greater blood concentrations of propellants 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>
<thead>
<tr>
<th>Preparation</th>
<th>Dosage</th>
<th>Convulsion Score (Max = 6)</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propellants 11 and 12</td>
<td>40 puffs</td>
<td>Continuous Administration: 5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interimtary Administration: 0</td>
<td>0</td>
</tr>
<tr>
<td>Propellants</td>
<td>40 puffs</td>
<td>Continuous Administration: 6</td>
<td>0</td>
</tr>
<tr>
<td>&amp; salbutamol 100 µg/puff</td>
<td></td>
<td>Interimtary Administration: 0</td>
<td>0</td>
</tr>
<tr>
<td>Propellants &amp; isoprenaline 100 µg/puff</td>
<td>40 puffs</td>
<td>Continuous Administration: 6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interimtary Administration: 0</td>
<td>0</td>
</tr>
</tbody>
</table>

*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 conceivably worsen asthma these results suggest that overdose with inhalers containing isoprenaline may present a special danger to hypoxic individuals. A likely reason for this is that isoprenaline, unlike salbutamol, is 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.4

Like Dollery et al.,4 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 to 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 individuals 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 Hanbursys Ltd.

Problems with Ketamine Anaesthesia

Str.—The advent of the phencyclidine conger: 2 (0-chlorophenyl)-2-methylamino cyclohexanone HCl (Parke Davis Cl7581, 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 severely agitated 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.

Proven Anosmia

Str.—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, G.E.R—GERDY (U.K.) Ltd.

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