiology and biochemistry of calcium metabolism are described.

Keywords: dairy calcium, skeletal development, osteoporosis, bone mas, dental caries, caseinophosphopeptide

Traditional Dairy Products in Developing Countries - Professor Jashbhai B Prajapati, India

Dairying is one of the prime sectors for socio-economic development in most developing countries. About 50-55% of the milk produced in developing countries is utilized for making traditional dairy products. Traditional products include fermented dairy products, cheese, coagulated mik, heat-desiccated products, frozen desserts and fat-rich products. Functional products are growing in importance. These products are important in promoting nutritional security in developing countries.

Keywords: Traditional Dairy Products, Nutrition, Developing Countries, Milk Products, Dairy Industry.

The anti-infective potential of milk products: Positive effects of milk to prevent gastrointestinal infection and inflammation - R. Corinne Sprong, Johannes Snel, Ingeborg M.J. Bovee-Oudenhoven, New Zealand

Bioactivity of milk includes antimicrobial activity, balancing gut microbiota composition, improving the gut barrier function, and immune modulation. Therefore, milk or its constituents may improve the defense against gut infection and may reduce gastrointestinal inflammation. This paper summarizes the effect of milk and milk constituents on gut infections and inflammation. However the anti-infective potential of single milk ingredients is tested rather than their contribution in the complete dairy matrix. Data from in vitro studies do not answer the question whether high dairy consumption is beneficial for human gut health. Well designed intervention trials are

needed to establish the role of milk and milk products in improving human resistance to gastrointestinal infection and inflammation. Keywords: antimicrobial, microbiota, gastrointestinal infection, inflammation, milk, gut permeability, inflammatory bowel disease, gut health 110 pp - English only Bulletin N° 457/2012 - Free of charge (electronic) - Date: 2012

INTERNATIONAL DAIRY FEDERATION

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1 Singh, H. & Creamer, L.K. Aggregation & dissociation of milk protein complexes in heated reconstituted skim milks. J. Food Sci. Example:

56:238-246 (1991).

2 Walstra, P. The role of proteins in the stabilization of emulsions. In: G.O. Phillips, D.J. Wedlock & P.A. William (Editors), Gums & Example:

Stabilizers in the Food Industry - 4. IRL Press, Oxford (1988).

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w	Usually double guotes and not single guotes
7	Usually double quotes and not single quotes Half-space before and after question marks, and exclamation marks
±	Half-space before and after
microorganisms	Without a hyphen
Infra-red	
	Not underlined nor italic
e.a., i.e	Spelled out in English - for example, that is
litre	Not liter unless the author is American
ml, ma,	Space between number and ml, mg,
	One word if adjective, two words if substantive
	Not sulphuric, sulphite, sulphate (as agreed by IUPAC)
AOAC International	
	Not program unless a) author is American or b) computer program
milk and milk product	rather than "milk and dairy product" - Normally some latitude can be allowed in non scientific texts
-ize, -ization	Not -ise, -isation with a few exceptions
Decimal comma	in Standards (only) in both languages (as agreed by ISO)
No space between figure and	l % - i.e. 6%, etc.
Milkfat	One word
USA, UK, GB	No stops
Figure	
1000-9000	No comma
10 000, etc	No comma, but space
hours	ø h
second	
litre	ø I
<u>t</u> he Netherlands	
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