



The Paleo Diet Update

www.ThePaleoDiet.com

Loren Cordain, Ph.D.

August 8, 2010 - Volume 6 Issue 24

Welcome to the latest edition of *The Paleo Diet Update*.

Articles on paleo nutrition, as well as answers to selected reader questions are published in my newsletter. Answers to selected reader questions are also posted on my [blog](#), and answers to commonly asked questions are posted on the [FAQ](#) page of my web site. Special reports and more lengthy papers are sold from my [web site store](#). You may also purchase [back issues](#) of my newsletters.

The content on the [Paleo Diet web site](#) and [Paleo Diet blog](#) is searchable. I encourage you to search my web site and blog, or browse my [FAQ](#) page to see if the information you're seeking has been documented. As always, you have my sincere thanks for your continued readership and for purchasing my writings on diet and paleo nutrition.

Loren Cordain, Ph.D., Professor



Loren Cordain, Ph.D.

In This Issue

[Announcements](#)

[The Adverse Effects of Milk](#)

[Recipe of the Week](#)

The Adverse Effects of Milk - by Loren Cordain & Pedro Bastos

Editor's note: Dr. Cordain was contacted over the summer by journalist Ben Hewitt, who was writing an article for *Men's Journal*. Mr. Hewitt inquired about the adverse effects of milk consumption, which prompted the following responses from Dr. Cordain and Pedro Bastos.

Hello Dr. Cordain,

I am working on an article for Men's Journal about the negative impact of dairy products on some people. Basically, can you explain why milk is problematic? My understanding is that, similar to gluten, milk is potentially inflammatory, which is why it's such a common allergen. Can you expand on this?

If someone is drinking milk now, and not feeling any negative effects, does that mean he doesn't have an issue with milk?

What sort of changes have you observed in people who've given up dairy?

Also, are all dairy products problematic, or is milk a particularly bad one?

What do you recommend in place of milk to fill that nutritional gap?

Thanks so much for your help.

Thanks,
Ben

Hi Ben,

I really am not a world expert when it comes to health problems associated with milk, but I will copy Pedro Bastos, a colleague who is, and who has written a few pieces on this that may help to answer your questions:

Milk has numerous properties that may adversely affect health.

- Paradoxically, milk has a low glycemic response, but has an insulin response similar to eating a chocolate chip cookie or candy. In a recent study of young boys, they became insulin resistance after 7 days on a high milk diet compared to 7 days of a high meat diet.
- In humans, milk drinking elevates a hormone called IGF-1 which increases growth in children, resulting in an increased adult stature, but it also increases the risk for breast, colon and most particularly prostate cancer. How milk drinking increases IGF-1 is not completely known, but two mechanisms have been proposed: 1) bovine milk contains IGF-1 which crosses the human gut barrier, and 2) IGF-1 concentrations in human blood vary with insulin -- because milk increases the insulin response so dramatically, then this response in turn may increase IGF-1.
- In numerous epidemiological studies, milk drinking has been associated with an increased risk for numerous autoimmune diseases including multiple sclerosis, rheumatoid arthritis and type 1 diabetes. Young children are particularly at risk for type 1 diabetes if bovine milk exposure occurs before the age of 1 year. In animal models of multiple sclerosis, a particular protein found in milk (butyrophilin) when injected into rats causes the animal equivalent of MS.

- In a series of epidemiological studies from the Harvard School of Public Health, milk drinking has shown to dramatically increase the risk for acne. Once again the mechanism has not been completely worked out but may once again involve milks highly insulinotropic effect and/or various hormones found in milk that bypass the gut barrier and enter circulation.
- In many epidemiological studies, milk drinking increases the risk for atherosclerosis and fatal myocardial infarctions independent of its saturated fat content. Again the mechanisms are unclear, but it likely involves chronic low level inflammation, or perhaps endocrine substances found in bovine milk that adversely interact with mechanisms known to underlie cardiovascular disease.
- Milk contains a hormone called betacellulin which binds a human gut receptor called the epidermal growth factor receptor (EGF-R). In many human cancers, there is massive over expression of this receptor which may be linked to chronic consumption of betacellulin in bovine milk.
- There are many more health problems associated with milk drinking, but these are the ones that come immediately to mind. I'm sure Pedro can add many more.

Are all dairy products problematic, or is milk a particularly bad one?

I believe that all dairy products are problematic. Cheeses do not cause the high insulin response as does milk, yogurt and other fermented dairy products, but is one of the most acidic of all foods. Paradoxically, despite its high calcium content, its net acidic load promotes calcium loss from the bones. Betacellulin is also found in cheese, but many of the other hormones found in milk do not survive the cheese making process.

If someone is drinking milk now, and not feeling any negative effects, does that mean he doesn't have an issue with milk?

We cannot feel whether or not we are insulin resistant or if bovine hormones are entering our bloodstream, or if our arteries are becoming clogged with the atherosclerotic process, but we can notice improvements in acne and symptoms of allergy (wheezing, sneezing, rashes etc.), or autoimmune disease.

What sort of changes have you observed in people who've given up dairy?

I am not a clinician, and generally the anecdotal responses I am privy to involve people not just giving up dairy only, but rather adopting a Paleo diet in which all dairy is eliminated, along with all grains, processed foods, salt, legumes and potatoes. If you go to my [website](#) and look at the [success stories](#) section, you can read about these people.

What do you recommend in place of milk to fill that nutritional gap?

I don't view it as a nutritional gap, but rather a liability which causes our health to suffer in the long run. We have run nutritional comparisons of the following food groups (meats, seafood's, fresh fruits, fresh vegetables, whole grains, nuts & seeds, milk) and published our results in the highest impact nutritional journal in the world, the *American Journal of Clinical Nutrition*. We found that for these 7 food groups, milk ranked third from last for the 14 most commonly lacking nutrients in the US diet. Hence, the commonly held notion that milk is a highly nutritious food is simply untrue.

Except for calcium, milk is a lightweight for many of the vitamins and minerals needed for

optimal human health. Healthy bones result from positive calcium balance. Calcium balance is like a bank account and results from how much calcium we put into our bodies minus how much we lose. The Dairy Council focuses their ads upon the input side of the calcium equation -- more, more, more. However, the calcium that we ultimately lose in our urine is just as important. If we lose more calcium in our urine than we take in, we will never be in calcium balance, no matter how much milk we drink.

The most important factor determining urinary calcium loss is acid base balance. A net acid yielding diet promotes calcium loss in the urine, whereas a net base yielding diet prevents urinary calcium loss. Foods which are base yielding are fruits and vegetables. Studies have shown that by consuming about 25-30 % of our daily energy as fruits and veggies, we can maintain calcium balance at low calcium intakes without milk consumption. Humans have existed on this planet for 2.5 million years, and only in the past 10,000 have we ever consumed milk or dairy products. Like all other mammals on the planet, we did quite well without milk (once we were weaned) for the rest of our adult lives. Have you ever thought about how an elephant can grow such large, health and strong bones without drinking the milk of another species?

I hope this helps.

Loren Cordain, Ph.D., Professor

Hi Ben,

There is a large body of evidence that up until 9,000 years ago in the Middle East¹ and 7,000 years ago in Northern Europe², no human being on the planet consumed non human milk or dairy products. So on an evolutionary time scale, non-human milk is a relatively newcomer into human diet. By using the evolutionary template, and knowing that that milk is species specific, we would expect this new habit to have unintended consequences, which go way beyond lactose intolerance (which is actually very common), since only a minor percentage of the world's population continues to produce lactase into adulthood³.

Indeed there are several lines of evidence raising concerns with milk and dairy intake, such as:

1) Milk and fermented milk (yoghurt, for instance), despite having a low glycemic index and load, elicit a very high insulin response and this has been shown repeatedly in intervention studies⁴⁻⁹.

As you may be aware, constantly increasing insulinemia may downregulate the insulin receptor, and hence lead to insulin resistance¹⁰⁻¹², which in turn is the primary metabolic defect underlying The Metabolic Syndrome¹³, and may be a driving force in obesity^{14,15}. It should also be mentioned that a chronic state of Hyperinsulinemia may set a hormonal cascade that ultimately results in cancer, acne and juvenile myopia, among other diseases¹³.

Indeed, a high bovine milk diet has been shown to cause insulin resistance in boys⁹. Moreover, dairy intake is strongly associated with a higher incidence of Acne¹⁶⁻¹⁸ and moderately associated with Prostate Cancer¹⁹⁻²³.

2) Cow's milk appears to be involved in certain autoimmune diseases (AD):

- Various epidemiological studies have associated it with Type 1 Diabetes²⁴⁻³¹, especially when the initial exposure begins in the first months of life.

- Epidemiological studies have repeatedly shown a strong correlation between Multiple Sclerosis and cow's milk consumption³²⁻³⁶.
- There is molecular mimicry between Bovine Serum Albumin and Human Collagen Type 1, which has implications for Rheumatoid Arthritis³⁷. Indeed, case studies have shown that elimination of milk and dairy products from the diets of patients with RA improved symptoms, and the disease was markedly exacerbated on re-challenge³⁷.
- Bovine milk is also implicated (or appears to have adverse effects) in other auto-immune diseases, such as Crohn's disease³⁸, Sjögren's syndrome³⁹, IgA nephropathy⁴⁰⁻⁴², Behçet's disease⁴³, and even Celiac disease⁴⁰.

3) Hormones in Milk:

In addition to proteins, fats, lactose, vitamins and minerals, milk contains various growth-stimulating steroid and peptide hormone and also catalysts, transporters and stabilizers that ensure their maximum bioactivity⁴⁵.

Here's a short list of some hormones present in cow's milk that could be problematic for humans:

Insulin

Cow's Milk, as well as human milk (and presumably milk from all mammals) contains insulin⁴⁶⁻⁴⁹, and we know that bovine insulin - BI (which differs from human insulin by three amino acids⁵⁰) survives pasteurization, because immunity to this hormone is common in children who consume cow's milk or who have been exposed to infant formulas containing cow's milk⁵¹⁻⁵⁴.

This not only confirms that BI is present in commercial pasteurized milk, but also in infant formulas and perhaps other dairy products (although direct evidence is lacking). Moreover, these studies provide evidence that BI survives the human digestive processes and crosses the gut barrier intact, although this could be related to the fact that infants have higher intestinal permeability than older children and adults⁵⁰. Nevertheless, various factors may cause the so called "leaky gut" in virtually everyone, so we shouldn't dismiss bovine insulin altogether.

IGF-1

Cow's milk contains active IGF-1⁵⁵, but this has been largely dismissed as relevant, since pasteurization (time and temperature are crucial factors) and fermentation appears to reduce its content^{56, 57}. Yet cow's milk consumption, compared to various foods, is associated with a higher plasma IGF-1 concentrations in humans (both children⁵⁸⁻⁶¹ and adults⁶²⁻⁶⁶), which could be due to calcium in milk (which has been shown to increase IGF-1 in boys and girls⁶⁷), the effect of milk upon insulinemia (the high elevation of plasma insulin caused by milk drinking⁴⁻⁹ could lead to a higher plasma IGF-1¹³) or indeed residual IGF-1 in casein⁶⁸ (the major protein in milk).

Betacellulin

Betacellulin (BTC) belongs to the Epidermal Growth Factor family of hormones⁶⁹, and is found not only in cow's milk⁷⁰ and whey⁷⁰, but also in cheese⁷⁰. Therefore, it survives pasteurization and processing. Although no direct evidence yet exists, bovine milk does contain peptidase inhibitors which prevent human gut enzymes from degrading EGF⁵ (and most likely BTC), and a low pH such as that found in the gut, it does not impair or prevent BTC from binding its receptor⁷¹. Finally, there is a lumenally expressed EGF receptor in the gut, through which BTC

may enter circulation⁶⁹.

Steroid Hormones

The major sources of animal-derived estrogens in the human diet are believed to be milk and dairy products, which presumably account for 70–80% of the total estrogens consumed^{72, 73}. Furthermore, it has been pointed out that most milk for human consumption is obtained from cows in the latter half of pregnancy when estrogen metabolites levels are greatly elevated⁷²⁻⁷⁴.

Confirming this, US researchers have measured estrogen metabolites in various milks and shown that buttermilk contains the highest total amount of estrogen metabolites, followed by skim milk, 2% milk and whole milk⁷². Therefore, estrogen metabolites appear to survive pasteurization, and estrone sulphate, which comprises 45% of the conjugated estrogens in Premarin and Prempro (the most frequently prescribed hormone replacement therapy for menopausal women⁷³) has high oral bioactivity⁷³, and is the most prevalent form of estrogen in cow's milk^{72, 73}.

There are also other steroid hormones in commercial pasteurized cow's milk, such as progesterone, 5 α -androstanedione and 5 α -pregnanedione, which are dihydrotestosterone (DHT) precursors⁷⁵.

As expected from the evidence presented, dairy intake is strongly associated with a higher incidence of acne¹⁶⁻¹⁸, moderately associated with prostate cancer¹⁹⁻²³, and mildly associated with ovarian cancer^{76, 77}.

Dairy consumption was also associated with an increased incidence of testicular^{78, 79}, kidney⁸⁰, and head and neck cancer⁸¹, but very few studies have been conducted to draw more significant conclusions.

Although epidemiological evidence can't show a clear cause and effect, and clearly much more studies need to be conducted, the current evidence strongly suggests that cow's milk may be implicated in a variety of autoimmune diseases, certain cancers, as well as acne.

4) Milk has a very high calcium/magnesium ratio and may contribute to some micronutrient imbalances.

5) There is evidence of higher fracture incidence rates in countries with higher milk and calcium intake⁸², some long term prospective studies have failed to show a benefit from drinking milk or taking calcium supplements⁸³⁻⁸⁵, and a recent meta-analysis, which analyzed seven prospective cohort studies (170,991 women), five prospective cohort studies (68,606 men), five clinical trials, (5,666 women, and 1,074 men), and four clinical trials with separate results for hip fracture (6,504 subjects), concluded that calcium intake doesn't decrease the risk for fractures⁸⁶.

Calcium intake is only part of the story; we need to consider GI absorption and renal excretion. In these regards, vegetables from the brassica family have a clear advantage over milk⁸⁷.

I know this may sound overly alarming, and possibly exaggerated, but given what I know about milk, I have a hard time recommending it - even though it has some positive effects, such as being a cheap source of high quality protein and various micronutrients.

For those who are fortunate and have access to good (real) food, supplements such as Vitamin D, (which by the way, may be needed in much higher doses than the ones provided by three or four servings of dairy a day), and adopt a diet that has a low glycemic load, is moderate in fructose, is net base yielding and provides sufficient protein, soluble fiber, essential fatty acids, especially EPA, DHA, GLA and AA (with a w6/w3 ratio < 4/1) and all the micronutrients, I

believe milk is not necessary.

I hope this helps.

Best regards,

Pedro Carrera Bastos

Nutrition Researcher, Lisbon, Portugal

References:

1. Evershed RP, Payne S, Sherratt AG, Copley MS, Coolidge J, Urem-Kotsu D, Kotsakis K, Ozdoğan M, Ozdoğan AE, Nieuwenhuys O, Akkermans PM, Bailey D, Andeescu RR, Campbell S, Farid S, Hodder I, Yalman N, Ozbaşaran M, Biçakci E, Garfinkel Y, Levy T, Burton MM. Earliest date for milk use in the Near East and southeastern Europe linked to cattle herding. *Nature*. 2008 Sep 25;455(7212):528-31.
2. Copley MS, Berstan R, Dudd SN, Docherty G, Mukherjee AJ, Straker V, Payne S, Evershed RP: Direct chemical evidence for widespread dairying in prehistoric Britain. *Proceedings of the National Academy of Sciences of the United States of America* 2003, 100(4):1524-1529.
3. Swallow DM. Genetics of lactase persistence and lactose intolerance. *Ann Rev Genet* 2003;37:197-219.
4. Gannon MC, Nuttall FQ, Krezowski PA, Billington CJ, Parker S. The serum insulin and plasma glucose responses to milk and fruit products in type 2 (non-insulin-dependent) diabetic patients. *Diabetologia*. 1986 Nov;29(11):784-91.
5. Holt SH et al. An insulin index of foods: the insulin demand generated by 1000-kJ portions of common foods. *Am J Clin Nutr*. 1997 Nov;66(5):1264-76.
6. Ostman EM, et al. Inconsistency between glycemic and insulinemic responses to regular and fermented milk products. *Am J Clin Nutr* 2001;74:96 –100.
7. Liljeberg Elmstahl H & Bjorck I. Milk as a supplement to mixed meals may elevate postprandial insulinaemia. *Eur J Clin Nutr* 2001; 55:994–999.
8. Hoyt G et al. Dissociation of the glycaemic and insulinaemic responses to whole and skimmed milk. *Br J Nutr*. 2005 Feb;93(2):175-7.
9. Hoppe C et al. High intakes of milk, but not meat increase s-insulin and insulin resistance in 8-year-old boys. *Eur J Clin Nutr*. 2005 Mar;59(3):393-8.
10. Rizza RA, Mandarino LJ, Genest J, Baker BA, Gerich JE. Production of insulin resistance by hyperinsulinaemia in man. *Diabetologia*. 1985 Feb;28(2):70-5.
11. Treadway JL, Whittaker J, Pessin JE. Regulation of the insulin receptor kinase by hyperinsulinism. *J Biol Chem* 1989;264:15136–15143.
12. DelPrato S, Leonetti F, Simonson DC, et al. Effect of sustained physiologic hyperinsulinaemia and hyperglycaemia on insulin secretion and insulin sensitivity in man. *Diabetologia* 1994;37:1025 -1035.
13. Cordain, L.; Eades, M.R.; Eades, M.D. Hyperinsulinemic diseases of civilization: more than just syndrome X. *Comp Biochem Physiol Part A*; 136:95-112, 2003.
14. Thomas DE, Elliott EJ, Baur L. Low glycaemic index or low glycaemic load diets for overweight and obesity. *Cochrane Database Syst Rev*. 2007 Jul 18;(3):CD005105.
15. Nishino N, Tamori Y, Kasuga M. Insulin efficiently stores triglycerides in adipocytes by inhibiting lipolysis and repressing PGC-1alpha induction. *Kobe J Med Sci*. 2007;53(3):99-106.
16. Adebamowo, C.A. et al. High school dietary dairy intake and teenage acne. *J Am Acad Dermatol*; 52(2):207-14, 2005.
17. Adebamowo, C.A. et al. Milk consumption and acne in adolescent girls. *Dermatol*

- Online J; 12(4):1, 2006.
18. Adebamowo CA, et al. Milk consumption and acne in teenaged boys. *J Am Acad Dermatol.* 2008 May;58(5):787-93.
 19. Kurahashi N, Inoue M, Iwasaki M, et al. Dairy product, saturated fatty acid, and calcium intake and prostate cancer in a prospective cohort of Japanese men. *Cancer Epidemiol Biomarkers Prev.* 2008 Apr;17(4):930-7.
 20. Mitrou PN, Albanes D, Weinstein SJ et al. A prospective study of dietary calcium, dairy products and prostate cancer risk (Finland). *Int J Cancer;* 120(11):2466-73, 2007.
 21. Rohrmann S, Platz EA, Kavanaugh CJ, et al. Meat and dairy consumption and subsequent risk of prostate cancer in a US cohort study. *Cancer Causes Control.* 2007 Feb;18(1):41-50.
 22. Gao X, LaValley MP, Tucker KL. Prospective studies of dairy product and calcium intakes and prostate cancer risk: a meta-analysis. *J Natl Cancer Inst.* 2005 Dec 7;97(23):1768-77.
 23. Qin LQ, Xu JY, Wang PY, Kaneko T, Hoshi K, Sato A. Milk consumption is a risk factor for prostate cancer: meta-analysis of case-control studies. *Nutr Cancer.*2004;48(1):22-7.
 24. Virtanen SM, Räsänen L, Ylönen K, Aro A, Clayton D, Langholz B, Pitkääniemi J, Savilahti E, Lounamaa R, Tuomilehto J, et al. Early introduction of dairy products associated with increased risk of IDDM in Finnish children. The Childhood in Diabetes in Finland Study Group. *Diabetes.* 1993 Dec;42(12):1786-90.
 25. Kostraba JN, Cruickshanks KJ, Lawler-Heavner J, Jobim LF, Rewers MJ, Gay EC, Chase HP, Klingensmith G, Hamman RF. Early exposure to cow's milk and solid foods in infancy, genetic predisposition, and risk of IDDM. *Diabetes.* 1993 Feb;42(2):288-95.
 26. Fava, D.; Leslie, R.D.G.; Pozzilli, P. Relationship between dairy product consumption and incidence of IDDM in childhood in Italy. *Diabetes Care* 1994;17: 1488-1490.
 27. Gimeno SG, de Souza JM. IDDM and milk consumption. A case-control study in São Paulo, Brazil. *Diabetes Care.* 1997 Aug;20(8):1256-60.
 28. Hyppönen E, Kenward MG, Virtanen SM, Piitulainen A, Virta-Autio P, Tuomilehto J, Knip M, Akerblom HK. Infant feeding, early weight gain, and risk of type 1 diabetes. Childhood Diabetes in Finland (DiMe) Study Group. *Diabetes Care.* 1999 Dec;22(12):1961-5.
 29. Kimpimäki T, Erkkola M, Korhonen S, Kupila A, Virtanen SM, Ilonen J, Simell O, Knip M. Short-term exclusive breastfeeding predisposes young children with increased genetic risk of Type I diabetes to progressive beta-cell autoimmunity. *Diabetologia.* 2001 Jan;44(1):63-9.
 30. Wahlberg J, Fredriksson J, Nikolic E, Vaarala O, Ludvigsson J; The ABIS-Study Group. Environmental factors related to the induction of beta-cell autoantibodies in 1-yr-old healthy children. *Pediatr Diabetes.* 2005 Dec;6(4):199-205.
 31. Wahlberg J, Vaarala O, Ludvigsson J; ABIS-study group. Dietary risk factors for the emergence of type 1 diabetes-related autoantibodies in 2 1/2 year-old Swedish children. *Br J Nutr.* 2006 Mar;95(3):603-8.
 32. Agranoff BW, Goldberg D . Diet and the geographical distribution of multiple sclerosis. *Lancet* 1974;2:1061-66.
 33. Butcher PJ. Milk consumption and multiple sclerosis--an etiological hypothesis. *Med Hypotheses.* 1986 Feb;19(2):169-78.
 34. Malosse D et al. Correlation between milk and dairy product consumption and multiple sclerosis prevalence: a worldwide study. *Neuroepidemiology.* 1992;11(4-6):304-12.
 35. Malosse D, Perron H. Correlation analysis between bovine populations, other farm animals, house pets, and multiple sclerosis prevalence. *Neuroepidemiology.* 1993;12(1):15-27.
 36. Lauer K. Diet and multiple sclerosis. *Neurology.* 1997 Aug;49(2 Suppl 2):S55-61.
 37. Cordain L, Toohey L, Smith MJ, Hickey MS. Modulation of immune function by dietary lectins in rheumatoid arthritis. *Brit J Nutr* 2000, 83:207-217.

38. van den Bogaerde J et al. Immune sensitization to food, yeast and bacteria in Crohn's disease. *Aliment Pharmacol Ther.* 2001 Oct;15(10):1647-53.
39. Lidén M, Kristjánsson G, Valtýsdóttir S, Venge P, Hällgren R. Cow's milk protein sensitivity assessed by the mucosal patch technique is related to irritable bowel syndrome in patients with primary Sjögren's syndrome. *Clin Exp Allergy.* 2008 Jun;38(6):929-35.
40. Fornasieri A, Sinico RA, Maldifassi P, Paterna L, Benuzzi S, Colasanti G, D'Amico G. Food antigens, IgA-immune complexes and IgA mesangial nephropathy. *Nephrol Dial Transplant.* 1988;3(6):738-43.
41. Yap HK, Sakai RS, Woo KT, Lim CH, Jordan SC. Detection of bovine serum albumin in the circulating IgA immune complexes of patients with IgA nephropathy. *Clin Immunol Immunopathol.* 1987 Jun;43(3):395-402.
42. Soylu A, Kasap B, Soylu OB, Türkmen M, Kavukçu S. Does feeding in infancy effect the development of IgA nephropathy? *Pediatr Nephrol.* 2007 Jul;22(7):1040-4.
43. Triolo G, Accardo-Palumbo A, Dieli F, Ciccio F, Ferrante A, Giardina E, Licata G. Humoral and cell mediated immune response to cow's milk proteins in Behçet's disease. *Ann Rheum Dis.* 2002 May;61(5):459-62.
44. Kristjánsson G, Venge P, Hallgren R. Mucosal reactivity to cow's milk protein in coeliac disease. *Clin Exp Immunol* 2007;147:449–55.
45. Walzem RL, Dillard CJ, German JB. Whey components: millennia of evolution create functionalities for mammalian nutrition: what we know and what we may be overlooking. *Crit Rev Food Sci Nutr.* 2002 Jul;42(4):353-75.
46. Ballard FJ, Nield MK, Francis GL, Dahlenburg GW, Wallace JC. The relationship between the insulin content and inhibitory effects of bovine colostrum on protein breakdown in cultured cells. *J Cell Physiol.* 1982 Mar;110(3):249-54.
47. Malven PV, Head HH, Collier RJ, Buonomo FC. Periparturient changes in secretion and mammary uptake of insulin and in concentrations of insulin and insulin-like growth factors in milk of dairy cows. *J Dairy Sci.* 1987 Nov;70(11):2254-65.
48. Oda S, Satoh H, Sugawara T, Matsunaga N, Kuhara T, Katoh K, Shoji Y, Nihei A, Ohta M, Sasaki Y. Insulin-like growth factor-I, GH, insulin and glucagon concentrations in bovine colostrum and in plasma of dairy cows and neonatal calves around parturition. *Comp Biochem Physiol A Comp Physiol.* 1989;94(4):805-8.
49. Aranda P, Sanchez L, Perez MD, Ena JM, Calvo M. Insulin in bovine colostrum and milk: evolution throughout lactation and binding to caseins. *J Dairy Sci.* 1991 Dec;74(12):4320-5.
50. Vaarala O. Is it dietary insulin? *Ann N Y Acad Sci.* 2006 Oct;1079:350-9.
51. Vaarala O, Paronen J, Otonkoski T, Akerblom HK. Cow milk feeding induces antibodies to insulin in children—a link between cow milk and insulin-dependent diabetes mellitus? *Scand J Immunol* 1998; 47: 131–135.
52. Vaarala O, Knip M, Paronen J et al. Cow's milk formula feeding induces primary immunization to insulin in infants at genetic risk for type 1 diabetes. *Diabetes* 1999; 48: 1389–1394.
53. Paronen, J. et al. The effect of cow milk exposure and maternal type 1 diabetes on cellular and humoral immunization to dietary insulin in infants at genetic risk for type 1 diabetes. *Diabetes* 2000;49: 1657–1665.
54. Vaarala, O. et al. The effect of coincident enterovirus infection and cow's milk exposure on immunization to insulin in early infancy. *Diabetologia* 2002; 45:531–534.
55. Blum JW, Baumrucker CR. Insulin-Like Growth Factors (IGFs), IGF Binding Proteins, and Other Endocrine Factors in Milk: Role in the Newborn. In Bosze Z. *Bioactive Components of Milk*, Springer, 2008, Pgs 397-422.
56. Collier RJ, Miller MA, Hildebrandt JR, Torkelson AR, White TC, Madsen KS, Vicini JL, Eppard PJ, Lama GM. Factors affecting insulin-like growth factor-I concentration in bovine milk. *J Dairy Sci* 1991; 74:2905-2911.
57. Kang SH, Kim JU, Imm JY, Oh S, Kim SH. The effects of dairy processes and storage

- on insulin-like growth factor-I (IGF-I) content in milk and in model IGF-I-fortified dairy products. *J Dairy Sci* 2006; 89:402-409.
58. Hoppe C, Mølgaard C, Michaelsen KF. Cow's milk and linear growth in industrialized and developing countries. *Annu Rev Nutr.* 2006;26:131-73.
 59. Rogers IS, Gunnell D, Emmett PM, et al. Cross-sectional associations of diet and insulin-like growth factor levels in 7- to 8-year-old children. *Cancer Epidemiol Biomarkers Prev* 2005; 14: 204-212.
 60. Hoppe C, Udam TR, Lauritzen L, et al. Animal protein intake, serum insulin-like growth factor I, and growth in healthy 2.5-year-old Danish children. *Am J Clin Nutr* 2004; 80: 447-452.
 61. Hoppe C, Mølgaard C, Juul A, et al. High intakes of skimmed milk, but not meat, increase serum IGF-I and IGFBP-3 in eight-year-old boys. *Eur J Clin Nutr* 2004; 58: 1211-1216.
 62. Ma J, Giovannucci E, Pollak M, et al. Milk intake, circulating levels of insulin-like growth factor-I, and risk of colorectal cancer in men. *J Natl Cancer Inst* 2001, 93:1330-1336.
 63. Giovannucci E, Pollak M, Liu Y, et al. Nutritional predictors of insulin-like growth factor I and their relationships to cancer in men. *Cancer Epidemiol Biomarkers Prev* 2003, 12:84-89.
 64. Norat T, Dossus L, Rinaldi S, et al. Diet, serum insulin-like growth factor-I and IGF-binding protein-3 in European women. *Eur J Clin Nutr* 2007; 61: 91-98.
 65. Morimoto LM, Newcomb PA, White E, et al. Variation in plasma insulin-like growth factor-1 and insulin-like growth factor binding protein-3: personal and lifestyle factors (United States). *Cancer Causes Control* 2005; 16: 917-927.
 66. Holmes MD, Pollak MN, Willett WC, et al. Dietary correlates of plasma insulin-like growth factor-I and insulin-like growth factor binding protein-3 concentrations. *Cancer Epidemiol Biomarkers Prev* 2002; 11: 852-861.
 67. Ginty F, et al. calcium carbonate supplementation is associated with higher plasma IGF-1 in 16-to 18-year old boys and girls. In Burckhardt P, Heaney R, Dawson-Hughes B. *Nutritional Aspects of Osteoporosis*. Elsevier, 2004, pp 45-57.
 68. Hoppe C, Mølgaard C, Dalum C, Vaag A, Michaelsen KF. Differential effects of casein versus whey on fasting plasma levels of insulin, IGF-1 and IGF-1/IGFBP-3: results from a randomized 7-day supplementation study in prepubertal boys. *Eur J Clin Nutr.* 2009 Sep;63(9):1076-83.
 69. Cordain L. Dietary implications for the development of acne: a shifting paradigm. In: *U.S. Dermatology Review II 2006*, (Ed., Bedlow, J). Touch Briefings Publications, London, 2006.
 70. Bastian SE, et al. Measurement of betacellulin levels in bovine serum, colostrum and milk. *J Endocrinol.* 2001 Jan;168(1):203-12.
 71. Rao RK, Baker RD, Baker SS. Bovine milk inhibits proteolytic degradation of epidermal growth factor in human gastric and duodenal lumen. *Peptides.* 1998; 19(3):495-504.
 72. Farlow DW, Xu X, Veenstra TD. Quantitative measurement of endogenous estrogen metabolites, risk-factors for development of breast cancer, in commercial milk products by LC-MS/MS. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2009 Jan 31. [Epub ahead of print]
 73. Ganmaa D, Sato A. The possible role of female sex hormones in milk from pregnant cows in the development of breast, ovarian and corpus uteri cancers. *Med Hypotheses* 2005; 65: 1028-37.
 74. Qin LQ, Wang PY, Kaneko T, et al. Estrogen: one of the risk factors in milk for prostate cancer. *Med Hypotheses.* 2004;62(1):133-42.
 75. Danby FW. Acne, dairy and cancer. *Dermato-Endocrinology* 1:1, 9-13; January/February 2009.
 76. Genkinger JM, Hunter DJ, Spiegelman D, et al. Dairy products and ovarian cancer: a pooled analysis of 12 cohort studies. *Cancer Epidemiol Biomarkers Prev.* 2006 Feb;15(2):364-72.

77. Larsson SC, Orsini N, Wolk A. Milk, milk products and lactose intake and ovarian cancer risk: a meta-analysis of epidemiological studies. *Int J Cancer*. 2006 Jan 15;118(2):431-41.
78. Stang, A.; Ahrens, W.; Baumgardt-Elms, C. et al. Adolescent milk fat and galactose consumption and testicular germ cell cancer. *Cancer Epidemiol Biomarkers Prev*; 15(11):2189-95, 2006.
79. Ganmaa D, Li XM, Qin LQ, et al. The experience of Japan as a clue to the etiology of testicular and prostatic cancers. *Med Hypotheses*. 2003 May;60(5):724-30.
80. Bravi F, Bosetti C, Scotti L, et al. Food groups and renal cell carcinoma: a case-control study from Italy. *Int J Cancer*. 2007 Feb 1;120(3):681-5.
81. Peters ES, Lockett BG, Applebaum KM, Marsit CJ, McClean MD, Kelsey KT. Dairy products, leanness, and head and neck squamous cell carcinoma. *Head Neck*. 2008 Sep;30(9):1193-205.
82. Klompmaker TR. Lifetime high calcium intake increases osteoporotic fracture risk in old age. *Med Hypotheses*. 2005;65(3):552-8.
83. Owusu W, Willett WC, Feskanich D, Ascherio A, Spiegelman D, Colditz GA. Calcium intake and the incidence of forearm and hip fractures among men. *J Nutr* 1997; 127:1782-7.
84. Feskanich D, Willett W et al. Milk, Dietary Calcium, and Bone Fractures in Women: A 12-Year Prospective Study. *Am J Public Health*. 1997 Jun;87(6):992-7.
85. Feskanich D, Willett WC, Colditz GA. Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women. *Am J Clin Nutr*. 2003 Feb;77(2):504-11.
86. Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, Burckhardt P, Li R, Spiegelman D, Specker B, Orav JE, Wong JB, Staehelin HB, O'Reilly E, Kiel DP, Willett WC. Calcium intake and hip fracture risk in men and women: a meta-analysis of prospective cohort studies and randomized controlled trials. *Am J Clin Nutr*. 2007 Dec;86(6):1780-90.
87. Heaney RP, Weaver CM. Calcium absorption from kale. *Am J Clin Nutr*. 1990 Apr;51(4):656-7.

ns