

Correspondence

Alcohol-induced bronchial asthma

To the Editor:

Shimoda et al. (J Allergy Clin Immunol 1996;97:74-84) are mistaken in stating that exacerbations of asthma do not occur in Caucasian populations.

We conducted a survey of patients with asthma attending a hospital, which indicated that 25% reported exacerbation of asthma by at least one form of alcoholic drink.¹ The major cause was red wine, followed by whisky. One subject reacted to all forms of alcohol, and I have seen two more subjects since who not only demonstrate wheezing and decreases in lung function after drinking ethanol in distilled water, but also have marked facial flushing and headache. None of these patients were of Chinese or Japanese origin. In most cases it is reasonable to assume that congeners within a drink are the cause of airway narrowing, but in some cases ethanol is the causal agent.

We have also found that this bronchoconstrictor response can be enhanced by the oral hypoglycemic agent, chlorpropamide.²

Alcohol given orally as a single bolus can also cause an immediate bronchoconstriction,³ which is usually followed by bronchodilation once the alcohol is absorbed. The immediate ("Schnapps") effect is presumably mediated by stimulation of pharyngeal or upper airway receptors, a different mechanism than that described by Shimoda et al., which would fit with the difference in time scale of the bronchoconstrictor effect in each case. The bronchodilator response has been confirmed with intravenous ethanol, showing a dose-response effect,⁴ of which the mechanism is unclear but is likely to relate to a direct effect on bronchial smooth muscle.

It is likely that the congeners in alcoholic beverages are usually the cause of the bronchoconstriction in Caucasian patients with asthma. Acetaldehyde is recognized as a common component of certain alcoholic drinks, which may thus be acting through a mechanism similar to that described by Shimoda et al., but through a pharmacologic rather than a metabolic pathway.

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1/8/76099

Alcohol-induced asthma: Not only in Asians

To the Editor:

I read with great interest the recent article by Shimoda et al. (J Allergy Clin Immunol 1996;97:74-84), describing the mechanism of alcohol-induced asthma.

The authors suggest that this phenomenon is restricted to

Asians and is not observed in Caucasians. Actually, we observed a case of well-documented alcohol-induced asthma in a Caucasian woman. The patient was a 39-year-old Swiss nurse with complaints of repetitive asthma, facial flushing, itching, and rhinorrhea after ingestion of alcoholic beverages and exposure to ethanol vapors (open containers in a surgical ward). Provocation tests with ingestion of 30% ethanol and exposure to ethanol vapors reproduced the symptoms and induced a drop in FEV₁. Partial protection was afforded by cromoglycate and ketotifen. The case was published in 1982 in the *Schweizerische Medizinische Wochenschrift*.¹

At the time of our observation, only one other case had been published in another Caucasian patient.²

This observation leaves open the possibility that some rare Caucasian patients share a common defect with Asian patients, leading to degranulation of mast cells under the influence of ethanol. The occurrence of respiratory and cutaneous symptoms under the influence of ethanol vapors suggests that another mechanism may be the cause, because a significant elevation of blood acetaldehyde level can hardly be expected to result from casual inhalation of minute amounts of ethanol vapors.

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Cetirizine overdose in a young child

To the Editor:

The effect of cetirizine overdose in small children has not previously been reported. Drowsiness is a known symptom of antihistamine overdose in adults and in older children in whom agitation can also occur.¹ We describe an accidental ingestion of over 50 times the prescribed dose in an 18-month-old boy.

The boy had eczema at the age of 6 months, which was treated conventionally. At 15 months he was entered into a trial and began receiving cetirizine drops, 3.5 mg (0.25 mg/kg) twice daily. At the age of 18 months, he drank approximately 18 ml of cetirizine solution, corresponding to a dose of 180 mg of cetirizine. He was admitted to the children's ward and given ipecac syrup, which induced vomiting at 75 minutes after ingestion of cetirizine. After administration of the ipecac, he became slightly agitated, excitedly running around the ward in a lively manner. This lasted approximately 2 hours. It is not clear whether this was due to ipecac, cetirizine, or the change in environment. All other vital and neurologic signs remained stable overnight, including pulse rate, blood pressure, respiration, and body temperature. Cardiac monitoring overnight showed a sinus rhythm with no episodes of arrhythmia or ectopic beats. A twelve-lead electrocardiogram, performed 15

hours after the overdose, showed no abnormalities. Concentrations of cetirizine in the blood and urine samples, collected 14 hours after the overdose, confirmed an intake of approximately 180 mg of cetirizine (2.4 µg/ml and 129.0 µg/ml, respectively). After a washout period of 3 days, the patient resumed taking his trial medication as prescribed and has exhibited no further clinical signs or symptoms relating to the overdose.

In this report the toddler tolerated the overdose with virtually no complications. Obviously, a single case is no proof for definite harmlessness of a major overdose. It should be noted that the commercially available form of cetirizine drops has a child-proof stopper, which would have prevented the incident described.

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Topical triclosan treatment of atopic dermatitis

To the Editor:

Kolmer et al. (J Allergy Clin Immunol 1996;98:702-7) recently reported the efficacy of itraconazole in the treatment of severe intractable atopic dermatitis. Any nontoxic treatment advance is to be applauded. We have been impressed with the daily use of a topical antiseptic wash containing 1% wt/vol triclosan (Irgasan DP 300, a synthetic diphenyl ether, 5-chloro-2-[2,4-dichlorophenoxy] phenol) in the treatment of infants and children with moderate to severe eczema. It is available, here in Australia, combined with a moisturizer and emollient as Microshield T (Johnson & Johnson Medical Pty. Ltd.). Triclosan has been shown to be an effective antimicrobial, useful in the eradication of methicillin-resistant *Staphylococcus aureus*,¹ an effective antifungal agent,² and to have antiinflammatory actions. It has been reported to markedly reduce the wheal produced by intradermal histamine,³ to reduce the effects of topical applications of nickel in sensitized individuals, to reduce the effects of topical applications of sodium lauryl sulfate, and to inhibit the cyclooxygenase and lipoxygenase pathways of arachidonic acid production and prostaglandin E₂ production in vitro. It has a low toxicity and a very low incidence of contact sensitization, and it is tolerated on weeping eczema. It is even being studied as an oral rinse for the treatment of gingivitis.

Topical triclosan appears to be worth considering in the treatment of atopic dermatitis because bacterial infections have a significant role in provoking cutaneous inflammation. In addition, triclosan's antiinflammatory and antifungal action may provide additional benefits.

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Flovent (fluticasone propionate inhalation aerosol)

To the Editor:

Flovent (fluticasone propionate [FP]) inhalation aerosol is currently marketed in the United States by Glaxo Wellcome. The pivotal clinical trials of FP that were presented to the Food and Drug Administration (FDA) were performed with a 10% wt/wt lecithin suspension; after the trials were undertaken, the concentration of lecithin was reformulated to 1% wt/wt to assure dose-to-dose consistency.¹ The original 10% formulation was 20% bioavailable,¹ whereas the reformulated 1% suspension, which is being marketed worldwide, is 30% bioavailable (Flovent package insert).

On my inquiry to Glaxo Wellcome's Medical Services Department, on August 8, 1996, a pharmacist/drug information scientist sent information regarding the reformulation of FP (Correspondence, Glaxo Wellcome Medical Services Department; August 26, 1996). The report stated, "The ratio of mean AUC₂₄ between the 1% formulation and the 10% formulation was 1.19 (90% CI: 1.05-1.35; p=0.024), the ratio of AUC_{last} was 1.25 (90% CI: 1.06-1.48; p=0.034) and the ratio of mean C_{max} was 1.30 (90% CI: 1.15-1.58; p=0.002). Since the 90% confidence intervals were outside the FDA accepted criteria of 0.80-1.25 for oral dose forms, a formal bioequivalence statement could not be made."

Further clarification of the reformulation was requested, and on August 26, 1996, a revised information sheet was sent, and one of the revisions was the deletion of the statement, "Since the 90% confidence intervals were outside the FDA accepted criteria of 0.80-1.25 for oral dose forms, a formal bioequivalence statement could not be made." (Correspondence, Glaxo Wellcome Medical Services Department; August 26, 1996)

In the Proceedings of the Pulmonary-Allergy Drugs Advisory Committee meeting of September 25, 1995, at which time FP was under review, on page 151 an FDA reviewer states, "In terms of safety, we also have some concern that the pharmacokinetic endpoints showed that the 1% was more bioavailable. So if we believe that, it means that systemic side effects may be a more serious concern with the 1% than the 10%. So on safety, we think the clinical studies and the PK studies do not conclusively show that the two are equivalent."¹

We as physicians must be given access to this type of information so that we can make informed choices for our patients. The pharmaceutical industry has the responsibility to provide a balanced database of information regarding their products.

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