

LETTERS TO THE EDITOR

Effect of aminophylline on brain tissue oxygenation in patients with chronic obstructive lung disease

Nishimura and colleagues (December 1992; 47:1025-9) introduce their study of blood gas changes immediately following intravenous theophylline and ethylenediamine by citing two unreliable and misleading references^{1,2} to the upsetting effect of theophylline on children's behaviour. They are only loosely related because ethylenediamine is not inert and these papers concern long term oral theophylline alone.

The first study which claimed that "teachers could easily discriminate between children on theophylline and on placebo" used 53 questions irredeemably skewed by restricting the answers to "average," "somewhat more," or "much more." Two questions, "gets into fights?" and "gets angry easily?" reached 5% significance. The rest—the same questionnaire to parents and four psychomotor tests—found nothing. These questions missed 13 of the 20 on treatment so the teachers' scores were actually twice as often wrong as right. The claim is therefore positively misleading. Even more so is the implication that teachers by themselves could tell which children were on theophylline. Not cited by the present authors is a more careful similar study³ with negative findings.

In the second study,² school behaviour problems "spontaneously raised" by earlier parents were not confirmed by comparing behaviour checklists and five psychomotor tests with controls. The authors noted the same degree of worsening in the control group in the remaining test as of improvement in the group changed to cromoglycate. They gave no data to support their further claim of "improvement on all concentration measures" in that group.

Choosing these two references indirectly and correctly implies that there is no evidence of impairment in adults. It is not mentioned in the many acute studies carried out over decades with aminophylline, and was not found by those who used appropriate tests. It would have been good to have simultaneous cognitive or psychomotor data from Nishimura's study since its uniquely valuable features cannot easily be repeated.

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- 1 Rachelefsky GS, Wo J, Adelson J, Mickey MR, Spector SL, Katz RM, et al. Behavior abnormalities and poor school performance due to oral theophylline use. *Pediatrics* 1986;78:1133-8.
- 2 Furakawa CT, DuHamel TR, Weimer L, Shapiro GG, Pierson WE, Bierman CW. Cognitive and behavioural findings in children taking theophylline. *J Allergy Clin Immunol* 1988;81:83-8.
- 3 Rappaport L, Coffman H, Guare R, Fenton T, DeGraw C, Twarog F. Effects of theophylline on behaviour and learning in children with asthma. *Am J Dis Child* 1989; 143:368-72.

AUTHORS' REPLY We appreciate Dr Addis' interest and comments on our paper. He seems to claim that we have introduced our study with two unreliable and misleading

references warning of possible adverse effects of long term oral theophylline on cognition and school performance in children. His concern mostly concentrates on the interpretations of the validity and clinical importance of the results of these early studies which have, indeed, generated considerable controversy on this issue.^{1,2} We feel it fair, however, to cite these two reports in the introduction of our paper, since our study was certainly encouraged by their findings. We would not have attempted to carry out the study without these reports. Our paper makes no attempt to judge the validity of these reports. However, we would like to stress the following points again in order not to leave readers with a wrong message from our study. We are not certain whether changes in blood gas tensions 15 minutes after intravenous infusion of aminophylline are sustained or not, and whether the lowering effect of aminophylline on jugular venous PO_2 has any relevance to the controversy mentioned above.

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- 1 Creer TL, McLoughlin JA. Editorial: The effect of theophylline on cognitive and behavioral performance. *J Allergy Clin Immunol* 1989;83:1027-9.
- 2 Lindgren S, Lokshin B, Stromquist A, Weinberger M, Nassif E, McCubbin M, et al. Does asthma or treatment with theophylline limit children's academic performance? *N Engl J Med* 1992;327:926-30.

Concentrations of the domestic house dust mite allergen *Der p I* after treatment with solidified benzyl benzoate (Acarosan) or liquid nitrogen

We are not entirely surprised by the failure of liquid nitrogen treatment to reduce house dust mite antigen levels within treated homes as reported in the study by Dr S Kalra and colleagues (January 1993;48:10-13). We conducted a double blind placebo controlled trial of liquid nitrogen in the homes of 30 asthmatic children with dust mite allergy confirmed both on skin testing and by specific IgE determination. The 15 homes in the active arm of the trial were treated with liquid nitrogen with a protocol similar to that of Kalra and colleagues—that is, the child's bedroom and the sitting room were treated—but we did not treat other areas of the house. After treatment a high pressure vacuum cleaner was used in an attempt to remove dead mites and their excreta. Dummy treatment consisted of treating a small area of bedroom carpet near the door (so that "smoke" could be seen emerging from under the door), followed by high pressure vacuum cleaning.

There was no effect on the quantity of *Der p I* antigen trapped in petri dishes exposed in the bedroom before and at intervals after the treatment and, not unexpectedly, there was no effect on asthma symptom scores, peak expiratory flows, bronchial reactivity to methacholine, or levels of specific IgE.

Despite this disappointing result, we have received numerous reports from individual patients of the success of this treatment which is available commercially in Aberdeen. Based on this anecdotal evidence, we have the impression (which we now propose to investigate in a further trial) that certain technical factors might be

important in determining the success of the treatment. Firstly, despite the expense involved, all soft furnishings must be soaked thoroughly—in particular the mattress must be treated until it looks completely wet. Secondly, if the treatment is followed by vacuum cleaning, this should be vented to the outside air in such a way that the dust cannot be blown back into the house. Thirdly, repeated treatments appear to give additional benefit by ensuring that mites do not recolonise the rooms before allergenic traces of their previous occupation have gone, a process which takes several months. Finally, few children react to only a single allergen, and it is important to focus this relatively expensive treatment on individuals whose spectrum of allergy is limited either to house dust mite alone, or to house dust mite plus seasonal or other allergens to which they will not be exposed continually.

Although on the basis of our trial work we cannot recommend the use of liquid nitrogen in the management of children with allergy to the house dust mite, we believe that investigation of this treatment should be continued. It has already given encouraging results in the homes of adults in whom it resulted in a significant reduction in bronchial hyperreactivity.¹

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- 1 Colloff MJ. Use of liquid nitrogen in the control of house dust mite populations. *Clin Allergy* 1986;16:41-7.

AUTHORS' REPLY It is encouraging that Drs Ninan and colleagues have obtained similar results to our own with liquid nitrogen treatment in their large study. Whilst research must continue, we are not enthusiastic about the principles of acaricidal treatment.

If a new drug for asthma were introduced into clinical practice, it would have to be proven to be efficacious and safe in long term use. Acaricides have become widely available and heavily marketed in spite of satisfying neither of these criteria. Nevertheless, they are still being bought by our patients. We question whether this is the correct approach. House dust mites are a domestic infestation directly analogous to mosquitoes in tropical countries. Malaria control incorporates barriers—that is, mosquito nets—and changing the natural habitat—that is, draining the swamp. Insecticides are only transiently effective.

Ultimately we are going to have to address the question of how we are going to change our domestic environment to make it less conducive to mite infestation. This involves controlling ventilation and humidity in addition to barrier methods.

Finally we are concerned about negative publication bias. We are aware of a large multicentre controlled study on acaricides and asthma which gave negative results when published in abstract form which has not yet been published as a full paper.

We do not believe that acaricides have a significant effect in reducing mite allergen exposure when used as currently recommended by the manufacturers.

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