Response to Anti-Raw Milk Position Paper by Bill Marler, JD Prepared by the Weston A. Price Foundation

Bill Marler, a personal injury and products liability attorney who frequently targets raw milk products in legal efforts and the blog posts of his web site MarlerBlog.com, argues in a post entitled "Raw Milk Pros: Review of the Peer-Reviewed Literature," that the claimed benefits of raw milk are scientifically unsubstantiated while the hazards of this food are clearly documented. In doing so Marler applies a double standard to the scientific evidence, failing to give a fair hearing to hypotheses about the benefits of raw milk that have gathered substantial preliminary evidence while simultaneously supporting claims about the hazards of raw milk with poor research or even opinion rather than solid scientific evidence.

Summary

- Marler defines the "hygiene hypothesis" in a way that clearly includes exposure to pathogens but does not clearly include or exclude exposure to nonpathogenic or symbiotic organisms. He dismisses the "probiotic" of raw milk because it does not fit an irrelevant definition of "probiotic" designed for formulated products rather than natural foods, but cites numerous studies in support of the "hygiene hypothesis" that could also be interpreted to support a probiotic effect of raw milk. In most cases, the authors of these studies themselves suggest such an effect, but Marler fails to disclose this in all but one case.
- Authors of studies cited by Marler suggest several other potential mechanisms for a protective effect of raw milk against allergic disorders such as the reduction in micronutrients, destruction of antimicrobial peptides, denaturation of whey protein induced by pasteurization and the fortification of pasteurized milk with vitamin D.
- Marler frequently cites the opinions or conclusions of researchers that raw milk is hazardous rather than citing specific hazards and discussing primary evidence of these putative hazards. In one case, he substantially misquotes an author by rendering "potentially hazardous" as simply "hazardous."
- In all cases, the opinions of these researchers about the hazards of raw milk rely on three or fewer (often one) citation(s) of reports of outbreaks or case reports of illnesses that – often inconclusively – were associated with raw milk, with no attempt to thoroughly review the published literature on the subject or to compare the safety of raw milk to the safety of pasteurized milk or other common foods.
- Marler dismisses claims that raw milk is more nutritious but makes no attempt to reconcile old claims of large nutrient destruction based on feeding studies

with modern claims of negligible nutrient destruction based on chemical assays.

- Marler judges the evidence in favor of raw milk by whether it can be "recommended" for certain uses. Raw milk advocates, however, are not currently fighting for governmental or other official agencies to recommend raw milk. Rather, they are fighting for the right of the producers and consumers of raw milk to engage in voluntary exchange and make their own decisions about what types of products to sell, buy, and consume.

RAW MILK PROS: REVIEW OF THE PEER-REVIEWED LITERATURE
June 5, 2008

Summary

- **There is substantial epidemiological evidence from studies in Europe that consumption of raw milk products in childhood has a "protective" effect for some allergic conditions (e.g., asthma, hay fever, eczema); other factors associated with living on a farm such as contact with animals and barns showed a similar effect in these studies. Plausible explanations for these observations exist including the "hygiene hypothesis" and modulation of the immune system early in life. At the same time, no author recommends raw milk as a preventive measure for allergies at this time because of the potential hazards due to foodborne pathogens such as EHEC and *Salmonella* known to occur in raw milk. The body of literature suggests that further studies are needed to identify the specific factors in raw milk (and other farm exposures) that lead to a protective effect for allergic conditions.**

- **No articles could be found substantiating an increased risk of autism due to pasteurized milk or a protective effect from raw milk consumption, respectively.**

- **Probiotics are increasingly recognized in the literature as an effective approach for managing some gastrointestinal and allergic conditions. Specific criteria that define "probiotics" have been published and raw milk does not fit this definition. No articles suggested that raw milk should be used as a probiotic.**

- **Raw milk and cheeses may contain microflora ("beneficial bacteria") that produce metabolites and other antibacterial compounds that may be toxic to foodborne pathogens. The presence and quantity of these specific compounds, the bacterial species involved, and the log reduction for different foodborne pathogens from these bacteria/compounds has not been defined in raw milk; therefore, these properties cannot be considered a substitution for a "kill step."**

- **Although studies have shown modest reductions in some vitamins and other nutrients after pasteurization of milk, these changes are insignificant according to a review by Potter et al (1984), human nutrition studies have shown no advantage of raw over pasteurized milk. A review of more recent literature did not reveal any changes in this position.**

- **No references could be found to support some benefits reported by raw milk advocates such as promotion of tooth development/reduction of dental caries; enhanced fertility; or existence of an undefined substance to protect against arthritis ("anti-stiffness" factor)**

Detailed Literature Review of the "Pros" of Raw Milk Consumption

I. Protection against allergic conditions (e.g., asthma, hay fever, excema)

a. Raw milk advocates frequently cite recent epidemiological studies that have demonstrated a statistically significant inverse relationship between "farm" or "unpasteurized" milk and allergic conditions in children. A number of studies, mostly among children in various European countries, provide convincing evidence that *a protective effect is associated with unpasteurized milk consumption during childhood*. However, the underlying mechanism for this observation remains unclear and the overwhelming consensus among authors of these papers is that because of the potential health hazards from foodborne pathogens (EHEC, Salmonella, etc.) *consumption of raw farm milk cannot be recommended as a preventive measure for allergic conditions.*

i. Historical perspective: The "Hygiene Hypothesis"

1. The "hygiene hypothesis" is an accepted phenomenon that states children without (or with reduced) exposure to infectious agents (especially parasites) and other microorganisms are more susceptible to developing allergic disease.
2. In the last decade, researchers documented an association between children from "farming environments" and protection against the development of allergies. A couple papers as examples:

Kilpelainen, M., E. O. Terho, H. Helenius, and M. Koskenvuo. 2000. Farm environment in childhood prevents the development of allergies. Clin Exp Allergy 30:201-8.

Riedler, J., W. Eder, G. Oberfeld, and M. Schreuer. 2000. Austrian children living on a farm have less hay fever, asthma and allergic sensitization. Clin Exp Allergy 30:194-200.

This description of the hygiene hypothesis is vague and it is unclear whether Marler intends to include the effect of probiotic organisms under "other microorganisms." A review published in 2005 (Rook and Brunet, Gut. 2005;54:317-20) pointed out that the original conception of the hygiene hypothesis focusing on infectious organisms had considerable evidence against it, and postulated a variation called the "old friends hypothesis," which refers to colonizing or transiently colonizing organisms that are recognized by the immune system as non-pathogenic or symbiotic. Among the evidence, many childhood infections are associated with increased rather than decreased risk of allergies, while exposure to day care, pets and farm environments – where exposure to helminthes, saprophytic mycobacteria and lactobacilli occurs – is associated with a decreased risk.

The failure to be clear about whether probiotic effects are included in the hygiene hypothesis at the outset allows Marler to continually cite studies as supportive of the hygiene hypothesis even when the authors of these studies postulate probiotic effects and when the data specifically concerns non-pathogenic or symbiotic organisms, while at the same time completely dismissing the possibility that raw milk can act as a probiotic by claiming it does not meet specific criteria for the term from one report he cites as definitively defining it.

ii. The next step in understanding the statistically significant association between children living in farm environments and reduced allergies involved dissecting out the specific factors that might be involved using epidemiological studies (conducted mostly in Europe). During these studies, raw milk was repeatedly identified as an independent "protective" factor for various allergic conditions. Raw milk was not the only independent factor found to be significant for rural children– others included "barn exposure" and "animal contact," for example. Some of the studies are contradictory (see below) and there were inconsistencies regarding which type of allergic conditions were influenced by raw milk exposure (e.g., asthma, atopy,

excema). Below are some of the articles most frequently cited by advocates of raw milk consumption as "evidence" to support using raw milk as a "treatment" or "preventive measure" for allergies in children. Highlights from the abstracts and text are in bullets.

The hygiene hypothesis has strong support and is a legitimate interpretation of some of these studies. It is not, however, the best-fitting interpretation of all of them. For example, the first study cited below (Waser et al. 2007) found that "farm milk," but not other foods produced on farms, was inversely associated with asthma and allergies across a number of populations, some of which were and some of which were not from farming environments. The data from this study, then, point squarely to an effect of the milk *per se.* The accompanying editorial (Perkin 2007) offers several other hypotheses of why unpasteurized milk may be protective (see below). Likewise, in the succeeding study (Perkin and Strachan 2006), the data suggests an effect of raw milk *per se* rather than general exposure to bacteria and the authors suggest several possibilities including a probiotic effect of raw milk.

Perkin, M. R. 2007. Unpasteurized milk: health or hazard? Clin Exp Allergy 37:627-30.

- **This is an editorial in the same issue with the Waser article below**
- **Reviews epidemiological evidence of the protective effect of raw milk for allergic disorders in children**
- **He concludes that the Waser paper "adds to the weight of evidence that a protective effect is associated with unpasteurized milk consumption….The key issue now is to determine what underlies this protective effect and whether it is possible to separate the protective effect from the hazardous [pathogens] substances."**

In addition to reviewing the epidemiological evidence supporting a protective effect of raw milk, this editorial offers several speculative hypotheses to explain the mechanism of this protection. Among them are the following: raw milk contains more bacteria and a greater diversity of bacteria as well as a greater content of endotoxin (present in the cell walls of gram-negative bacteria) and these factors may influence the maturation of the immune system directly or indirectly by influencing gut flora; pasteurization marginally destroys vitamin A and riboflavin while it substantially destroys antimicrobial substances and denatures whey proteins; vitamin D fortification of pasteurized milk may increase the risk of allergies; and homogenization may have some unknown adverse effect(s) on the milk.

Marler substantially misquotes the author and leaves out the word "potentially" that modifies "hazardous" in the original document. The quote according to the .pdf file as accessed on June 27, 2008, reads, "The key issue now is to determine what underlies this protective effect and whether it is possible to separate the protective from the potentially hazardous elements."

There is only one citation to support the presence of "potentially hazardous elements" in raw milk, which is a UK report that found *L. monocytogenes, Salmonella* spp., *Campylobacter* spp., and *E. coli* "in raw milk samples but not in pasteurized milk." This report can be found at the following URL:
http://www.foodstandards.gov.uk/multimedia/pdfs/milksurvey.pdf.

This report, however, found that pasteurized milk contains its own potentially hazardous elements: "Viable MAP [*Mycobacterium avium* subsp. *paratuberculosis*] was found to be present in a small percentage of pasteurized milk samples, which "appears to confirm laboratory studies demonstrating the relative heat resistance of this organism," and suggests "that MAP will survive HTST (high temperature short time) pasteurization." This latter finding was of concern, according to the report, because some evidence indicates that MAP may be associated with the development of Crohn's disease. This pathogen was present in 1.8% of raw milk samples and 1.6% of pasteurized milk samples. MAP bacteria were not present in greater concentration in raw milk than in pasteurized milk, contrary to the authors' expectations. They suggested that this may be because the greater number of other (mostly harmless) bacteria in raw milk may keep the growth of MAP in check (they made this suggestion specifically about the growth of these bacteria in culture plates, but there is no reason the same phenomenon would not operate in the milk).

This report examined raw milk exclusively from operations that produce milk intended for pasteurization. The presence of pathogens in a minority of raw milk samples cannot be taken to reflect the quality of raw milk intended for consumption *as raw milk.* This report therefore provides no evidence that cleanly produced, high-quality raw milk is in any way hazardous.

Waser, M., K. B. Michels, C. Bieli, H. Floistrup, G. Pershagen, E. von Mutius, M. Ege, J. Riedler, D. Schram-Bijkerk, B. Brunekreef, M. van Hage, R. Lauener, and C. Braun-Fahrlander. 2007. Inverse association of farm milk consumption with asthma and allergy in rural and suburban populations across Europe. Clin Exp Allergy 37:661-70.

- **NOTE: a major limitation of this study – raw milk was not distinguished from boiled "farm milk"**

This is a valid criticism, especially since half of the subjects reported boiling the milk and boiling status had no effect on the outcome. The authors dismissed this finding primarily because they expected high reporting bias due to the vigorous recommendations of researchers and government agencies against feeding raw milk to children. It should also be noted that the authors tested many other farm-produced foods and only the milk showed an inverse association. This does not in any way demonstrate that the rawness of the milk was responsible for the putative effect, but because the association is milk-specific and many milk-specific compounds such as whey proteins are denatured by pasteurization (as described in the accompanying editorial – see above), it certainly strengthens the likelihood of this possibility.

- **Study enrolled 14,893 children aged 5-13 from 5 European countries**
- **"A strong and consistent inverse association was observed for the prevalence of asthma, wheeze, rhinoconjunctivitis, and pollen, in children who consumed farm milk since their first year of life." [Odds ratios/CIs are in the paper].**
- **No association with eczema (versus other studies showing an association)**

The inverse association with eczema lost statistical significance after adjusting for a history of food avoidance, but without this adjustment there was a statistically significant OR of 0.80 for eczema diagnosis and 0.84 for current eczematous symptoms. Adjusting for confounding variables may make the findings more or less accurate depending on whether the cause-and-effect relationships between the

primary variables and the putative confounders are correctly judged. This study may, then, have found an inverse association with eczema like other studies did, but it may have been an artifact of an association between consumption of farm milk and food avoidance.

- **"At present, we can only speculate about the components of farm milk responsible for the observed protective effect."**
- **"The underlying mechanism of the farm milk effect is not known."**

The authors do, in fact, speculate about these components and provide supporting evidence for the various possibilities. Experimental alternations of gut flora in laboratory animals by antibiotics and probiotics, for example, can respectively cause or reverse immunological abnormalities and allergic symptoms; thus, "[c]ommensal [symbiotic] microorganisms in farm milk might therefore be responsible for the decreased risk of respiratory allergies such as asthma and hay fever." They also suggested the possibility that grass-fed animal fats may be protective, which would not be dependent on pasteurization status.

- **"In conclusion…Dietary interventions are an attractive means for primary prevention. However, raw milk may contain pathogens such as salmonella or EHEC, andits consumption may therefore imply serious health risks. A deepened understanding of the relevant "protective" components of farm milk and a better insight into the biological mechanisms underlying the reported epidemiological observation are warranted as a basis for the development of a safe product for prevention. <u>At this stage, consumption of raw farm milk cannot be recommended as a preventive measure</u>."**

The authors cite a single study in support of their contention that raw milk consumption implies serious health risks: Allerberger et al. Int J Infect Dis 2003;7:42-5. This is a case report of two children who contracted *E. coli* O26:H- infections and associated hemolytic uremic syndrome (HUS), of which only the abstract is available to me at the moment. According to the abstract, the two children stayed at the same hotel room and drank unpasteurized milk from a breakfast buffet. The feces samples of cows from which the milk came were positive for the organism, and one of these three samples were positive with the same strain. Within the abstract, the authors of the case report do not state how common this organism is in cattle feces, how common the particular strain is, nor do they report having demonstrated contamination of milk or testing any of the other foods or drinks offered at the buffet.

The fact that the evidence in support of raw milk is not conclusive (it could not be conclusive at this point because raw milk is understudied) and does not justify an evidence-based recommendation is entirely independent from whether a reasonable person may choose to act on a reasonably supported but yet-unproven hypothesis and whether such a person should have the legal right to engage in such an action.

Perkin, M. R., and D. P. Strachan. 2006. Which aspects of the farming lifestyle explain the inverse association with childhood allergy? J Allergy Clin Immunol 117:1374-81.

- Cross sectional survey of 879 children in rural England
- Raw milk was the exposure mediating the protective effect on skin prick test positivity (a measure of allergic disease)
- Like others, they speculate that the "diverse milieu" of bacteria in raw milk may explain the association ("hygiene hypothesis), but say these associations do not confirm a causal relationship

On the other hand, only raw milk and not other elements consistent with the hygiene hypothesis – such as farming status, early and current farm animal exposure, barn or stable exposure, and endotoxin exposure – had a statistically significant relationship.

The authors also offered a second hypothesis – that raw milk has a probiotic effect. They stated the following: "Unpasteurized milk can also contain lactobacilli, and our finding of a protective effect for eczema is consistent with the evidence of a protective effect of lactobacilli- and *Bifidobacterium* species-containing probiotics on eczema."

This stands in direct contrast to Marler's dismissive comments on the probiotic value of raw milk further below and it is rather remarkable that Marler fails to acknowledge this suggestion.

- **They conclude with "However, it is important to mention that unpasteurized milk consumption is not hazard free, and milk-related outbreaks of Cryptosporidium species and Campylobacter species and E. coli O157 have all been described. <u>It is thus premature to recommend unpasteurized milk as a putative protective agent for allergic disease.</u>**

The authors cite three reports of illness associated with raw milk.

The first is a brief report of eight cases of cryptosporidiosis traced to raw milk in Queensland, Australia: Harper, et al. CDI. 2002; 26(3):449-50. The authors reported that the ten milk samples were of unacceptable quality for unpasteurized milk because of elevated total plate, coliform, or *E. coli* counts (they do not report the counts or the legal standards of this district). Since raw milk is not legal for human consumption in Queensland, it was sold as pet milk. The authors wrote that the incident highlighted the dangers of consuming unpasteurized milk, but it actually highlighted the dangers of prohibiting raw milk consumption and relegating the product to an illegal market. Had the milk been subjected to regular tests for total plate counts and coliforms that are common where raw milk can be sold legally, the milk would have been discarded. The authors cite one other incident of cryptosporidiosis tied to milk consumption: Gelletlie, et al. Lancet. 1997;350:1005. In this case, the milk was pasteurized school milk – although the on-farm pasteurizer may have been faulty – and 48 children became ill.

The second is a report of an outbreak of *Campylobacter* at a large festival: Morgan, et al. Eur J Epidemiol. 1994;10(5):581-5. A case-control study showed consumption of raw milk to be associated with incidence of illness, but none of the samples of milk tested positive for *Campylobacter*.

According to the CDC, between 1990 and 2005, this organism has also been associated with numerous outbreaks of foodborne illness reported to the CDC as relating to the consumption of the following foods: beef, pork, quail, grilled chicken, baked chicken, barbecued chicken, chicken liver, oysters, chicken and beef fajita, potato salad, Caesar salad, tuna salad, green salad, taco salad, fruit salad, pasta salad, green peas, baked beans, lettuce, melon, strawberries and pasteurized milk. (CDC, Annual Listing of Foodborne Disease Outbreaks, United States, 1990-2005. http://www.cdc.gov/foodborneoutbreaks/outbreak_data.htm.)

The third is a report of two cases of *E. coli* O157:H7, one involving hemolytic uremic syndrome, one of which was suggested to be associated with raw milk: Allerberger et al. Euro Surveill. 2001;6:147-51. Only one of these children developed HUS. Neither case was conclusively linked to raw milk; in the HUS case, raw milk was explicitly ruled out. In the first case, the boy was visiting a rural farm on a school trip where he had direct contact with farm animals and their manure. He did not develop HUS. The authors of the report concluded that it was more likely that he contracted *E. coli* from drinking raw milk than from contact with manure. Nevertheless, they only found *E. coli* present in manure and none of the milk samples they tested were contaminated. One teacher and 13 other school children also drank the milk and did not get sick. Of the second case, the authors concluded: "Although the child with HUS was given unpasteurized cows' milk regularly by his parents, his severe illness . . . was not related to consumption of raw milk." Both children fully recovered.

As stated above, it may be premature for a government agency or scientific body to make an evidence-based recommendation to use raw milk to prevent allergic disease, but parents and others should have the legal right to make informed decisions to act on the reasonably supported but yet-unproven hypothesis that raw milk consumption supports proper immune development and lowers the risk of allergies.

Riedler, J., C. Braun-Fahrlander, W. Eder, M. Schreuer, M. Waser, S. Maisch, D. Carr, R. Schierl, D. Nowak, and E. von Mutius. 2001. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. Lancet 358:1129-33.

- **Cross sectional survey involving 2,618 parent of 6-13 yo children in rural areas of 3 European countries**
- **Overall findings: "long term and early life exposure to stables and farm milk induces a strong protective effect against development of asthma, hay fever, and atopic sensitization.**
- **Speculate that farm milk contains more gram negative bacteria and lipopolysaccharide (LPS, endotoxin) than pasteurized milk, which may be a factor in the allergic effect**
- **The authors do not comment on the pros or cons of raw milk consumption, per se**

This study adds further support to the possible protective effect of raw milk against allergic disorders.

Wickens, K., J. M. Lane, P. Fitzharris, R. Siebers, G. Riley, J. Douwes, T. Smith, and J. Crane. 2002. Farm residence and exposures and the risk of allergic diseases in New Zealand children. Allergy 57:1171-9

- Smaller epidemiological study (293 children) from New Zealand
- Consumption of raw milk as part of the infant diet was associated with less allergic disease, especially eczema and allergic rhinitis; exposure to animals also significant
- Speculate that exposure to bacteria in raw milk in early life may stimulate an immune response that protects against allergies
- Supports the hygiene hypothesis
- No recommendation to promote raw milk (pro or con)

Exposure to farm animals in early life was as often associated with an increase in risk of allergies than a decrease (exposure to poultry tended to be associated with increased risk while exposure to pig tended to be associated with a decreased risk) and living on a farm had no inverse association. The two strongest protective factors that best withstood adjustment for confounding variables were the consumption of yogurt and the

consumption of unpasteurized milk. This is not a basis for concluding, but certainly suggests, a probiotic effect of the raw milk.

The authors even suggested a probiotic effect of raw milk in the discussion section of this paper: "It has been shown that the probiotics found in yoghurt, lactobacilli (ref) and bifidobacteria (ref), influence development of the immune system towards a Th1 response. This is consistent with our finding of an inverse effect of yoghurt consumption at least once a week in infancy on the prevalence of hayfever, allergic rhinitis and AEDS [atopic eczema dermatitis syndrome] at age 7-10 years. . . . A similar mechanism may explain the reduced prevalence of some allergic diseases, especially AEDS and allergic rhinitis, that we found in association with the consumption of unpasteurized cow's milk early in life, because bacteria found in unpasteurized milk (ref) would stimulate a Th1 immune response.

The authors do not refer to the presence of lactobacilli and bifidobacteria in raw milk, but nevertheless these bacteria are indeed found in raw milk:

Desmasures N, Bazin F, Guéguen M. Microbiological composition of raw milk from selected farms in the Camembert region of Normandy. J Appl Microbiol. 1997;83(1):53-8.

Beerens H, Hass Brac de la Perriere B, Gavini F. Evaluation of the hygienic quality of raw milk based on the presence of bifidobacteria: the cow as a source of faecal contamination. Int J Food Microbiol. 200.54(3):163-9.

The first study found lactic acid bacteria in all raw milk samples tested. The second found bifidobacteria in 88 percent of raw milk samples. The authors suggested, but without any direct evidence, that the origin was fecal contamination. All that is supported by direct evidence, however, is the presence of lactobacilli and bifidobacteria in most raw milk samples.

Other articles

Barnes, M., P. Cullinan, P. Athanasaki, S. MacNeill, A. M. Hole, J. Harris, S. Kalogeraki, M. Chatzinikolaou, N. Drakonakis, V. Bibaki-Liakou, A. J. Newman Taylor, and I. Bibakis. 2001. Crete: does farming explain urban and rural differences in atopy? Clin Exp Allergy 31:1822-8.

- **They hypothesize that rates of atopy would be lower among the rural children compared with urban children because of contact with farm animals ("or perhaps raw milk") in early childhood. The "hygiene hypothesis"**
- **Regression analysis showed independent protective effects from raw milk consumption on atopy for children under 5 years**
- **They also found a significant association with animal contact (independent of raw milk consumption)**
- **The differences between rural/urban were not clear**
- **No statement regarding raw milk consumption (pro or con)**

This study adds further support to the possible protective effect of raw milk against allergic disorders.

Bieli, C., W. Eder, R. Frei, C. Braun-Fahrlander, W. Klimecki, M. Waser, J. Riedler, E. von Mutius, A. Scheynius, G. Pershagen, G. Doekes, R. Lauener, and F. D. Martinez. 2007. A polymorphism in CD14 modifies the effect of farm milk consumption on allergic diseases and CD14 gene expression. J Allergy Clin Immunol 120:1308-15.

- **These authors explore the genetic mechanism that might explain the protective effect of raw milk consumption and asthma in children**
- **They find a change in a specific gene (CD14)**

In the introduction, the authors offer several possibilities of why "farm milk" may be protective, which include the presence of viable lactobacilli. In other words, a probiotic effect, which Marler dismisses without serious consideration further below.

In the discussion, the authors offer several hypotheses to explain the association with CD14 polymorphisms, one of which is a probiotic effect: "Second, strains of probiotic bacteria contained in farm milk might have a balancing effect on the intestinal microflora, and their degradation products might interact with CD14 after absorption." (The first suggestion alluded to in this sentence is that microbial compounds present in the milk before consumption, as opposed to being produced in the intestine, interact with CD14.)

The authors argue against a role for endotoxin from gram-negative species (such as *E. coli*, as opposed to gram-positive species like lactobacilli), citing a submitted paper showing similar endotoxin levels in farm and non-farm milk in rural Europe. They suggest that the CD14 interaction could be based on differences in phospholipid composition of farm milk in addition to or instead of differences in microbial composition.

As stated previously, it is remarkable that Marler dismisses the probiotic potential of raw milk so quickly below while completely failing to point out where such an effect is postulated by the authors of the studies he cites within this document.

The fact that genetic polymorphisms affect the association with raw milk could explain why there are some inconsistencies between the results of epidemiological studies.

Debarry, J., H. Garn, A. Hanuszkiewicz, N. Dickgreber, N. Blumer, E. von Mutius, A. Bufe, S. Gatermann, H. Renz, O. Holst, and H. Heine. 2007. *Acinetobacter lwoffii* and *Lactococcus lactis* strains isolated from farm cowsheds possess strong allergy-protective properties. J Allergy Clin Immunol 119:1514-21.

- **The authors show that 2 bacterial species from cowsheds were able to reduce allergic reactions in mice through alterations in the innate immune system.**
- **They conclude that their findings "strongly support the hygiene hypothesis, which states that an environment rich in microbiologic structures, such as a farming environment, might protect against the development of allergies.**

In the introduction, they state that bacteria that *colonize the intestine* are important for normalizing immune function, and list three citations that refer to probiotics, prebiotics, and the disruptive effect of antibiotics on the microflora of the gut. The authors refer to the organisms they used as "nonpathogenic organisms." The form of the "hygiene hypothesis" that this study supports, then, is not the form emphasizing infectious agents, which are emphasized in the definition for the hypothesis that Marler describes at the beginning of this document, but rather the "old friends hypothesis" described by Rook and Brunet (cited in the beginning of this response), which includes nonpathogenic and symbiotic organisms.

Ege, M. J., R. Frei, C. Bieli, D. Schram-Bijkerk, M. Waser, M. R. Benz, G. Weiss, F. Nyberg, M. van Hage, G. Pershagen, B. Brunekreef, J. Riedler, R. Lauener, C. Braun-Fahrlander, and E. von Mutius. 2007. Not all farming environments protect against the development of asthma and wheeze in children. J Allergy Clin Immunol 119:1140-7.

- Epidemiological study involving 8,263 school age children from rural areas in 5 European countries
- Statistically significant protective effect against asthma by several farm factors (odds ratios and CIs are in the text): farm milk consumption; pig keeping; animal sheds

This study adds further support to the possible protective effect of raw milk against allergic disorders.

Hebeisen, D. F., F. Hoeflin, H. P. Reusch, E. Junker, and B. H. Lauterburg. 1993. Increased concentrations of omega-3 fatty acids in milk and platelet rich plasma of grass-fed cows. Int J Vitam Nutr Res 63:229-33.

- They find higher omega 3 fatty acids in milk grass fed cattle
- Black-Sharpe Dietary Fat Hypothesis suggests that omega 3 fatty acids may have a beneficial effect on allergies
- They conclude, “milk from grass fed cows may be nutritionally superior to milk from cows eating conserved grass with regard to omega 3 FAs
- Not stated here, but pasteurization should have no significant effect on FA composition (in other words, do not need to use ‘raw milk” for this possible benefit, but whole—full fat—milk may be a factor)

This is a legitimate hypothesis but does not constitute evidence against competing hypotheses.

Radon, K., D. Windstetter, J. Eckart, H. Dressel, L. Leitritz, J. Reichert, M. Schmid, G. Praml, M. Schosser, E. von Mutius, and D. Nowak. 2004. Farming exposure in childhood, exposure to markers of infections and the development of atopy in rural subjects. Clin Exp Allergy 34:1178-83

- **Survey of 321 young adults from rural environments in Germany**
- **No independent effect of raw milk and atopy**
- **Combined protective effect of raw milk + barn animal exposure before age 7**
- **No comment on use of raw milk (pro or con)**

The effect of raw milk was only statistically significant after adjustment for visits to animal houses and when combined with positive IgG to *H. pylori*, but there was a non-significant inverse association with raw milk in the absence of IgG to *H. pylori.* Although it is not strong support, this study does add further support to the possible protective effect of raw milk against allergic disorders.

Remes, S. T., K. Iivanainen, H. Koskela, and J. Pekkanen. 2003. Which factors explain the lower prevalence of atopy amongst farmers' children? Clin Exp Allergy 33:427-34.

- Finish study of 366 farmers and non farmers children
- No association with raw milk and allergic disease
- Less atopy among fresh vegetable eaters
- This study conflicts with other studies

Like many of the others, this study looked at “farm milk” rather than pasteurization status. This fact, recall bias, population genetics, or many other factors could contribute to the difference between the findings of this study and those of most of the other relevant studies.

Von Ehrenstein, O. S., E. Von Mutius, S. Illi, L. Baumann, O. Bohm, and R. von Kries. 2000. Reduced risk of hay fever and asthma among children of farmers. Clin Exp Allergy 30:187-93

- **Study purpose: to test the hypothesis that children living on a farm have lower prevalences of allergic disease**
- **Cross sectional survey of children aged 10,163 (5-7 years)**
- **Farmer's children had significantly lower prevalences of hay fever, asthma, and wheeze than children not living in an agricultural environment; increasing exposure to livestock was significant**
- **Consumption of whole but not skim milk was associated with decreased hay fever and asthma**
    - **Speculate that protective effect might be from foods rich in fatty acids**
    - **Suggest that raw milk may have a higher microbial load (especially *Lactobacillus*) than industrially processed skim milk**

Lactobacillus species are probiotic organisms.

II. Raw milk is protective against autism

Nothing in the literature was found to support this in the literature. WAPF cites this article, which seems irrelevant.

Meisel, H. 2005. Biochemical properties of peptides encrypted in bovine milk proteins. Curr Med Chem 12:1905-19

There is anecdotal evidence that raw milk may be useful in treating autism in some cases. While controlled experimental evidence may not exist, parents of autistic children should have the right to try what *may* work for their own children and autistic children deserve to possibility of what good may come.

III. Raw milk is a probiotic

An entire issue of Clinical Infectious Diseases was dedicated to probiotics in 2008, but no mention of raw milk as a recommended source of probiotics could be found. The article below is by one of the experts in the field and *defines probiotics*; raw milk does not meet this definition.

Clinical Infectious Disease Journal, February 2008
http://www.journals.uchicago.edu/toc/cid/2008/46/3

Sanders, M. E. 2008. Probiotics: definition, sources, selection, and uses. Clin Infect Dis 46 Suppl 2:S58-61; discussion S144-51.

- **The term "probiotic" should be used only for products that meet the scientific criteria for this term-namely, products that contain an adequate dose of live microbes that have been documented in target-host studies to confer a health benefit.**
- **Probiotics must be identified to the level of strain, must be characterized for the specific health target, and must be formulated into products using strains and doses shown to be efficacious.**
- **NOTE: raw milk does not meet this definition**

Obviously raw milk will not meet a definition designed specifically for formulated products, because raw milk is not a formulated product. It does, however, contain live organisms that have been documented in target-host studies to confer health benefits (such as lactobacilli and bifidobacteria). Whether the doses are adequate has not been studied directly, but most researchers in the field apparently consider it plausible, since many of the studies cited within this document offer the presence of these organisms in raw milk as one of several hypotheses to explain their evidence.

Another recent article concerning probiotics and milk

Ivory, K., S. J. Chambers, C. Pin, E. Prieto, J. L. Arques, and C. Nicoletti. 2008. Oral delivery of *Lactobacillus casei* Shirota modifies allergen-induced immune responses in allergic rhinitis. Clin Exp Allergy.

- **Lactic acid bacteria are among the most important probiotic organisms**
- **Probiotics are believed to reduce allergic symptoms by modulating the immune system**
- **The authors provide a rationale for probiotic use by demonstrating 2 lactic acid bacterial species that modified the allergic response, specifically indicators of seasonal allergic rhinitis (SAR)**
- **They suggest that "probiotics hold much promise as a functional food," but nowhere is it suggested that "raw milk" would be a recommended food for this purpose**
- **NOTE: the experiment was carried out by *inoculating the specific bacterial species* into a milk drink (not explicitly stated, but no indication it was raw milk: "all dairy milk drinks were supplied by…with HACCP certification for the safety…"**

If this study added bacteria to a milk drink that was not made from raw milk, it is clearly completely irrelevant.

IV. Raw milk contains "beneficial" bacteria.

There is evidence that there may be metabolites toxic to foodborne pathogens and antibacterial compounds that are produced by other bacterial species in raw milk. These compounds may help the bacteria that produce them to survive and compete in the food environment. Some of these properties are exploited by the food industry, but often to promote food quality, not foodborne pathogen control per se (at least not as the only method to control pathogens). The presence of these compounds in raw milk has not been defined and thus should not be relied upon as *a "kill step"* for dangerous foodborne pathogens that may also be present in raw milk.

Representative examples from the literature

Doyle, M. P., and D. J. Roman. 1982. Prevalence and survival of *Campylobacter jejuni* in unpasteurized milk. Appl Environ Microbiol 44:1154-8.

- **This study compared the survival of 8 *C. jejuni* strains in sterile and raw milk**
- **The survival time (number of days) of *C. jejuni* strains varied depending on the specific strain**
- ***Campylobacter* survived longer in sterile milk than raw milk at refrigeration temperatures**
    - **The authors speculated that other microflora in raw milk may have produced toxic metabolites that inactivated the *C. jejuni* (for example, lactoperoxidase)**
    - **Although *Campylobacter* levels dropped off sooner in raw milk over the study period, there could still be enough surviving bacteria to represent an "infectious dose" (see Figure 2)**
- **The authors conclude: "our results indicate the presence and possible persistence of *C. jejuni* in raw grade A milk and reaffirm the need for pasteurization."**

The authors showed that when they inoculated a laboratory culture medium meant for growing the brucellosis pathogen, sterile milk, and raw milk with a massive dose of *C. jejuni,* the *C. jejuni* survived well in the culture medium but rapidly died in the milk. One of their key findings was that the organism survived twice as long in sterile milk as it did in raw milk.

It is true that the authors concluded that their results reaffirmed the need for pasteurization, but their data can easily be seen in a different way. The "presence" of *C. jejuni* was found in only one out of 108 bulk tank milk samples, with no references to the production practices on any of the farms. They did not state the concentration of *C. jejuni* in this sample, but the sensitivity was 0.1 (CFU) per milliliter (mL). Thus, the concentration may have been very low. The "persistence" of the *C. jejuni* was six days in raw milk when they inoculated it with 10,000,000 CFU/mL. In other words, they only observed the "persistence" of *C. jejuni* in raw milk when they inoculated it with up to 100 million times the amount they found naturally in one out of 108 samples of bulk tank milk that, for all we know, may have been of the absolute worst quality.

Data from a number of other studies suggest that it is very difficult for *C. jejuni* to persist in raw milk under natural conditions.

Hutchinson and others (1985) tried blaming an outbreak of *C. jejuni* in a village where virtually everyone drank raw milk from a single farm on the milk. They found the organism in rubbish heaps and watering holes, but not in milk or milk filters. Frustrated with this result, they cultured samples right on the farm instead of carrying them in sterile containers to a sterile working space in the laboratory as is usually done, and the milk and milk filters proved contaminated. They claimed the reason they had to culture the milk on the farm was because the *C. jejuni* was unable to tolerate the "natural antibacterial effect of fresh milk" for the several hours it took to transport the milk to the lab, but offered no explanation of how the milk could have gotten anyone sick if all the *C. jejuni* within it would die within hours of milking. When they tried quantifying two of the positive samples after some unspecified time, the milk turned up negative. When they tried subtyping two other samples soon after collection, they failed because the bacteria could not survive long enough for them to finish the procedure.

Warner (1986) found *C. jejuni* in bile samples from cows culled from their herds, but found no *C. jejuni* in milk filter samples, despite the visible presence of fecal contamination, giving indirect support to the idea that the "natural antibacterial effect of fresh milk" may have killed any *C. jejuni* that would have found its way into the milk filters.

Over and over again, investigators blame *C. jejuni* outbreaks on raw milk despite negative milk samples. In explaining how certified raw milk could cause *C. jejuni* infection without being contaminated with *C. jejuni*, Potter (1983) wrote the following:

> *C. jejuni* has been cultured with relative facility from a number of different environments, including human and animal feces, bile, poultry meat, and water. However, despite the frequent association of raw milk with *C. jejuni* infections, attempts to recover the organism from milk have usually been unsuccessful.

What these researchers never explain is why *C. jejuni* would fail to grow from milk when transferred to a broth specifically formulated to cause its proliferation, but would easily transmit infection to humans within an organ – the stomach – specifically designed to cause its death.

While Hudson (1984) provided convincing evidence of *C. jejuni* illness transmitted by raw milk, most of the studies claiming to find such evidence have instead supported the concept that it is incredibly difficult for the organism to survive in such a medium. This never stops investigators from blaming raw milk, however. Even Schmid (1987) blamed a local outbreak of *C. jejuni* on raw milk when all of the milk tested negative and 360 samples of locally sold chicken tested positive!

See the following references:

Hutchinson, D. N., F. J. Bolton, P. M. Hinchliffe, H. C. Dawkins, S. D. Horsley, E. G. Jessop, P. A. Robertshaw, and D. E. Counter. Evidence of udder excretion of Campylobacter jejuni as the cause of milk-borne campylobacter outbreak. J Hyg (Lond). 1985; 94:205-15

Warner, D. P., J. H. Bryner, and G. W. Beran. Epidemiologic study of campylobacteriosis in Iowa cattle and the possible role of unpasteurized milk as a vehicle of infection. Am J Vet Res. 1986;47:254-8.

Potter, M. E., M. J. Blaser, R. K. Sikes, A. F. Kaufmann, and J. G. Wells. Human Campylobacter infection associated with certified raw milk. Am J Epidemiol. 1983;117:475-83.

Hudson, P. J., R. L. Vogt, J. Brondum, and C. M. Patton. Isolation of Campylobacter jejuni from milk during an outbreak of campylobacteriosis. J Infect Dis. 1984;150:789.

Schmid, G. P., R. E. Schaefer, B. D. Plikaytis, J. R. Schaefer, J. H. Bryner, L. A. Wintermeyer, and A. F. Kaufmann. A one-year study of endemic campylobacteriosis in a midwestern city: association with consumption of raw milk. J Infect Dis. 1987;156:218-22.

V. Raw milk has a higher nutritive value

a. Historical perspective

i. Raw milk advocates frequently cite older articles about pasteurization with nutritional claims that were never substantiated by later research/nutrition studies. For example:

Hess AF. Infantile scurvy: its influence on growth. The American Journal of Diseases of Children. 1916; 152-165.

Bell RW. The effect of heat on the solubility of the calcium and phosphorus compounds in milk. The Journal of Biological Chemistry. 1925;64(2):391-400.

Pottenger FM. Effect of heat-processed foods and metabolized vitamin D milk on dentofacial structures of experimental animals. Am J Orthod 1946;32:467-485.

- **In Pottenger article, raw milk advocates erroneously cited this article as having reported that disease occurred in cats fed *pasteurized* milk (see Potter et al, below).**

b. Current literature

i. Potter et al wrote a review discussing the hazards and purported benefits of raw milk consumption for JAMA in 1984.

Potter, M. E., A. F. Kaufmann, P. A. Blake, and R. A. Feldman. 1984. Unpasteurized milk. The hazards of a health fetish. Jama 252:2048-52.

In table 1, they summarize the argument against the purported nutritive benefits as follows:

Pasteurization causes insignificant decreases in thiamine, vitamin B12, and vitamin C content; no effect has ever been demonstrated on the bioavailability of other raw milk constituents with known nutritive value; human nutrition studies have shown no advantage of raw over pasteurized milk.

No current peer-reviewed literature directly supporting "a higher nutritive value" for raw milk was found. One example of a questionable article that the raw milk advocates cite:

Rajakumar, K. 2001. Infantile scurvy: a historical perspective. Pediatrics 108:E76.

- **This article is confusing/misleading when compared with other descriptions of the emergence of scurvy (vitamin C) deficiency in infants at the end of the 19th century**
- **The author repeatedly refers to *“”the increased incidence of infantile scurvy during that period was attributed to the usage of heated milk and proprietary foods.”***
- **From other readings, these “ready to eat” formulas became popular and replaced other vitamin C sources in the infant’s diet during this time period. Since milk (raw or pasteurized) is not an important source of vitamin C, the most likely explanation for the epidemic was the removal of fruit and vegetable juices from the infant’s diet; adding these foods back into the diet resolved the problem.**
- **This is not a “current day” issue with our diverse food including fruit and vegetable sources for infants.**

The cited article also refers to Hess’s experimental evidence that raw but not pasteurized milk could prevent or treat scurvy.

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