

CORRESPONDENCE

Measurement of vitamin D₃ metabolites in smelter workers exposed to lead and cadmium

We note with interest the paper of Chalkley *et al*¹ on the measurement of vitamin D metabolites in smelter workers, where they suggest that exposure to both cadmium (Cd) and lead (Pb) increased the concentration of 1,25 dihydroxyvitamin D. We also reported a significant association between blood Pb concentrations and serum 1,25 dihydroxyvitamin D in Pb workers.² However, our subjects were not occupationally exposed to Cd and in vivo measurements of tibial Pb, as an index of cumulative exposure, were also made. Our data suggested that the increase in 1,25 dihydroxyvitamin D was associated with blood Pb, reflecting recent or current exposure rather than tibial Pb, and that the relation was not significant in those subjects with blood Pb <60 µg/dl. Our study found no effect on serum calcium, phosphate, or parathyroid hormone concentrations.

We think that it is important to highlight the difference between this Pb induced renal effect in adults and the reported opposite finding in children of a decrease of serum 1,25 dihydroxyvitamin D associated with increasing blood Pb.^{3,4} Whatever the cellular or biochemical events that cause such contrary findings between children and adults, it should renew our caution in any sort of extrapolation from dose effect relations or "no observable effect levels" derived from adult, occupational studies to other potentially susceptible groups such as children. It is also feasible that biomarkers of nephrotoxic effect may have different usefulness or applicability in studies of adults and children. The maturing kidney during childhood and lifestyle habits, such as hand-mouth contact, means that children with potential exposure to any nephrotoxin should remain a group of special concern for professionals in environmental medicine or public health.

HOWARD MASON
HSL, Sheffield, UK

DAVID CHETTLE
McMaster University, Ontario, Canada

- 1 Chalkley S, Richmond J, Barltrop D. Measurement of vitamin D₃ metabolites in smelter workers exposed to lead and cadmium. *Occup Environ Med* 1998;55:446-52.
- 2 Mason H, Somerville L, Wright A, *et al*. Effect of occupational lead exposure on serum 1,25 dihydroxyvitamin D levels. *Hum Exp Toxicol* 1990;9:29-34.
- 3 Rosen J, Chesney R, Hamstra A, *et al*. Reduction in 1,25 dihydroxyvitamin D in children with increased lead absorption. *N Engl J Med* 1980;302:1128-31.
- 4 Mahaffey K, Rosen J, Chesney R, *et al*. Association between age, blood lead and serum 1,25 dihydroxycholecalciferol levels in children. *Am J Clin Nutr* 1982;35:1327-31.

Author's reply—I thank Mason and Chettle for their interest in our paper describing the effects of lead (Pb) and cadmium (Cd) on plasma 1α, 25-dihydroxycholecalciferol (1α,25(OH)₂ D₃).¹ We were aware of their excellent paper on the relation between blood

Pb and 1α,25(OH)₂ D₃ concentrations,² but we thought that a direct comparison of our work with theirs was not possible due to the difference in the concentrations of Pb exposure, the fact that they had measured tibial Pb, and also that our subjects were primarily exposed to Cd. Mason and Chettle² raise two separate issues, the first about the correlation between blood Pb and plasma 1α,25(OH)₂ D₃, and the second draws attention to the need for caution when assuming that values derived from adult studies may be applied to children.

About the correlation between blood Pb and plasma 1α,25(OH)₂ D₃, our interest lay in the fact that concurrent exposure to Cd seemed to enhance the positive correlation between blood Pb and plasma 1α,25(OH)₂ D₃ at concentrations below the appearance of lead toxicity, with no threshold effect.

The second point raised was not an intentional part of our study, as we only mentioned the results of other studies on children in our discussion to suggest possible mechanisms for these opposite findings. However, we are in full agreement with this suggestion of caution when extrapolating results obtained from adults to children and also that children may be more susceptible to environmental hazards than adults. We found that blood Pb concentrations were significantly increased in children who did not wash their hands before eating compared with those who did (Chalkley SR, Hardman T, Strehlow CD, *et al*; Report on project to study the impact of lead in gasoline regulations in the UK; 1999, manuscript in preparation). In London schoolchildren with concentrations of mean cell volume (MCV), mean cell haemoglobin (MCH), and serum ferritin below the reference ranges, the blood Pb and erythrocyte protoporphyrin (EPP) concentrations were significantly higher than concentrations found in children whose MCV, MCH, and serum ferritin values were within the reference ranges.³ Monitoring the concentrations of Pb in air in the school playgrounds indicated that these children were all exposed to similar concentrations of Pb in air (Chalkley SR, Hardman T, Strehlow CD, *et al*; Report on project to study the impact of lead in gasoline regulations in the UK; 1999, manuscript in preparation).

SYLVIA CHALKLEY
Department Academic Child Health, Imperial College Medical School, London, UK

- 1 Chalkley SR, Richmond J, Barltrop D. Measurement of vitamin D₃ metabolites in smelter workers exposed to lead and cadmium. *Occup Environ Med* 1998;55:446-52.
- 2 Mason HJ, Somerville LJ, Wright AL, *et al*. Effect of occupational lead exposure on serum 1,25- dihydroxyvitamin D levels. *Hum Exp Toxicol* 1990;9:29-34.
- 3 Chalkley SR, O'Donohoe J, Richmond J, *et al*. Blood lead concentrations and indices of anaemia in London schoolchildren. *Clin Sci* 1998; 95:1-22.

Exposure-response relations of α-amylase sensitisation in British bakeries and flour mills

EDITOR—The publication of this paper by Nieuwenhuijsen *et al*¹ was accompanied by an unusually high level of media interest in the United Kingdom with typical banner headlines that read "exposure to α-amylase is a significant health risk for those employed in

bakeries and flour mills". The authors' press release included a comment that "urgent action is needed to reduce these high levels of fungal amylase and the high sensitisation rates of up to 30%". Although the assay for amylase and the data on exposure response are new, the risk of sensitisation to fungal amylase in bread bakeries has been recognised for some time.² On the basis of research carried out within one of the large food companies in the United Kingdom,^{2,5} the trade organisations representing the milling and baking industries have taken a proactive stance in both proposing exposure standards and producing training material to reduce the risk of sensitisation to fungal amylase. Unfortunately the Anglo-Dutch authors of the paper have not made mention of these facts.

On a slightly more disturbing note, there are two conclusions in the paper which are difficult to justify on the basis of the data presented. The first is the statement that "exposure to α-amylase is a significant health risk". Although there is no dispute about the high prevalence of markers of sensitisation to amylase, in this case a positive skin prick test, or the large numbers with respiratory symptoms, these are essentially independent observations. To show a causal relation between the observations would require detailed history taking (rather than administration of a respiratory questionnaire) to establish the relation between the occurrence of symptoms and working patterns which give rise to high levels of amylase exposure. It is worth noting that there are reasons quite apart from sensitisation which could explain the high level of symptoms. The groups of milling and baking employees with the highest exposures to fungal amylase are also those who may have high total inhalable dust exposures (>10 mg.m⁻³).² It is entirely possible that their symptoms (the health effect) may simply be the result of a non-specific irritant response.

The second conclusion which is difficult to defend is that amylase produces a health risk in flour mills. Unlike the data from the dispensing and mixing category in bread bakeries, which show a consistently high exposure in a group who handle fungal amylase in relatively concentrated form (bread improvers), the conclusion on risk in flour mills is based on limited and inconsistent data. Essentially it relates to a small sample with a high arithmetic mean but widely distributed results in a single category (flour mill) at one of the four milling and packing sites, with lesser support from the hygiene group at the same site and at one other site. The authors do not seem to have an understanding of the milling process and hence how amylase exposure may arise. Firstly, not all mills add fungal amylase to flour. Only those which make flour for bread baking add amylase, and even then, only to some of their products. When fungal amylase is added, it goes into the final stream of product from the mill. Thus potential high exposures are limited to a small group of the workforce who make these additions. Subsequent handlers of the flour, such as packers, will be exposed to a concentration of fungal amylase in the final flour mix of around 0.0001% by weight. There is some evidence to suggest that typical exposures to dust from flour that contains amylase do not present a risk of sensitisation.¹ Incidentally, the findings of Nieuwenhuijsen *et al* of low exposures in the packing and warehousing groups support this viewpoint.

In summary, it seems a pity that a paper which presents new and important data on sensitisation in bakery workers should be spoiled by pressing the interpretation of findings too far.

T A SMITH
Ranks Hovis McDougall

N BENNETT
National Association of British and Irish Millers

M T BITHELL
Federation of Bakers

- 1 Nieuwenhuijsen MJ, Heederik D, Doekes G, *et al.* Exposure-response relations of α -amylase sensitisation in British bakeries and flour mills. *Occup Environ Med* 1999;56:197-201.
- 2 Smith TA, Smith PW. Respiratory symptoms and sensitisation in bread and cake bakers. *Occup Med* 1998;48:321-8.
- 3 Smith T, Lumley KPS. Work-related asthma in a population exposed to grain, flour, and other ingredient dusts. *Occup Med* 1996;46:37-40.
- 4 Smith T, Lumley KPS, Hui EHK. Allergy to flour and fungal amylase in bakery workers. *Occup Med* 1997;47:21-4.
- 5 Smith T, Patton J. Health surveillance in milling, baking, and other food manufacturing operations: five years experience. *Occup Med* 1999 (in press).

EDITOR—You recently reported on this paper by Nieuwenhuijsen *et al.*¹ A great deal of research has been carried out in a range of manufacturing companies in the United Kingdom, particularly in milling and baking. This research highlighted the specific risks of exposure to enzymes such as fungal α -amylase at high concentrations. These high concentrations are present in flour treatment agents (bread improvers) used in bread baking.

As a result bakers have introduced specific controls to minimise the risk of exposure for all our employees, with a recommended exposure of $1\text{mg}/\text{m}^3$ or flour treatment agents. The controls include the use of special dust booths, local exhaust ventilation, personal protective equipment, guidance on reducing dust exposure and training packages for handling dusty ingredients.

The guidance and training packages are developed in conjunction with all the industries that use flour and are supported by the Health and Safety Executive, the plant and craft baking industries and the trade unions representing employees. Details of the training package follow.

The Federation of Bakers represents all the leading bakery companies in the United Kingdom who produce 80% of the nation's bread.

ANNE LINEHAN
The Federation of Bakers, 6 Catherine Street, London WC2B 5JW, UK. Telephone 0044 171 420 7190; fax 0044 171 379 0542.

Breathe easy: training programme

From the Federation of Bakers

The successful management of dust is a vital function in the baking industry—from the traditional craft baker producing and selling his own range of bread and confectionery, to the large wholesale bakery producing up to 10 000 loaves an hour.

This comprehensive training programme explains the potential hazards and the action that management and individual workers should take to make sure their workplace is a safe and healthy environment.

The video section of the programme demonstrates the correct way to handle dusty ingredients and highlights the practical steps

that can be taken to reduce the level of dust in the atmosphere.

Contents

- Trainer's notes
- Training video (running time about 20 minutes)
- Topic cards—eight cards with broad questions for group or individual use
- Multiple choice questions
- *Guidance on dust control and health surveillance in bakeries*—a 16 page booklet compiled by the Health and Safety in Bakeries Liaison Committee
- Important contacts and addresses.

Processes covered in the training programme

- Tipping and sieving ingredients
- Weighing and dispensing ingredients
- Mixing
- Dusting—hand and mechanical
- Choosing and wearing the right personal protective equipment
- Local exhaust ventilation—choosing, maintaining and using correctly
- Hygiene—cleaning, clearing spillages
- Health surveillance.

Price £34.99 plus VAT, postage and packaging

Available from: The Federation of Bakers,
6 Catherine Street, London WC2B 5JW
Tel: 0171 420 7190; Fax: 0171 379 0542

- 1 Nieuwenhuijsen MJ, Heederik D, Doekes G, *et al.* Exposure-response relations of α -amylase sensitisation in British bakeries and flour mills. *Occup Environ Med* 1999;56:197-201.

Authors' reply—Although the statement that “urgent action is needed to reduce these high levels of fungal amylase and the high sensitisation rates of to 30%” was not ours, but that of OEM's press release, we support this conclusion and greatly welcome the initiatives that apparently have already been taken by the bakery industry. We suggest, however, that the organisations take care if they want to use the results of the studies in one of the large food companies to set an exposure standard¹⁻³ given the limited information on exposure including the representativeness, level, duration, and definition of exposure (workers with “regular” exposure), the labour turnover, including how many left and why, bearing in mind the aims of the studies and the basic statistical analyses. The main aims of the other papers seemed to be to categorise any symptoms or sensitisation into diagnostic categories—for example, respiratory irritation or occupational asthma, and to describe their overall (relatively low) prevalence rather than exploring any exposure-response relation as we aimed for in our work.^{4,5} We found that the overall prevalence of sensitisation was relatively low (about 5%) and that only by categorising workers by exposure levels and taking into account movement of workers it became clear that in highly exposed areas a large proportion of the workers became sensitised (about 30%). This is important information for the prevention of sensitisation.

We do not agree with the suggestion by Smith *et al.* that sensitisation is not a relevant end point. In the previous study in The Netherlands sensitisation to α -amylase was strongly associated with reported work related respiratory symptoms, of both upper

and lower airways.⁶ In this study we found no association, but this could, for example, be due to the movement of workers away from exposure or the relatively short duration of exposure. We further know from other studies among workers exposed to typical high molecular weight sensitisers that sensitised workers have more symptoms than non-sensitised workers,⁷ and that the likelihood of the presence of symptoms in sensitised workers is associated with the level of exposure.⁶ Few longitudinal studies are available, but the limited evidence published suggests that sensitised workers develop bronchial hyperresponsiveness and symptoms soon after sensitisation.⁸ It is likely that those who become sensitised to α -amylase are more likely to develop occupational asthma (when exposed) than those not sensitised, and reducing the risk of sensitisation will reduce the risk of occupational asthma. We acknowledge that respiratory symptoms occur in the absence of sensitisation. The concentrations at which these symptoms occur are not well described, but it is unlikely that these symptoms occur below the inhalable dust or allergen concentrations at which sensitisation occurs. For risk assessment purposes it seems therefore reasonable to take sensitisation as a critical end point for the risk evaluation.

For exposure-response modelling as performed in our studies, there is no need to include a cross section of the whole industry as long as the study is not hampered by different forms of bias, well known to most epidemiologists. Whether the risk assessment is appropriate for other exposed populations than the study population is a matter of generalisability and comparability. Other exposure settings, where workers are exposed to the same allergens, but possibly at different concentrations, are usually within the limits of generalisability. A well designed exposure assessment study throughout the United Kingdom baking and milling industry would be welcomed, and would provide information on exposure levels and for risk assessment. We found detectable, and sometimes high, concentrations of α -amylase at half the flour milling sites, site 1 and site 10, among, for example, flour millers, packers, and cleaners (hygiene). As we stated in our paper the great majority of our population was exposed to non-detectable or very low concentrations of α -amylase, and only a small proportion to high concentrations. We think that these high concentrations of α -amylase should be reduced. This would most likely lead to a reduction in sensitisation in α -amylase.

MARK J NIEUWENHUIJSEN
DICK HEEDERIK
GERT DOEKES
KATHERINE M VENABLES
ANTHONY J NEWMAN TAYLOR

Correspondence to: Dr Mark J Nieuwenhuijsen, Th Huxley School of Environment, Earth Sciences, and Engineering, Centre for Environmental Technology, Imperial CU of Science, Technology, and Medicine, 48 Prince's Gardens, London SW7 2PE, UK.

- 1 Smith TA, Smith PW. Respiratory symptoms and sensitisation in bread and cake bakers. *Occup Med* 1998;48:321-8.
- 2 Smith T, Lumley KPS. Work-related asthma in a population exposed to grain, flour and other ingredient dust. *Occup Med* 1996;46:37-40.
- 3 Smith T, Lumley KPS, Hui EHK. Allergy to flour and fungal amylase in bakery workers. *Occup Med* 1997;47:21-4.