Consumption of unprocessed cow's milk protects infants from common respiratory infections

Georg Loss, PhD,[a,b,c] Martin Depner, PhD,[a] Laurien H. Ulfman, PhD,[d] R. J. Joost van Neerven, PhD,[d,e] Alexander J. Hose, MPH,[a] Jon Genuneit, MD,[f] Anne M. Karvonen, PhD,[g] Anne Hyvärinen, PhD,[g] Vincent Kaulek, PhD,[h] Caroline Roduit, MD,[i,j] Juliane Weber, MD,[a] Roger Lauener, MD,[j,k] Petra Ina Pfefferle, PhD, DrPH,[l,m] Juha Pekkanen, MD, PhD,[g,n] Outi Vaarala, MD, PhD,[o] Jean-Charles Dalphin, MD, PhD,[h] Josef Riedler, MD,[p] Charlotte Braun-Fahrländer, MD,[b,c] Erika von Mutius, MD,[a,q] Markus J. Ege, MD,[a,q] and the PASTURE study group*

Munich, Ulm, and Marburg, Germany, Basel, Zürich, Davos, and St Gallen, Switzerland, Amersfoort and Wageningen, The Netherlands, Kuopio and Helsinki, Finland, Besançon, France, and Schwarzach, Austria

Background: Breast-feeding is protective against respiratory infections in early life. Given the co-evolutionary adaptations of humans and cattle, bovine milk might exert similar anti-infective effects in human infants.

Objective: To study effects of consumption of raw and processed cow's milk on common infections in infants.

Methods: The PASTURE birth cohort followed 983 infants from rural areas in Austria, Finland, France, Germany, and Switzerland, for the first year of life, covering 37,306 person-weeks. Consumption of different types of cow's milk and occurrence of rhinitis, respiratory tract infections, otitis, and fever were assessed by weekly health diaries. C-reactive protein levels were assessed using blood samples taken at 12 months.

Results: When contrasted with ultra-heat treated milk, raw milk consumption was inversely associated with occurrence of rhinitis (adjusted odds ratio from longitudinal models [95% CI]: 0.71 [0.54-0.94]), respiratory tract infections (0.77 [0.59-0.99]), otitis (0.14 [0.05-0.42]), and fever (0.69 [0.47-1.01]). Boiled farm milk showed similar but weaker associations. Industrially processed pasteurized milk was inversely associated with fever. Raw farm milk consumption was inversely associated with C-reactive protein levels at 12 months (geometric means ratio [95% CI]: 0.66 [0.45-0.98]).

Conclusions: Early life consumption of raw cow's milk reduced the risk of manifest respiratory infections and fever by about 30%. If the health hazards of raw milk could be overcome, the public health impact of minimally processed but pathogen-free milk might be enormous, given the high prevalence of respiratory infections in the first year of life and the associated direct and indirect costs. (J Allergy Clin Immunol 2015;135:56-62.)

***Key words:** Respiratory infections, rhinitis, otitis, fever, inflammation, C-reactive protein, infancy, milk, prevention, epidemiology*

Cow's milk has been a readily available source of protein and energy for humans ever since the Neolithic period. Mutations in the human lactase gene prevented downregulation of lactase

From [a]Dr von Hauner Children's Hospital, Ludwig Maximilian University, Munich; [b]the Swiss Tropical and Public Health Institute, Basel; [c]the University of Basel; [d]FrieslandCampina, Amersfoort; [e]Cell Biology and Immunology, Wageningen University; [f]the Institute of Epidemiology and Medical Biometry, Ulm University; [g]the Department of Environmental Health, National Institute for Health and Welfare, Kuopio; [h]the Department of Respiratory Disease, UMR/CNRS 6249 chrono-environment, University Hospital of Besançon; [i]Children's Hospital, University of Zürich; [j]the Christine Kühne Center for Allergy Research and Education, Davos; [k]Children's Hospital of Eastern Switzerland, St Gallen; [l]the Institute for Laboratory Medicine and Pathobiochemistry, Molecular Diagnostics, Philipps University of Marburg; [m]Member of the German Center for Lung Research; [n]Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio; [o]the Department of Vaccination and Immune Protection, National Institute for Health and Welfare, Helsinki; [p]Children's Hospital, Schwarzach; and [q]Comprehensive Pneumology Center Munich (CPC-M), German Center for Lung Research, Munich.

*The members of the PASTURE study group are (in alphabetical order by study center): Marie-Laure Dalphin (France); Gert Doekes (The Netherlands); Remo Frei (Switzerland); Maija-Riitta Hirvonen, Sami Remes, Marjut Roponen, and Pekka Tiittanen (Finland); and Sabina Illi, Michael Kabesch, Harald Renz, and Bianca Schaub (Germany).

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Corresponding author: Georg Loss, PhD, Dr von Hauner Children's Hospital, Ludwig Maximilian University Munich, Lindwurmstrasse 4, D-80337 Munich, Germany. E-mail: georg.loss@med.uni-muenchen.de.

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Abbreviations used
GEE: General estimation equation
hsCRP: High-sensitivity C-reactive protein
aOR: Adjusted odds ratio
PASTURE: Protection against Allergy—Study in Rural Environments
RTI: Respiratory tract infection
UHT: Ultra-heat treatment

levels, thereby rendering native cow's milk digestible also to adolescents and adults. The enormous pace—in genetic terms—by which the mutations spread across the populated world emphasizes the evolutionary advantage of cow's milk consumption and its impact on population fertility.[1]

This indicates that consumption of bovine milk matches human needs remarkably well despite varying proportions of fat, protein, and carbohydrate contents. Reasons for this relatively fast mutual adaptation might be found in successful breeding of animals, effectively a form of co-evolution. In turn, additional genetic and epigenetic changes in humans might have occurred in analogy to the lactase mutations. Beyond using nutrients and energy, the human organism might also profit from functional properties of cow's milk, such as host-defense proteins.[2,3] In a way, cow's milk might provide passive immunity to humans, in analogy to human breast milk, and might also prevent or attenuate infections in humans. Indeed, numerous agents with beneficial anti-microbial or immune-modulatory effects are shared in bovine and human milk, such as immunoglobulins, cytokines, growth factors, lactoferrin, oligosaccharides, and milk fat globule membranes.[4]

The price humankind had to pay for the advantages of cow's milk was the risk of serious infections that can be transmitted by raw milk, such as tuberculosis, brucellosis, listeriosis, or enterohemorrhagic *Escherichia coli* causing hemolytic-uremic syndrome.[5-7] By the introduction of pasteurization and other industrial processing techniques, the critical issue of milk-borne infections has effectively been solved. In contrast to the mutual adaptation between humans and cattle, which evolved over several millennia, the replacement of fresh raw milk by processed milk was a rather recent change, which in itself might bear unknown disadvantages. For instance, heat-susceptible milk ingredients such as proteins or even microbial components might be altered by industrial processing,[8,9] possibly losing some of their properties that are beneficial for human health. Despite maintained nutritional value, functional proteins are denatured by ultra-heat treatment (UHT).[10,11]

The question remains whether industrial processing could abolish the postulated anti-infective effects, because these might be tightly linked to heat-sensitive molecules, such as whey proteins.[11] In other words, the rationale for the present analysis was the assumption that children consuming raw cow's milk were less affected by common infections as compared with children fed with processed milk. Though in most European countries, consumption of raw milk is vigorously discouraged, it is still practiced by many farming families. Infants are particularly susceptible to infective agents, because their immune system is immature. For the same reason, however, this age group might profit most from the beneficial immunomodulatory qualities of unprocessed cow's milk.

The aim of this study was to assess the effects of consumption of raw, boiled, and industrially processed milk types on common infections in the first year of life in a prospective multi-center birth cohort in 5 European countries.

METHODS

For the prospective birth cohort Protection against Allergy—Study in Rural Environments (PASTURE), pregnant women were recruited during the third trimester of pregnancy in rural areas of Austria, Finland, France, Germany, and Switzerland; half of the women lived and worked on livestock farms.[12] Questionnaire information on lifestyle and parental background was obtained within the third trimester of pregnancy and at 2 and 12 months of the child's age. In addition, parents reported information on feeding practices, farm-related exposures, and the occurrence of infection outcomes using weekly diaries kept between 8 and 53 weeks of life. The study was approved by the local research ethics committees in each country, and written informed consent was obtained from all parents.

Presence of infections was registered by the diaries, in particular occurrence during the last 7 days of a cold or runny nose (rhinitis), fever (at least 38.5°C), otitis, cough, or diarrhea for at least 2 days. These outcomes were defined as occurrence or absence in a given week between week 8 and 53 of life. Respiratory tract infections (RTI) were any occurrence of rhinitis or cough in the absence of other respiratory symptoms such as wheeze.[13] Cough was defined as cough without concomitant wheeze, in order to minimize confounding by allergy.

Explanatory variables based on diaries were defined as occurrence or absence in a given week and included exclusive or any breast-feeding, infant formula, contact with cow, pig, or horse stables, and quarterly seasons of milk sampling. Consumption of cow's milk, which was either bought at a shop (industrially processed milk, ie, UHT or pasteurized milk) or obtained directly from a farm (farm milk), was coded for weekly intervals in the following categories: (1) UHT milk and no farm milk, (2) pasteurized milk and no UHT and no farm milk, (3) boiled farm milk irrespective of any shop milk, (4) raw farm milk irrespective of any shop milk. Weekly diaries provided data on the quantity of milk (in units of 200 mL) and whether farm milk was consumed. Every 4 weeks, parents were asked whether they had boiled the milk and whether they had fed the infant shop milk. The type of shop milk was asked at 12 months of age by the following question: Did your child consume i) pasteurized cow's milk or ii) UHT milk after 8 weeks of life?

Covariables were selected *a priori* and included farming (living on a farm vs not), siblings, maternal education, parental history of atopic disease (asthma, hay fever, or atopic dermatitis) (derived from pregnancy questionnaires), and sex, mode of delivery, birth weight, and use of hypoallergenic infant formula (derived from 2-month questionnaires). To avoid collinearity, farming was replaced by contact to stables where applicable. Variables based on 1-year questionnaires were contact with dogs or cats and exposure to environmental tobacco smoking. Introduction of complementary foods during the first year of life was described by a food diversity score.[14] Age or follow-up time was entered as a continuous variable in weeks.

Statistical analyses considered a follow-up time from week of life 8 to 53 with non-missing information on variables used in present analyses in more than half of the average follow-up time (40 weeks). The median follow-up time was 42 weeks, with an interquartile range of 4 weeks. In total 983 individuals, ie, 87% of the originally included 1,133 children,[15] contributed to this analysis, with 37,306 person-weeks of observation. Weekly period prevalences refer to children with information available for the respective week. In a subsample of 602 children, high-sensitivity C-reactive protein (hsCRP) was measured at age 1 year.[16]

Longitudinal associations of individual outcomes and exposures were derived from general estimation equations (GEE) and expressed as adjusted odds ratios (aOR) with 95% CI. Due to the given data structure with unequal spacing and gaps, an exchangeable correlation structure was used; sensitivity analyses assuming unstructured and autoregressive matrices yielded similar effect estimates. When data on exposures or outcomes were missing from a