greater blood concentrations of propellents were achieved by dosing conscious dogs progressively with aerosol preparations with a maximum of four puffs per kilo, or about 40 puffs in all. Two dosing schedules were used. In the first, the preparations were given in bursts of 5 or 8 puffs; the dogs were allowed a few breaths of air between bursts. In the second, progressive asphyxiation was achieved by giving one puff of aerosol with each inspiration without allowing access to air. The preparations used and the results obtained are shown in the Table.

TABLE.—*Acute Toxicities of Aerosol Preparations in Beagle Dogs with and without Access to Air*

Preparation	Dosage		Convulsion Score (Max = 6)	Deaths
Propellants 11 and 12 mixture 60 µlitres/puff	40 puffs	Continuous Administration	5	0
		Intermittent Administration	0	0
Propellants & salbutamol 100 µg/puff	40 puffs	Continuous Administration	6	0
		Intermittent Administration	0	0
Propellants & isoprenaline 100 µg/puff	40 puffs	Continuous Administration	6	2*
		Intermittent Administration	0	0

*Another dog revived with difficulty

All preparations were well tolerated when the dogs were allowed even modest access to air. Excessive dosing with the propellants alone in the asphyxiated animals caused struggling, tremor, loss of consciousness, and convulsions. The animals recovered quickly when allowed to breathe air. Exactly the same results were obtained with the salbutamol inhaler, but with the isoprenaline inhaler two out of six animals died.

Although excessive use of any effective aerosol bronchodilator may conceal seriously worsening asthma these results suggest that overdosage with inhalers containing isoprenaline may present a special danger to hypoxic individuals. A likely reason for this is that isoprenaline, unlike salbutamol, is fairly rapidly absorbed from the respiratory tract; a specific absorption mechanism like the uptake-2 mechanism for catecholamines may be involved. Once the isoprenaline is in the general circulation, its cardiovascular effects are particularly dangerous in hypoxia because its chronotropic and inotropic effects increase the oxygen requirement of heart muscle, and its hypotensive effect may decrease the coronary perfusion pressure and, therefore, the oxygen supply to the heart. Cardiac arrest is known to occur in dogs under these conditions.[5]

Like Dollery *et al.*[6] we have found that the blood levels of Freons 11 and 12 in human beings after large doses of aerosols are small compared with those achieved in the dog experiments. For example only about 1 µg/ml of Freon 11 is found after 10 to 30 puffs of the inhaler. It is extremely unlikely, therefore, that the propellants have played a significant part in unexpected deaths from asthma in the human beings. Deaths following "sniffing" of organic solvents may be another matter because these individauls inhale relatively large amounts of organic material without air. Asthma patients must inhale air with the propellants because of the design of the inhalers.

Preliminary results of these experiments were sent to the Committee on Safety of Drugs in December 1970 and a detailed report in April 1971. A full account of the work will be published elsewhere.—I am, etc.,

DAVID JACK
Research Director,
Allen and Hanburys Ltd.
Ware, Herts

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Problems with Ketamine Anaesthesia

SIR,—The advent of the phencyclidine congener 2 (0-chlorophenyl)-2 methylamino cyclohexanone HCl (Parke Davis CI-581, Ketamine) means that a totally intramuscular technique of anaesthesia is available for infants or others with difficult veins. The following case report is illustrative.

A healthy 10 kg female was admitted with an extensive laceration of the lower lip. Atropine 0·3 mg intramuscularly was given and 30 minutes later one was faced with the problem of inducing anaesthesia in a struggling chubby child with no visible veins. Ketamine hydrochloride was selected for the induction and maintenance of anaesthesia for the following three reasons:

(1) It may be given intramuscularly.

(2) There is a very low vomiting hazard, and even if it occurs the protective pharyngeal reflexes are preserved.

(3) The lacerations around the patient's mouth contraindicated a mask induction.

Ketamine hydrochloride 150 mg was given into the vastus lateralis muscle. This is the dosage recommended by Phillips *et al.*[1] A quiet, trouble free induction followed, but during subsequent wound toilet an unsuspected tongue laceration started to bleed. Blood from this ran back into the pharynx and caused severe continuous coughing illustrating the preservation of the protective reflexes. While the child was in no danger it was impossible to continue due to the upset, so it was decided to paralyse and intubate, thus securing the airway and providing the surgeon with a still patient. This was accomplished with a total of two doses of 50 mg succinyl choline given intramuscularly with a ten minute interval. The patient was ventilated throughout with pure oxygen delivered from an Ayre's T-piece with Jackson-Rees attachment. As the operation was completed, spontaneous respiration returned and the patient extubated.

Induction of anaesthesia with intramuscular ketamine is so easy that the inexperienced anaesthetist may be encouraged to use it. The case further demonstrates that although induction was simple, the provision of a still patient required paralysis and intubation. The ability to perform these last two functions is in our view mandatory in those using this useful drug.—We are, etc.,

T. R. AUSTIN
D. R. BEVAN
Military Hospital,
Tidworth, Hants

1 Phillips, L. A., Seruvatu, S. G., Rika, P. N., and Tirikula, U., *Anaesthesia*, 1970, **25**, 36.

Hiccup

SIR,—With reference to your leading article "Hiccup" (1 May, p. 234), in a first-aid attempt to cure hiccup the patient was given two liqueur-glasses of kummel as a carminative with immediate success. This was in 1922, and I have never known the treatment to fail. The appropriate reference to its extreme usefulness in hiccup appeared under "Notes and Comments" (see *B.M.J.*, 13 March 1948, p. 532).—I am, etc.,

W. K. MORRISON
Edinburgh

Intractable Hiccuping in Acute Myocardial Infarction

SIR,—The report of Dr. H. Ikram and others (29 May, p. 504) prompts me to suggest that metoclopramide (Maxolon) 10 mg intravenously is worthy of trial in such an emergency. Although the drug is established as an antiemetic and antinauseant its power to suppress hiccup is less known. If an intravenous dose is effective treatment may be continued by mouth in 10 mg doses t.i.d. The original reports from Paris emphasized its value in this complaint, a fact which has been overlooked because persistent hiccup is rare.—I am, etc.,

A. H. DOUTHWAITE
London W.1

Prolonged Anosmia

SIR,—A male chemical process worker, aged 24, inhaled fumes of phosphorous oxychloride in June 1970. He complained of the usual symptoms but in addition a loss of taste and smell. His pulmonary function was unaffected and he has remained well except that some 11 months later he still complains of anosmia.

I wonder if any other readers have encountered this symptom?—I am, etc.,

IVAN MACINTYRE
Industrial Medical Officer,
Industrial Chemicals Division,
CIBA-GEIGY (U.K.) Ltd.
Manchester