

The A2 Milk Debate: Searching for the Evidence

Keith Woodford
Professor of Farm Management and Agribusiness
Lincoln University
woodfork@lincoln.ac.nz

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Introduction

The debate about A2 milk has been in the public arena for at least five years. There have been lots of claims and counter claims about whether 'ordinary milk', which is a mixture of A1 and A2 milk, is linked to a range of disease conditions, and whether selecting for cows that produce only A2 milk can avoid these problems. Despite the claims and counter claims, the substance of the arguments has not been widely aired in public. Instead, most people have only heard the assertions. Therefore it has been a case of making a judgement as to which of the two competing sides has most credibility.

In early August 2004 the New Zealand Food Safety Authority (NZFSA) released the 'Swinburn Report' (Swinburn 2004). The NZFSA had contracted Professor Boyd Swinburn back in March 2003 to review the scientific evidence for and against the A1/A2 hypothesis. Depending on which media report people were exposed to, it would have been reasonable to accept either that the Swinburn Review had found that there was no difference between A1 and A2 milk, or that there were indeed significant concerns about the health implications of A1 milk. And so the issues remain as muddy as ever.

The purpose of this paper is to present the evidence for and against. In that way dairy farmers and their consultants can make their own judgements as to whether or not this is an issue that they need to be concerned about.

Captured Interests

One of the problems of the A2 debate is that the participants are widely seen to be less than independent. A2 Corporation is obviously a commercial organisation whose success depends on convincing the public that the issues are real. On the other hand, life would be simpler for existing mainstream players in the dairy industry if the A2 issue would disappear. Even the scientists are often seen as 'captured interests' in that their livelihood can depend on the next grant, and much of their funding comes from commercial interests. Reputable scientists do not manipulate results, but there is often more than one potentially valid interpretation that can be placed on their results. Unconscious bias can exist.

In recent months I have made a number of statements in relation to the A2 issue, and so I regularly get asked as to the nature of my relationship with the various protagonists. Am I independent or is Keith Woodford also a captured interest?

My interest in A2 milk arose by chance towards the end of 2003. I had noticed that Dr Jock Allison had become a Director of A2 Corporation. Jock will be known to many professional agriculturalists as a former Director of Invermay Research Station and also through his involvement in the introduction of exotic sheep such as the East Friesian. He has been part of many industry organisations (such as a Director of the Wool Board and Director of AgResearch) and in 2003 he was Lincoln University's Bledisloe Medallist. Jock's involvement with A2 Corporation intrigued me, and so when I next met Jock I asked him why he was associated with an organisation that many people might think was a bit shonky. Jock told me in no uncertain terms what he thought, and pulled a paper from his bag for me to read. I was sufficiently impressed that I began to do a lot more reading.

As part of getting on top of the issues I have talked and continue to talk to as many people as I can from both sides of the fence. However, I have no contractual association with any of the organisations involved. Subsequent and consequent to my interest, I have family members who have purchased a small shareholding in A2 Corporation, although I do not myself hold any shares. I do by choice drink A2 milk, which for Christchurch dwellers like me is currently freighted from Hamilton.

Where Did It Start?

The A2 story started in 1993 with Professor Bob Elliott from Auckland University. Bob was Professor (now Emeritus Professor) of Child Health, and as part of his work had been looking at the incidence of Type 1 diabetes amongst Samoan children. Type 1 diabetes is an immune response disease where the pancreas loses its ability to produce insulin. The disease usually strikes in childhood, but only a small proportion of people seem to be susceptible. Once a person has Type 1 diabetes that person will need to take insulin injections for the rest of his or her life. The incidence of Type 1 diabetes has been steadily rising throughout the world and it has been a real puzzle as to why this is happening.

There are two types of diabetes. In contrast to Type 1, Type 2 is mainly a disease of older people. The Type 2 disease is also related to an inability to produce sufficient insulin to digest sugars. But unlike Type 1, the causes of Type 2 are well known, even if the precise biological mechanisms are still unclear. The way to prevent or at least very much reduce the risk of Type 2 diabetes is through exercise and weight control. In contrast, there are no generally accepted health strategies for avoiding Type 1 diabetes.

Bob Elliott was aware that Samoan children living in New Zealand were very susceptible to Type 1 diabetes whereas Samoan children living in Samoa had an extremely low incidence. This difference could only be explained by an environmental or dietary factor. Bob suspected that at least part of the answer related to the consumption of milk, but he also knew that the answer was not going to be anywhere near as simple as that.

Accordingly, Bob telephoned the New Zealand Dairy Research Institute (now the Fonterra Research Centre) and asked to speak to someone who knew something about

milk protein biochemistry. Dr Jeremy Hill took the call. His advice was that it could be worth looking at the beta-casein proteins. It would be a long shot but worth a look.

The Initial Research

Bob Elliott took Jeremy Hill's advice, and indeed started working with Jeremy. There were two strands to their initial research. One was to look at the epidemiology of Type 1 diabetes. This involved comparing the incidence of Type 1 diabetes in a range of countries with the intake of A1 milk, versus the same comparisons with intake of A2 milk. This was possible because the proportion of A1 to A2 beta-casein proteins varies considerably between the herds in different countries. The second strand was to see what happened to mice when some were fed A1 milk and the remainder fed A2 milk.

In both cases the outcomes from this initial work were startling. Yes, the inter-country comparisons did show a strong association between intake of A1 milk (but not A2 milk) and the incidence of diabetes. And yes, the mice that were fed A1 milk did develop a very high incidence of diabetes whereas the mice fed A2 milk did not.

At this stage Dr Corann McLachlan was asked to review the epidemiology. Not only was he impressed by the results, but he also quickly saw that there was a similar association between countries with high levels of heart disease and the intake of A1 milk. Corann was himself the inventor of a cholesterol free butter but he knew that the association between intake of cholesterol and heart disease was tenuous. This link with A1 beta protein looked much more exciting.

Corann McLachlan then dedicated the rest of his life to working on A1 beta protein and assembling data that might prove the link. In 2000 he teamed up with entrepreneur Howard Patterson to form A2 Corporation. However, both Corann McLachlan and Howard Paterson died within a few weeks of each other in mid 2003. A2 Corporation subsequently went close to insolvency but a cash rights issue in early 2004 has rectified that situation.

A2 Corporation does not sell A2 milk. Rather, it licenses the technology to test the DNA of cattle to see whether they are producers of A1 milk, A2 milk, or an A1/A2 combination. It also licenses the use of the A2 trademarks and logos to marketers of A2 milk.

The Difference between A1 and A2 milk

Milk is about 88% water and 12% solids. The solids include milk fat, protein, lactose and minerals. The protein is of two general types, these being whey and casein. The casein proteins can be further divided into three types, these being alpha, beta and kappa casein. In a litre of milk there is about 15grams of beta-casein.

The difference between A1 and A2 milk is a tiny difference in the beta-casein protein. Both of these proteins contain 209 amino acids strung together and only one of these amino acids is different. Whereas the A1 protein contains the amino acid histidene at

position 67, the A2 protein contains proline. Both German and Japanese scientists (Hartwig et al 1997, Jinsmaa and Yoshikawa 1999) have shown under conditions of in vitro digestion that A1 beta-casein breaks down to form the peptide beta-casomorphin-7 (BCM7) but that this does not occur with the A2 beta-casein. Fonterra stated in one of their patent applications (Patent Number WO 02/19832 A1) that they also obtained this same result in their work.

It is well known that this beta-casomorphin-7 (hereafter referred to as BCM7) is a powerful opioid. This means it acts in similar ways to morphine. With many people it breaks down further in the gut and causes no opioid problem. But in some people it passes through into the bloodstream. Then it has the potential to cause mayhem. Not all of the effects of the BCM7, and also the sub particles such as BCM4 and BCM5, are necessarily due to it being an opioid. There is also emerging evidence that it oxidises the low density lipoproteins (or LDL) and this is linked to heart disease. (LDL carries cholesterol from the liver to the tissues and in common parlance it is LDL cholesterol that is the 'bad cholesterol'.)

Which is Normal: A1 or A2?

Originally, all cows' milk was A2. Then about 5000 years ago (although no-one knows the date with any accuracy) a mutation occurred in European cattle and some cows started producing the A1 protein. Typically in New Zealand milk about half the beta-casein protein is A1 and the rest is A2. This proportion varies from country to country depending on the particular breed. The native cattle of Africa and Asia produce only A2 milk. Also, goats milk and sheep milk is essentially A2 in that the amino acid at the equivalent position is proline rather than histidine. It is the same story with humans. So there is a good argument that it is really A2 milk that is 'normal milk' and it is A1 milk that is 'abnormal'. There seems to be no argument that A2 milk is the 'original milk'.

Some More Epidemiology.

Following the initial findings, Elliott, McLachlan and others beavered away refining their data and analyses. The most impressive papers are one that was authored by McLachlan and published in the journal *Medical Hypotheses* (McLachlan 2001), and another by Murray Laugeson (from New Zealand Health) and Bob Elliott published in the *New Zealand Medical Journal* (Laugeson & Elliott 2003). The relationships that they found, both for heart disease and Type 1 diabetes, are remarkably strong and there are no doubts about the statistical significance. Unless the data has been selectively chosen, either accidentally or fraudulently (and no-one has ever suggested the latter) then the relationships are extremely unlikely to be due to chance. But that is not the same as saying that A1 milk is causing heart disease and diabetes. In theory, there could be something else out there that is linked to both A1 milk and these diseases.

To take a simplistic example (but one that has been used by those arguing against the A2 milk hypothesis), there is a very strong association between people who wear dresses and people who get breast cancer. Similarly, there is a very strong association between

people who wear trousers and people who get prostate cancer. We all know the reason why this is so, and therefore no-one suggests that wearing dresses causes breast cancer or trousers cause prostate cancer, despite the very strong statistical associations. Instead, it is all about gender.

The difference with the A1 and A2 milk hypothesis is that no-one can come up with what the other factor or factors might be, beyond a generic statement such as 'lifestyle'. There is no other factor that has been found to give the high statistical associations, despite a lot of searching.

In Iceland, where the cows are predominantly A2, there is a low to moderate level of heart disease, whereas in Finland, where the people are of similar ethnicity to the Icelanders but the cows are mainly A1, the incidence of heart disease is very high. McLachlan even found in the various regions of Germany that there are marked changes in level of heart disease and this correlates with different breeds of cattle and hence different levels of A1 in the milk. In Japan, where A1 consumption is very low, heart disease is also very low despite Japanese being heavy smokers. (Smoking is usually considered a big risk factor). The Masai people in Kenya drink very high levels of milk but have very low levels of heart disease. All of their milk is A2.

Rats and Mice

Following Professor Bob Elliott's initial work there was a much bigger trial funded by the Dairy Research Institute (now part of Fonterra) (Beales et al. 2002). The trials used genotypes of rats and mice that were susceptible to diabetes, and involved research teams in New Zealand, Canada and Britain. The Canadian trials showed some evidence supporting Bob Elliott's earlier work but the British trials did not. The New Zealand animals died of an infection. The work was published in the Journal Diabetologia in 2002. Subsequently it became known that the trials were confounded by contamination of the base diets, such that both the so-called A1 and A2 diets contained lots of BCM7, which those who believe in the A2 hypothesis think is the cause of the A1 problem. So the trial was a total mess and many people think the data should have been thrown away rather than published. But it was published, without acknowledgement of the problem in diet formulation, despite at least one of the authors (by his own writing elsewhere) indicating that he knew prior to publication there was a problem.

Heart Disease in Rabbits

Professor Julie Campbell from the University of Queensland is a specialist in vascular heart disease. Her research team fed A1 milk and A2 milk to rabbits. The rabbits fed A1 milk had higher cholesterol levels than the rabbits fed A2 milk. Much more importantly, the A1 rabbits developed lesions and thickening on the artery walls. Professor Campbell's work was published in 2003 in the international medical journal 'Atherosclerosis' (Tailford et al. 2003). The conclusions were that A1 milk is 'atherogenic' (causes heart disease) and that A2 milk may have a protective effect. Particularly important (and worrying) is that the lesions in the arteries of rabbits fed A1

milk were very similar to what is known as ‘juvenile fatty streaks’ in humans. These are believed to be a forerunner of heart disease. The scientific community seems satisfied that Professor Campbell’s work was very well done, although Professor Swinburn has expressed reservations about some aspects of the methodology. Also, Professor Mann and Dr Skeaff from Otago University (Mann and Skeaff 2003) have cautioned that it may be a big step extrapolating from rabbits to humans, and have criticised Professor Campbell and her co-authors for going too far in their claims.

The Gatorade man

Professor Robert Cade from the University of Florida invented ‘Gatorade’, which is a nutrient balanced drink used by many athletes and sports people. The royalties have provided the funds for Cade’s research into autism and schizophrenia. He has published many papers on these conditions, but perhaps the most important is the one published in *Nutritional Neuroscience* in 2000 (Cade et al. 2000). He found that many autistics and schizophrenics have extremely high levels of BCM7 (up to 100 times normal) in their urine. However, when placed on a gluten and casein free diet not only does the BCM7 eventually disappear from the urine, but there is also a marked reduction in the disease symptoms that the patients display. Cade and his co-workers have also shown that when rats are injected with BCM7 that the BCM7 enters the brain and causes symptoms that are similar to those of autism and schizophrenia. With humans, Cade has shown that when people suffering from autism are placed on a gluten and casein free diet it may take some weeks before there is any improvement. There may even be a deterioration as they go through the withdrawal phase from the addiction. But once the improvement starts it is ongoing, and continues for at least 12 months, by which stage the symptoms of autism are very much reduced.

The relevance for the A2 debate is that it should be possible for these susceptible people to consume A2 milk. Interestingly, Fonterra themselves filed for a patent in March 2002 claiming that A2 milk (which they called milk containing beta-casein with proline at position 67) does not, unlike A1 milk, aggravate neurological disorders. They presented very strong epidemiological data that deaths from neurological disorders were much higher in countries where there was a high incidence of A1 milk. However, they subsequently abandoned their patent application, and have not formally published their findings in the scientific literature.

The Counter Arguments from Fonterra’s scientists

Over the last two years Fonterra’s scientists have been increasingly critical about the A2 hypothesis. This is despite the Dairy Research Institute (now called the Fonterra Research Centre) having applied for two patents in relation to A2 milk. One of these patents (which was granted) relates to diabetes, and the other application (subsequently abandoned) relates to neurological effects.

The Fonterra scientists have put forth their arguments in a number of poster presentations at an international dairy conference and most of these have subsequently been published as poster papers in the Australian Journal of Dairy Technology in 2003. Another paper has been published in the Proceedings of the NZ Society of Animal Production in 2002.

It would be fair to say that the peer reviewing of all of these papers has been very limited. Publishing in this way does not have the scientific prestige of publishing full papers in the international journals such as *Atherosclerosis* or *Diabetologia* or similar. The poster papers are only one page and details of methods are not provided. But it is a very good way of getting a short sharp message across to a professional audience.

Most of these papers have several joint authors. However, the name that most people immediately think of in relation to Fonterra's research into A1 and A2 milk is Jeremy Hill. Jeremy was there from the start. It was he who set Bob Elliott off down the path of looking at the beta-caseins. His name is on the early patent applications, he co-authored Bob Elliott's early work, and it is also now on the papers arguing against the A2 hypothesis.

The data is no good

One of the Fonterra arguments has been that the assumptions behind the studies of people like Laugesen, McLachlan and Elliott are flawed. In particular they have argued that the data on A1 composition of the herds in various countries is quite limited and potentially unreliable. However, one of the characteristics of poor data is that it inevitably leads to poor correlations rather than good correlations. The statistical tests of the data undertaken by Laugesen, Elliott and McLachlan are designed to test that relationships are very unlikely to be due to chance. And the data passed those tests. So we know that there is something there that cannot be ignored. It is not just a freak of the data.

The Fonterra scientists have also said that they are unable to replicate the results of Laugesen, Elliott and McLachlan. In one paper the Fonterra scientists have presented data that indicate that whereas there was a relationship between heart disease and the level of milk intake back in the 1980s, this is no longer the case (Hill et al. 2002). There are two problems with that argument. The first is that they have worked with milk protein intake rather than A1 intake. Bob Elliott knew back in the early 1990s that it was not simply a case of milk protein intake that mattered. So the lack of correlations does not come as any surprise.

But the second problem became evident when I referred to the World Health Organisation (WHO) Database that the Fonterra scientists said they had used for their data. I wanted to see if I could get the same results as Fonterra. However, I found that the WHO had subsequently withdrawn the database because they had found there were too many anomalies in it. So that seemed to explain very easily why Fonterra could no longer find any correlations. Quite simply, the data that Fonterra had used had too many holes in it, and the provider of the data has now withdrawn it.

The importance of cheese

The Fonterra scientists have also argued that McLachlan's work was flawed because he excluded cheese intake from his analyses (Norris et al 2003a). Fonterra scientists have questioned whether this was valid because they have shown that there is some BCM7 within cheese (presumably obtained from the A1 component). However, they have also shown that the amount of BCM7 is very dependent on the type of cheese (with blue vein apparently being easily the worst). In fact, McLachlan obtained very high correlations when he included the consumption of cheese, but not quite so high as when he excluded it. The fact that there is such a variation in BCM7 depending on the type of cheese, and the fact that the types of cheese also varies between countries, gives a very clear explanation as to why McLachlan got better correlations after excluding the cheese. So if anything, this work supports the A2 hypothesis.

Human milk can produce BCM7

Another Fonterra argument is based on the fact that they have been able to demonstrate the presence of very small amounts of BCM7 in human milk (Norris et al 2003b). This is very interesting research, and it may link very nicely with developing evidence that post partum psychosis in women is linked to BCM7. But there are two very important points that need to be made. The first is that the amounts of BCM7 are minute compared to what is released by digestion of bovine A1 milk. The second is that human BCM7 is not the same as bovine BCM7. Amazingly, both are indeed called beta-casomorphin-7 (BCM7). This is because they are both peptides with seven amino acids starting with a tyrosine, and both have opiate properties – hence the last two syllables being ‘morphin’. But the reality is that two of the seven amino acids are different. And there is plenty of irrefutable scientific evidence that the biological properties of the human and bovine versions are quite different, with the morphine-like qualities of the bovine version being much stronger (about 10 times). So this Fonterra research (which has some Massey co-authors) is really very interesting. Perhaps even exciting. Given that the amount of BCM7 produced varied considerably between the women it may help to further explain the very distressing condition of post-partum psychosis. But it does nothing to disprove the A2 hypothesis.

If A1 milk is the problem, why is diabetes increasing but heart disease decreasing?

The argument from the Fonterra scientists (Crawford et al 2003) is that if the A1 beta casein found in A1 milk is the problem in relation to both diabetes and heart disease, how can it be that the incidence of one is increasing and the other is decreasing? They have used Switzerland as their example, but the same argument could have been mounted for many other countries. In Switzerland the intake of milk, and the A1 composition of that milk has remained stable over many years. Why then are the disease incidences changing?

The counter argument is that no-one is saying that A1 milk is the only cause of heart disease. To make such a claim would be ridiculous. Heart disease rates are dropping for a range of reasons related to lifestyle, less smoking, and also much better drugs such as the statins and even the good old aspirin. But there are still far too many people who die of heart disease despite leading the recommended lifestyles, not smoking, and taking

cholesterol reducing drugs. It is these unexplained deaths, which vary so much between countries, that are hypothesised to be related to intake of A1 beta casein.

The level of type 1 diabetes is increasing and the cause is perplexing. It is known to be an auto immune disease, and something is causing the body to destroy its own insulin producing cells in the pancreas. Some people think that A1 beta casein is the fundamental cause, and the presence of high antibody levels against the A1 beta casein in many people with Type 1 diabetes gives credence to this hypothesis. There is also evidence from Finland that amongst genetically susceptible children (i.e. those who have an older sibling with Type 1 diabetes) there is a relationship between the amount of cows milk that is drunk and the chance of getting diabetes. It would also seem that as we move to more and more sterile environments the level of auto immune diseases such as Type 1 diabetes increases. So yes, there is certainly a lot more to learn. And yes, it is also quite clear that if A1 beta-casein is the culprit then it is not working in isolation from everything else.

The Swinburn Review

Professor Boyd Swinburn from Deakin University in Australia was contracted by the New Zealand Food Safety Authority to undertake a review of the A1 and A2 evidence. Professor Swinburn submitted his review in July 2003 but it was not released until 3 August 2004 (Swinburn 2004). The delay of over a year was apparently caused by difficulty in finding people to review his draft report.

Some of the protagonists in the A1 versus A2 debate have attempted to hijack the report for their own devices. So I will use some direct quotes. However, the first of these quotes actually comes from Professor Swinburn's 'Lay Summary' which NZFSA deleted at the last moment from the published version. It was a great pity that this lay summary was omitted from the final report, as it encapsulated in just over a page of non scientific language the essence of his findings. Instead, most of the media focused on the NZFSA interpretation which was rather different.

The A1/A2 hypothesis is both intriguing and potentially very important for population health if it is proved correct. It should be taken seriously and further research is needed. In addition, the appropriate authorities have a responsibility to communicate the current state of evidence to the public, including the uncertainty of the evidence. Further public health actions, such as changing dietary advice or requiring labeling of milk products are not considered to be warranted at this stage."(Lay Summary)

Changing dairy herds to produce more A2 producing cows may significantly improve public health, if the A1/A2 hypothesis is proved correct, and it is highly unlikely to do harm. (p6)

As a matter of individual choice, people may wish to reduce or remove A1beta casein from their diet (or their children's diet) as a precautionary measure. This may be particularly relevant for those individuals who have or are at risk of the diseases

mentioned (type 1 diabetes, coronary heart disease, autism and schizophrenia). However, they should do so knowing that there is considerable uncertainty about the benefits of such an approach. (p6)

I have some criticisms of the Swinburn Review. For example, he totally omitted the work of Professor Cade (the 'Gatorade man'). Presumably he was unaware of this work. I believe this omission influenced his conclusions that the evidence in relation to autism was weak. Also, having clearly identified that the formation of BCM7 upon digestion was the key difference between A1 and A2 milk, he then failed to follow this through and review the extensive biochemistry and pharmacology related to BCM7 (which is found in science rather than medical journals). Professor Swinburn also appeared to place considerable weight on the 2002 Diabetologia paper on diabetes in rats and mice, without apparently being aware of the confounding in this work (referred to in an earlier section of this paper). Finally, he stated that there was no obvious mechanism by which the heart disease mechanism might operate, when there is a significant literature on how the BCM7 peptide might act in this way.

The question I ask, therefore, is how much stronger would the Swinburn Review have been if all of this work had been reviewed and included. There are at least another 40 scientific papers that should have been considered, and arguably over 60.

What do the Medics Say?

Both sides of the debate can call in their medical experts to state a position. On the one hand there are people like Professor Jim Mann from Otago University who makes it clear that he does not believe the A2 hypothesis. On the other hand there are people such as Professor Sir John Scott, an eminent retired cardiologist and former President of the NZ Royal Society (the peak body for NZ science) who said on Australian television last year that to ignore the A2 hypothesis was "ostrich like".

Most lay people get very frustrated that scientists can not agree on matters such as this. But that is the way that science always works. All big advances start off as being controversial and ridiculed. Over time some of these ridiculed theories fade away and others eventually become the new established wisdom. If anyone doubts this, they should read Bill Bryson's book 'A Short History of Nearly Everything' which is currently widely available in bookshops.

Consumer Response

A2 milk has been marketed in New Zealand since about March 2003 and is slowly becoming increasingly available. In Australia the uptake has been faster, largely due to considerable television exposure on current affairs programs on Channels 7 and 9 (the major commercial channels) and also the ABC (which ran a forty minute 'Four Corners' documentary in 2003). Currently, daily sales of A2 milk in Brisbane alone are believed to exceed total NZ weekly sales, despite the later start-up in Australia. The growth in the Australian market is currently constrained by the rate at which cows can be tested and the A2 herds set up.

As in NZ, the mainstream Australian industry sees A2 as a threat and argues against A2 milk.

In America, the company Ideasphere has been licensed to market A2 milk. They have 5000 health stores to initially market through, and are in the process of testing their first 100,000 cows. However, A2 milk has yet to hit the market over there.

What's in the Pipeline?

It is unlikely that there will be any sudden breakthrough, at least in the short term, that will lead to the issue being settled. Rather, it will be a case of gradually filling in the pieces of the jigsaw.

There is a trial currently underway at University of Otago that is testing the effect of A1 and A2 milk on cholesterol levels, but I doubt if that will prove much. Testing the A2 hypothesis requires testing for BCM in the bloodstream and urine, and also testing for LDL oxidation. Whether or not there will be a differential effect on cholesterol is doubtful, and my best guess based on what is already known about casein is that they may find that both the A1 and A2 diets lead to a reduction in blood cholesterol over the period of the trial. I have tried to convince the researchers involved to take blood samples, centrifuge the contents, and then store on ice for subsequent detailed analysis when funds are available. But alas, it is not happening.

There has also been an Australian trial that has been very drawn out as a result of difficulties in both trial design and implementation. It is therefore questionable as to whether any major insights will come from this trial.

The trials that have been published over the last few years (and mentioned in this article) have definitely stimulated interest amongst overseas scientists. My expectation is that there will be a flow of trial results, particularly but not only from the United States, within the next two years.

My other best guess is that some time in the next two years there will be a major review article published in a pre-eminent international medical journal. This will integrate the disparate knowledge that already exists across the science disciplines of protein chemistry and pharmacology with the empirical results published in the medical journals. At that point, when all the disparate knowledge is brought together, the A2 hypothesis will genuinely become mainstream. However, it will remain controversial for a lot longer than that.

The question for people in the dairy industry, therefore, is whether they should ignore the threat in the hope it will go away, or are there appropriate risk management strategies that can be taken. The answer is that there are possible strategies, but they take time to implement. This issue of farmer strategies will be taken up in a following article.

References

- Beales P.E., Elliott R.B., Flohé S., Hill J.P., Kolb H., Pozzilli P., Wang G.S., Wasmuth H. and Scott F.W. (2002), A multi-centre, blinded international trial of the effect of A1 and A2 beta casein variants on diabetes incidence in two rodent models of spontaneous Type 1 diabetes, *Diabetologia* 45, 1240-1246.
- Cade R, Privette M, Fregly M, Rowland N, Sun Z, Zele V, Wagemaker H, Edelstein C (2000), Autism and schizophrenia: intestinal disorders. *Nutritional Neuroscience* 3:57-72
- Crawford R.A., Boland M.J., Norris C.S., & Hill J.P. (2003a), Changes in milk consumption are not responsible for the increase in the incidence of Type-1 diabetes or decrease in the incidence of deaths due to ischaemic heart disease in Switzerland, *Aust. J. Dairy Tech.* 58: 188.
- Hartwig A., Teschemacher H., Lehmann W., Gaulty M., & Erhardt G. (1997), Influence of genetic polymorphisms in bovine milk on the occurrence of bioactive peptides. *In Milk Protein Polymorphism*, Int. Dairy Fed., Brussels, Belgium, pp459-460
- Hill J.P., Crawford R.A. & Boland M.J. (2002), Milk and consumer health: a review of the evidence for a relationship between the consumption of beta-casein A1 with heart disease and insulin-dependent diabetes mellitus. *Proc.NZ Soc. Animal Production* 62:111-114
- Jinsmaa Y. & Yoshikawa M. (1999), Enzymatic release of neocasomorphin and beta-casomorphin from bovine beta-casein. *Peptides* 20(8):957-962
- Laugeson M. and Elliott R. (2003), Ischaemic heart disease, Type 1 diabetes, and cow milk A1 beta-casein, *New Zealand Medical Journal* 116(1168).
- Mann J. and Skeaff M. (2003), Editorial - β -casein variants and atherosclerosis – claims are premature, *Atherosclerosis* 170, 11-12.
- McLachlan C.N. 2001. Beta-casein A1, ischaemic heart disease mortality, and other illnesses, *Medical Hypotheses* 56:262-72
- Norris C.S., Coker C.J., Boland M.J. and Hill J.P. (2003a), Analysis of the water-soluble fraction of a selection of cheeses for beta-casomorphin, its precursors and its analogues, *Aust. J. Dairy Tech* 58:201.
- Norris C.S, Darragh A., Booth C., Boland M.J. and Hill J.P. (2003b), Human milks release beta-casomorphin-7 during simulated digestion, *Poster paper presented at the 2003 International Dairy Federation Conference.*
- Swinburn, B (2004) Beta casein A1 and A2 in milk and human health. Report to New Zealand Food Safety Authority. Available at www.nzfsa.govt.nz
- Tailford, Kristy A., Berry, Celia L., Thomas, Anita C. and Campbell, Julie H. (2003), A casein variant in cow's milk is atherogenic, *Atherosclerosis* 170:13-19.

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