The City of Birmingham Environmental Department analysed the paint and concluded that the solvent consisted of mixed isomers of amyl acetate, and did not contain any trace of benzene, toluene, xylene, or other substances known to be toxic. Its composition was similar to commercially available and widely used car paints. Although amyl acetate is not considered particularly toxic, its use is advised only in well-ventilated areas.

We can find no similar cases either in medical journals or after discussion with the medical officer at a local motorcar factory where such paint is in use. In the absence of any evidence to the contrary we are led to think that the paint caused this man's illness, and that the lack of any ventilation was important.

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Theophylline poisoning in adults

With the widespread availability of theophylline preparations and their extensive use for pulmonary conditions clinicians should be aware of the possible complications and risk of death from theophylline overdose. We report nine cases of theophylline poisoning in adults with special reference to plasma drug concentrations, features of poisoning, and outcome.

Patients, methods, and results

During January to July 1979 we followed up nine patients aged 15-72 years who had been referred to the National Poisons Information Service (Guy's Hospital, London) with theophylline poisoning. Information noted at the time of referral included age, sex, amount of drug thought to have been ingested, and any initial clinical manifestations of toxicity. Also a blood sample was taken for determination of plasma theophylline concentration. Further data regarding symptoms, management, and subsequent outcome were obtained from case summaries and, usually, by consultation with the clinicians concerned. Eight cases were of deliberate self-poisoning with oral preparations, and the ninth resulted from intravenous administration of theophylline. Four patients had a history of chronic obstructive pulmonary disease. Plasma theophylline concentrations were determined in eight patients by either a liquid chromatographic method (D Berry, unpublished data) or an enzyme immunoassay technique (Syva Co Ltd, Palo Alto, USA), the two methods giving comparable results.

There was a fivefold variation in plasma theophylline concentrations (table), which in general correlated poorly with the stated ingested dose. Signs of severe toxicity, such as hypotension and cardiac arrhythmias, were common in patients aged over 50, whereas three of the younger patients

(cases 2, 6, and 9) with high plasma theophylline concentrations (69 mg/l, 50.2 mg/l, and 64.2 mg/l respectively) had only minimal symptoms. Convulsions occurred in three patients, and, although they were successfully controlled by intravenous diazepam, they were associated with a uniformly fatal prognosis, the patients subsequently dying from cardiovascular complications of theophylline poisoning. In two cases (7 and 8) convulsions were the first sign of serious toxicity. Tachycardia (heart rate above 100 beats/min) was noted in all cases, and hypotension (systolic blood pressure 90 mm Hg or less) occurred in four. Hypokalaemia (serum potassium concentration below 3.0 mmol (mEq)/l) was recorded in three patients who developed ventricular arrhythmias. All three deaths were associated with plasma theophylline concentrations exceeding 65 mg/l, convulsions, hypotension, and finally cardiorespiratory arrest.

Comment

Tachycardia, nausea, and vomiting are poor indicators of the severity of theophylline poisoning and do not always precede more serious symptoms.¹ Seizures may be the first indication of poisoning, as occurred in our cases 7 and 8. Zwillich *et al*² noted a mortality of 50% in patients with theophylline-induced seizures, and this poor prognostic factor was confirmed in our series.

Hypotension and cardiac arrhythmias should alert the clinician to the severity of poisoning, and hypokalaemia should be sought and corrected. Age appears to be a further consideration. Jacobs *et al*³ found that toxicity was more common in patients over 50, and our results suggest that the manifestations of theophylline poisoning are also more severe in this age group. Increased susceptibility to the toxic effects of theophylline is also associated with chronic obstructive pulmonary disease and may have been relevant in four patients in our series. Until recently withdrawal of the drug and supportive treatment were regarded as the mainstay of the treatment for theophylline poisoning. Reports of successful management with resin haemoperfusion⁴ or charcoal haemoperfusion,⁵ however, suggest that this technique may be valuable for severely intoxicated patients and should be considered in those with signs of severe poisoning and high plasma theophylline concentrations before terminal events supervene.

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¹ Hendeles, L, and Weinberger, M, *New England Journal of Medicine*, 1979, **300**, 1217.

² Zwillich, C W, *et al*, *Annals of Internal Medicine*, 1975, **82**, 784.

³ Jacobs, M H, Senior, R M, and Kessler, G, *Journal of the American Medical Association*, 1976, **235**, 1983.

⁴ Lawyer, C, *et al*, *Annals of Internal Medicine*, 1978, **88**, 516.

⁵ Ehlers, S M, Zaskie, D E, and Sawchuk, R J, *Journal of the American Medical Association*, 1978, **240**, 474.

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Toxicity and outcome in nine cases of theophylline poisoning

Case No	Age (years)	Sex	Amount of theophylline ingested (g)	Maximum heart rate (beats/min)	Arrhythmias	Clinical features	Plasma theophylline concentration (mg/l)	Outcome
1*	57	M	6.25	150	Ventricular ectopic beats	Impaired consciousness, vomiting, hyperreflexia, hypotension	24.5†	Survived
2	15	M	4.5 (SR)	118		Abdominal pain, headache, vomiting	69.0	Survived
3*	49	F	2.4	136		Impaired consciousness, vomiting	Not done	Survived
4*	68	M	11.2 (SR)	220	Supraventricular tachycardia, asystole	Impaired consciousness, hyperventilation, vomiting, hypotension, convulsions	120.0	Died
5	50	F	Unknown	190	Ventricular ectopic beats	Impaired consciousness, hyperreflexia, hypotension, vomiting	60.0	Survived
6	22	M	11.2 (SR)	130		Hyperventilation	50.2	Survived
7	20	F	10.5 (SR)	190	Ventricular fibrillation	Impaired consciousness, hyperventilation, hypotension, convulsions	85.0‡	Died
8*	72	F	11.5 intravenously over 36 h	150	Asystole, idioventricular rhythm	Convulsions, hypotension	66.0	Died
9	18	F	3.5 (SR)	150		Agitation, vomiting, hyperventilation, hyperreflexia	64.2	Survived

SR = Sustained-release preparation.

*Patient with underlying chronic obstructive pulmonary disease.

†Salbutamol ingested.

‡Glutethimide ingested (plasma concentration 4 mg/l).