Comment

The rapid ascent to 4560 m caused minor symptoms of acute mountain sickness such as headache, nausea, and insomnia in all participants. We did not, however, find any influence of this short term exposure to high altitude on the morphology of the red cells. Our results are in contrast to the morphological changes observed by Rowles and Williams at a similar altitude (4600 m) during an expedition with ascents to 6200 m and 7200 m between blood samplings.[2] We cannot exclude the possibility that the ascents to the higher altitudes had an influence on the morphology. More probably, however, those morphological changes, which developed gradually over five weeks, reflected adaptive changes to high altitude, such as the increased erythropoiesis regularly observed at high altitude, rather than a short term effect. Our results indicate that changes in red cell morphology can be ruled out as a pathophysiological factor in acute mountain sickness.

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1 Heath D, Williams DR. *Man at high altitude. The pathophysiology of acclimatization and adaptation.* 2nd ed. Edinburgh: Churchill Livingstone, 1981:136-50.
2 Rowles PM, Williams ES. Abnormal red cell morphology in venous blood of men climbing at high altitude. *Br Med J* 1983;**286**:1396.
3 Meiselman HJ. Rheology of shape-transformed human red cells. *Biorheology* 1978;**15**:225-37.
4 Bessis M. Red cell shapes: an illustrated classification and its rationale. In: Bessis M, Weed RI, Leblond PF, eds. *Red cell shape.* New York: Springer Verlag, 1973:1-25.

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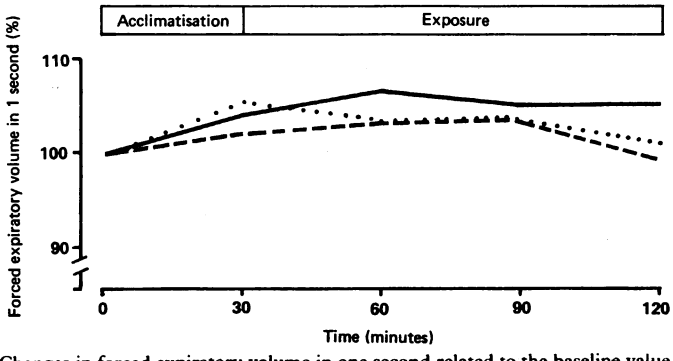
Low concentrations of formaldehyde in bronchial asthma: a study of exposure under controlled conditions

We have studied the effect on the lower airways of formaldehyde at concentrations similar to those found in the indoor environment. Participants in the study had severe bronchial hyper-responsiveness, thus representing the extreme in respiratory sensitivity to inhaled irritants.

Patients, methods, and results

Fifteen non-smoking volunteers (mean age 25·1 years) who had substantial bronchial hyper-reactivity were studied. The mean provocation concentration of histamine producing a 20% decrease (PC_{20}) in peak expiratory flow rate was 0·37 g/l (SD 0·36). All except one patient regularly required bronchodilator treatment. None used methylxanthines or corticosteroids.

Patients were exposed to formaldehyde once a week for three consecutive weeks. The experiments were carried out in a double blind randomised fashion under controlled conditions in a climate chamber with particle free air. All participants underwent the same three experiments, with mean formaldehyde concentrations of 0·85 mg/m³ (SD 0·07), 0·12 mg/m³ (SD 0·07), and zero. The mean exposure time at a steady state concentration was 89·4 minutes (SD 9·5). Bronchodilator drugs were withheld for four hours before the experiments. During the exposure each participant rated his symptoms of asthma every 15 minutes on a visual analogue scale, and forced expiratory volume in one second was measured on a spirometer every 30 minutes.



Changes in forced expiratory volume in one second related to the baseline value (100%) during exposure of 15 asthmatic patients to formaldehyde. Concentrations of formaldehyde: solid line 0·85 mg/m³; dashed line 0·12 mg/m³; dotted line 0 mg/m³.

Before and after exposure to formaldehyde functional residual capacity and airways resistance were determined in a body plethysmograph, and flow-volume curves were measured. Immediately after exposure a histamine challenge test was performed.

No significant changes in forced expiratory volume in one second, airways resistance, functional residual capacity flow-volume curves, or subjective ratings of symptoms of asthma were found in the group as a whole or among the nine participants with high histamine reactivity (PC_{20}<0·50 mg/ml) (figure). Histamine challenge tests were highly reproducible and were unaffected by exposure to formaldehyde.

After exposure the participants measured peak expiratory flow rate every two hours for the rest of the day and once again the next morning. These recordings showed a considerably lower value in the morning than in the evening, but this was not related to the formaldehyde exposure. No appreciable symptoms were reported after exposure.

Comment

Formaldehyde is known to irritate the upper respiratory tract and mucous membrane, but its effect on the lower respiratory tract is uncertain. Exposure of normal subjects in a climate chamber showed no changes in lung function after five hours in an atmosphere containing 2·0 mg/m³ formaldehyde.[1]

Several epidemiological surveys have shown adverse effects on the lower airways after chronic exposure to formaldehyde at concentrations below 0·8 mg/m³. Reports of occupational asthma claimed to be due to hypersensitivity to formaldehyde refer to reactions at concentrations below 0·5 mg/m³.[2]

Using sensitive methods for measuring dynamic changes in bronchomotor tone we found no evidence of bronchoconstrictive reactions and no changes in bronchial reactivity during exposure to formaldehyde at concentrations well above standards recommended for the indoor environment. Our length of exposure exceeded the time necessary to produce the maximum adverse effect of other irritating agents such as sulphur dioxide.[3]

The lack of response of the lower respiratory system to low concentrations of formaldehyde could be explained by complete clearance of formaldehyde in the upper airways. Theories of adverse effects on the lower airways, due to a reflex mechanism elicited in the upper airways,[4] are contradicted by the negative findings in our group of hyper-reactive patients.

An important difference between epidemiological surveys and the present study seems to be that our experiments were carried out with formaldehyde vapour in clean air, whereas the epidemiological studies dealt with conditions where other potential irritants and particles were present in the air.

In conclusion, our results suggest that concentrations of formaldehyde found in the indoor environment are of minor importance in the development of pulmonary symptoms.

1 Andersen I. Formaldehyde in the indoor environment—health implications and the setting of standards. In: Fanger PO, Valbjorn O, eds. *Indoor Climate.* Copenhagen: Danish Building Research Institute, 1979: 77-87.
2 Burge PS, Harries MG, Lam WK, O'Brien IM, Patchett PA. Occupational asthma due to formaldehyde. *Thorax* 1985;**40**:255-60.
3 Koenig JQ, Pierson WE, Frank R. Acute effects of inhaled SO_2 plus NaCl droplet aerosol on pulmonary function in asthmatic adolescents. *Environ Res* 1980;**22**:145.
4 Alexandersson R, Hedenstierna G, Kolmodin-Hedman B. Exposure to formaldehyde: effect on pulmonary function. *Arch Environ Health* 1982;**37**:279-84.

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