LETTERS TO THE EDITOR

Consumption of milk fat and reduced asthma risk in pre-school children

We read the paper by Wilga et al published in the July 2003 issue of Thorax with great interest. The authors found that the consumption of specific food items such as full cream milk, butter, and brown bread can contribute to a decrease in the risk of asthma and wheezing in pre-school children. These findings agree with previous studies in adults, but there are a few methodological problems in the analyses used in the study which may have influenced the results obtained.

Our first area of concern is that trans-generational traditions of families with atopic diseases are not taken into consideration. For instance, families with a history of atopy tend to smoke less, which is described as a "healthy passive smoker effect". Grandparents and parents who have asthma tend to smoke less, which may lead to a similar "healthy pet keeping effect". For related reasons, families may also alter their diets resulting in a "healthy cow's milk effect". These potential changes within families are supported by avoidance strategies propagated by various national medical associations. Children of atopic parents therefore tend to experience different exposures. Hence, before using statistical models we need to investigate the extent to which the diet of children differs according to the atopic status of their parents. An additional table is therefore needed, comparable to table 2, with consumption frequencies in columns for allergic and non-allergic parents as well as "allergic mothers" and "allergic fathers". In this respect, we were surprised to see the different proportion of mothers (14.2%) and fathers (29.1%) with allergy. Previous studies have reported the proportions of atopy in both mothers and fathers to be consistently around 30–35%.

This leads to our second area of concern which deals with the logistic regression model used in table 3. By modelling, the authors attempted to control for the effects of maternal and paternal atopy by considering them as confounding variables. We see the child's diet acting as an intervening variable in the association between parental atopic history and the risk of the child developing asthma (fig 1). The standard epidemiological rule is that intervening variables should not be considered as confounders. By neglecting this rule the authors may have achieved biased odds ratios. In addition, children with a parental history of allergy are likely to have a different genetic make up. It is therefore very likely that they react differently—for instance, to cow's milk—which requires the investigation of interactive effects of parental atopy and diet on asthma in the offspring. To overcome these two challenges the authors need to present another table stratifying for parental allergy. The child's risk of wheezing should be estimated for each stratum. This would then adequately control for the intervening effects of parental allergy and provide an indication of any interaction. Additionally, information on the risk of exposure to cow's milk in children with and without parental atopy would help either to change or—since we expect no protective effect in atopic families—to sustain the recommendation to avoid early exposure to cow's milk. To add to this argument, the authors also failed to differentiate between allergic and non-allergic (transient?) wheezing. We look forward to seeing additional informative tables.

W Karmaus, C Fussman
Michigan State University, College of Human Medicine, Department of Epidemiology, East Lansing, Michigan 48823, USA, karmaus@msu.edu

References

Authors' reply

The first point made by Karmaus and Fussman is that the association we observed between consumption of products containing milk fat (full cream milk, milk products, butter) and a reduced risk of asthma in pre-school children could be the result of a "healthy cow's milk effect". This is unlikely as avoidance of cow's milk is uncommon in the Netherlands. Dutch guidelines do not advise avoidance of cow's milk for children with familial allergy after the age of 12 months unless the child has cow's milk allergy. The popular belief is that young children need milk for healthy growth and few parents see milk as potentially harmful. 99% of Dutch children aged 1–4 years use milk (products). In the PIAMA population, too, nearly all children used milk—either full cream or semi-skimmed. Apart from 64 children with cow's milk allergy who were excluded from the analyses, only 27 children (<1%) had not used milk (products) in the previous month. Of these children, 16 had an allergic parent and 11 had non-allergic parents. The data requested by Karmaus and Fussman do not show an association between parental allergy and the prevalence of daily consumption of the foods that we found to be associated with reduced risk of asthma or wheeze: full cream milk, milk products (mainly flavoured and unflavoured yoghurt, either full cream or low fat), butter and brown bread (table 1, first column).

Karmaus and Fussman correctly point out the imbalance between the percentages of allergic mothers and allergic fathers in the study. This imbalance is due to the study design. Maternal allergy was used as the criterion to allocate participants to subgroups of the PIAMA study and in the natural history part of the study non-allergic mothers were oversampled.

The second point of concern raised by Karmaus and Fussman deals with our logistic regression model. They state that, by treating parental allergy as a confounder, we neglected the potential role of other unmeasured confounding variables. We see the parental allergy as a confounder, we neglected the potential role of other unmeasured confounding variables. We see the parental allergy.
allergy is not an intervening variable between the exposure of interest (diet) and the effect studied (child’s asthma). Parental allergy would only be an intervening variable when the child’s diet at age 2 is a cause of parental allergy. Instead, in their figure parental allergy is a classical confounder—that is, it is a factor that is a cause of both the exposure and the disease of interest and was therefore dealt with correctly in our analyses.

We agree with Karmas and Fussmann, however, that effect modification might be present in that children of allergic parents might react differently to dietary exposures, because of the small numbers, even large differences were not statistically significant in most cases (table 1, data shown for only three subgroups). Adjusted logistic regression analysis was carried out in only two subgroups because numbers were too small in the other groups. The adjusted odds ratios for daily consumption of full cream milk, milk products, and butter were consistently below 1 both in children of allergic and in children of non-allergic parents; however, because of the small numbers, the confidence intervals were wider than in the analysis of the group as a whole (see table 3 in our paper).

The last point made by Karmas and Fussmann is that they would have liked us to differentiate between allergic and non-allergic (transient?) wheezing. IgE measurements were not available for these children and they were too young for us to be able to differentiate between transient and persistent wheezers. We look forward to future analyses when a more reliable asthma diagnosis can be made.

We conclude that there is no evidence in our population for a “healthy full cream cow’s milk effect”, that we adjusted correctly for parental allergy in our analyses, and that our data do not suggest that the reported associations between daily consumption of products containing milk fat and reduced risk of asthma and wheeze are only present in children of non-allergic parents.

**Table 1** Percentages and (numbers) of 2 year old children who consumed different foods on 6 or 7 days/week, crude prevalences of asthma and wheeze at age 3 in children who, at age 2, used different foods on a daily basis (“daily use”) compared with children with lower consumption frequencies (others) and adjusted odds ratios for the relationship between daily consumption of different foods at age 2 and prevalence of asthma and wheeze at age 3, stratified for parental allergy

<table>
<thead>
<tr>
<th>Foods</th>
<th>Percentage (n) daily users</th>
<th>Crude % prevalence</th>
<th>Adjusted OR (95% CI)</th>
<th>Percentage (n) daily users</th>
<th>Crude % prevalence</th>
<th>Adjusted OR (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Full cream milk</td>
<td></td>
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<tr>
<td>Parental allergy</td>
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<tr>
<td>Full cream milk</td>
<td>32.9 (n = 97)</td>
<td>11.1</td>
<td>5.4</td>
<td>8.5</td>
<td>19.2</td>
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<tr>
<td>Milk products</td>
<td>73.9 (n = 218)</td>
<td>10.1</td>
<td>8.4</td>
<td>16.0</td>
<td>14.8</td>
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<tr>
<td>Brown bread</td>
<td>84.8 (n = 259)</td>
<td>18.6</td>
<td>6.9</td>
<td>15.6</td>
<td>14.5</td>
<td>22.2</td>
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<tr>
<td>Butter</td>
<td>71.7 (n = 21)</td>
<td>9.9</td>
<td>0.0</td>
<td>8.8</td>
<td>1.0</td>
<td>16.8</td>
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<tr>
<td>Mother and/or father allergy</td>
<td>41.5 (n = 390)</td>
<td>8.61</td>
<td>0.01</td>
<td>8.0</td>
<td>0.67</td>
<td>1.05</td>
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<tr>
<td>Full cream milk</td>
<td>31.2 (n = 547)</td>
<td>3.3</td>
<td>0.04 (0.22 to 0.91)</td>
<td>2.3</td>
<td>4.5</td>
<td>0.37 (0.16 to 0.84)</td>
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<tr>
<td>Milk products</td>
<td>75.1 (n = 1736)</td>
<td>4.6</td>
<td>0.70 (0.39 to 1.34)</td>
<td>3.4</td>
<td>4.8</td>
<td>0.73 (0.41 to 1.30)</td>
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<tr>
<td>Brown bread</td>
<td>82.8 (n = 1030)</td>
<td>7.3</td>
<td>0.67 (0.36 to 1.30)</td>
<td>3.8</td>
<td>5.2</td>
<td>0.49 (0.26 to 0.93)</td>
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<tr>
<td>Butter</td>
<td>7 (n = 126)</td>
<td>5.2</td>
<td>0.80 (0.32 to 2.18)</td>
<td>2.9</td>
<td>4.0</td>
<td>0.59 (0.17 to 2.05)</td>
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<td>Crude % prevalence</td>
<td></td>
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<tr>
<td>“Ever asthma”</td>
<td>22.9% (n = 97)</td>
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<tr>
<td>“Recent asthma”</td>
<td>15.4% (n = 218)</td>
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<tr>
<td>“Recent wheeze”</td>
<td>18.6% (n = 259)</td>
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</table>

* p < 0.05, † p < 0.10 for difference in asthma or wheeze prevalence between daily users and less frequent consumers.

† Adjusted for consumption frequencies of foods shown in the table, consumption frequency of semi-skimmed milk, consumption frequency of margarine, sex, birth weight, presence of older sibling(s), maternal education, having been breast fed for >8 weeks, and parental smoking in the home.

For full cream milk and butter odds ratios are shown for daily consumption (on 6–7 days/week) compared with consumption less than once a week; for milk products and brown bread the prevalence of consumption less than once a week is less than 3% and therefore odds ratios are shown for daily consumption versus all others.

**References**


**BIS/BTS SARS guidelines**

The guidelines on severe acute respiratory syndrome (SARS) published by the British Infection Society (BIS) and the British Thoracic Society (BTS) in July 2003 recommend giving adult patients with suspected or probable SARS an N95 or equivalent mask and request that they wear this continuously.1 This recommendation was apparently provided to prevent the spread of the SARS coronavirus from the patient to the surrounding environment.

An N95 respirator (mask) is a negative pressure respirator which only filters air entering the mask, not leaving it.2 Those wearing this respirator will experience an additional burden on the breathing system in moving air in and out of the respirator.3 For this reason, occupational protection agencies such as the United States Occupational Safety and Health Administration4 require those using these types of respirator to be medically qualified because of physiological5 and psychological6 stresses that may occur. Patients wearing this respirator will experience an additional burden on the breathing system in moving air in and out of the respirator.7 For this reason, occupational protection agencies such as the United States Occupational Safety and Health Administration require those using these types of respirator to be medically qualified because of physiological stresses that may occur. Patients wearing this respirator may react differently to dietary exposures, because of the small numbers, even large differences were not statistically significant in most cases (table 1, data shown for only three subgroups). Adjusted logistic regression analysis was carried out in only two subgroups because numbers were too small in the other groups. The adjusted odds ratios for daily consumption of full cream milk, milk products, and butter were consistently below 1 both in children of allergic and in children of non-allergic parents; however, because of the small numbers, the confidence intervals were wider than in the analysis of the group as a whole (see table 3 in our paper).

The last point made by Karmas and Fussmann is that they would have liked us to differentiate between allergic and non-allergic (transient?) wheezing. IgE measurements were not available for these children and they were too young for us to be able to differentiate between transient and persistent wheezers. We look forward to future analyses when a more reliable asthma diagnosis can be made.

We conclude that there is no evidence in our population for a “healthy full cream cow’s milk effect”, that we adjusted correctly for parental allergy in our analyses, and that our data do not suggest that the reported associations between daily consumption of products containing milk fat and reduced risk of asthma and wheeze are only present in children of non-allergic parents.

A H Wijga, H C Boshuizen, H A Smit National Institute of Public Health and the Environment, Department of Chronic Disease Epidemiology (CZE), The Netherlands

M Kerkhof, J Gerritsen Department of Paediatric Respiratory Medicine, University Hospital Groningen, Groningen, The Netherlands

J C de Jongste, H J Neijens (deceased) Department of Paediatrics, Erasmus University Medical Center/Sophia Children’s Hospital, Rotterdam, The Netherlands

B Brunkereef Institute for Risk Assessment Sciences, University of Utrecht, Utrecht, The Netherlands

Correspondence to: Dr A Wijga, National Institute of Public Health and the Environment, Department of Chronic Disease Epidemiology (CZE), P O Box 1, 3720BA Bilthoven, The Netherlands; aleth.wijga@rvn.nl
suggested that a high ventilation rate in hospital wards with SARS patients results in lower infectivity of healthcare workers. The most adequate form of protection is therefore proper use of personal protective equipment, including respirators, by healthcare workers together with a high ventilation rate. The guidelines should be adjusted to recommend that patients should not wear a respirator.

J H Lange
Environisate Training and Consultants, P O Box 114022, Pittsburgh, PA 15229, USA; johnlange@worldnet.att.net

References
2 Lange JH. A revising of the appropriate respiratory protection against SARS. Can Med Assoc J 2004;174:445-6

Authors’ reply
We thank Mr Lange for his comments on the BTS/BIS SARS guidelines of July 2003. He and other Thorax readers will be pleased to know that the guidelines have been rewritten over the last few months and are now on the BTS website under the title “Hospital management of adults with SARS if SARS re-emerges”.

The new BTS/BIS/HPA guidelines recommend that all possible or probable SARS patients should wear a surgical face mask rather than an N95 respirator, and that healthcare workers should wear a respirator complying with the European standard EN149:2001 FFP3 or higher filtration. Healthcare workers should note that wearing a respirator is just one way of preventing the spread of SARS; other important precautions include good personal hygiene (especially hand hygiene) and gloves, aprons, gowns, visors, and goggles when appropriate. For further up to date information please visit the UK Health Protection Agency (HPA) website.

The UK Health Protection Agency continues to urge healthcare workers to remain vigilant to the possibility of SARS even though the level of risk in the UK remains very low.

S R Anderson, W S Lim
SARS Guidelines Committee of the British Thoracic Society, the British Infection Society and the Health Protection Agency
Correspondence to: Dr W S Lim, Respiratory Infection Research Group, Respiratory Medicine, Nottingham City Hospital, Nottingham NG5 1PB, UK; m s l im @ doctors.org.uk

References

Authors’ reply
We thank Dr Lee for his interest in our reports. However, he appears to confuse the terms “treatment failure” and “non-responder”. “Treatment failure”, as defined in the original report for our study, referred to a clinical outcome (a composite end point of hospitalisation, need for excluded mediation, or need for prolonged acute asthma treatment in the emergency setting). In contrast, “non-responder” generally refers to a subset of patients who fail to surpass a defined threshold of response. As we have commented previously using chronic asthma as an example, simplistic “responder/non-responder” analyses often fail to account for clinically important aspects of disease variability and the impact of a treatment intervention. Moreover, in our initial report of intravenous montelukast in acute asthma, a systematic analysis of baseline variables did not identify any factor which predicted response to intravenous montelukast in terms of either forced expiratory volume in 1 second (FEV1) or treatment failures, with the exception of baseline FEV1.

The present report addressed the relationship between FEV1 and cysteinyl leukotriene production as measured by LTE4 excretion. A similar analysis of treatment failures and LTE4 levels is complicated by the fact that, unlike baseline FEV1, which was measured before administration of the study drug, treatment failures tended to be reduced by intravenous montelukast. Nevertheless, 27 of 201 patients (13.1%) in the montelukast group and 12 (18.2%) in the placebo group met one or more of the criteria for treatment failure during the study. Of these, 20 patients had LTE4 data for analyses. Compared with patients who did not meet the criteria for treatment failures and who had LTE4 data available (n = 161), LTE4 levels were numerically higher at baseline in the treatment failure group although this did not reach statistical significance (121.6 pg/mg creatinine (95% CI 91.5 to 161.6) vs 111.6 pg/mg creatinine (95% CI 100.0 to 128.5)). If Dr Lee’s hypothesis is correct, LTE4 levels should have been lower among the treatment failure group. However, data therefore suggest that, rather than serving as a useful predictor of clinical outcome, increased LTE4 levels are more likely to be a marker of worsened acute asthma severity, consistent with our analyses of LTE4 levels and FEV1. Taken together, the data provide a strong biological rationale for the observed benefit of antileukotriene therapy in acute asthma.

S A Green
Respiratory and Allergy, Merck Research Laboratories, 126 East Lincoln Avenue, Rahway, NJ, USA; stuart.green@merck.com

References