1, first mild symptom of upper respiratory infection; 2, moderate symptoms; 3, fever; 4, patients confined to the infirmary. Because the nurses and physicians had no way of positively diagnosing a true upper respiratory infection from an allergic response, psychosomatic upset, etc., they recorded all symptoms. We consider a true upper respiratory infection as one which persists for five or more days.

Table 1 gives the number of patients who had upper respiratory infection of 2, 3, 4 and 5 or more days duration for the entire investigation, control and experimental. The results indicate a lower incidence of upper respiratory infection in experimental wards for the 77-day observation period than in the wards with the placebo for the same time period. If we consider an upper respiratory infection of 5 or more days duration to be the ones representing a true upper respiratory infection in man, then viractin reduced the incidence to 0 in the experimental wards while the placebo wards had 11 patients with upper respiratory infection.

The cumulative evidence has shown that viractin holds promise as an effective prophylactic agent for upper respiratory infections. Additional evidence from several hundred other individuals and families over the past seventeen years is also worthy of note.

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## Solubility Relations of Fluorine Compounds and Inert Gas Narcosis

Two main physicochemical theories of inert gas narcosis have been put forward. The Meyer–Overton[1] theory postulates that the intensity of narcotic action varies as the concentration of narcotic in the lipids. More recently, Pauling[2] and Miller[3] have suggested that the aqueous phases play a dominant part and relate narcotic activity to the tendency to form hydrates or more generally to induce structure ('icebergs') in water.

For most simple narcotics the predictions of both theories are in substantial agreement as the narcotic effects of simple molecules are broadly in keeping with many of their thermodynamic properties, boiling points, ideal solubilities or polarizabilities[4,5]. However, in the case of fluorinated compounds these general relations break down and provide a means of discrimination between the theories. Such substances deviate very markedly from ideality in solution. Certain fully fluorinated gaseous compounds have the lowest recorded solubilities in water although their solubilities in organic solvents are less exceptional.

Though the dissociation pressures of hydrates at 0° C have been used to estimate the degree of structure a solute induces in water another indication is provided by the entropies of solution[6]. The entropy of solution of $SF_6$ has been estimated as $-22$ e.u. at 25° C using measurements of its solubility in water over a range of temperatures[7]. The results are in good agreement with those of Friedman[8], though both sets differ by a factor of five

Table 1

| Gas | Anæsthetic pressure (atm.) | Diss. pressure hydrate 0° C (atm.) | $-\Delta S$ soln (25°C) (cal. deg$^{-1}$ mole$^{-1}$) | Bunsen coeff. olive oil (37° C) |
|---|---|---|---|---|
| He | ~200 | — | 3 | 0·015 |
| $N_2$ | 29 | 160 | 7 | 0·067 |
| A | 20 | 95·0 | 9 | 0·14 |
| Kr | 2·9 | 14·5 | 13 | 0·43 |
| $CH_4$ | 4·6 | 26·0 | 11 | 0·28 |
| $SF_6$ | 3·0 | 1·0 | 22 | 0·25 |
| Xe | 0·85 | 1·2 | 16 | 1·70 |

from another determination[9]. Such a high entropy of solution would suggest a narcotic activity much higher than that observed (as would the dissociation pressure of its hydrate). Table 1 summarizes the data for a typical series of gases[10] and illustrates that solubility in the lipids (as represented by olive oil) is the best indication of narcotic activity, other factors showing little correlation when fluorinated compounds are considered. In the case of $CF_4$ for which no anæsthetic data are available the predictions of the two theories are very different. The hydrate theory would suggest an anæsthetic pressure of ~0·5 atm., a degree of narcotic activity unlikely to have gone unnoticed during the search for fluorocarbon anæsthetics, whereas the lipid solubility theory would indicate about 5 atm*.

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*Note added in proof. Preliminary experiments have shown that $CF_4$, at a partial pressure of 3 atm., does not produce anæsthesia in mice.

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## Effects of Insecticide Synergists on Duration of Sleep induced in Mice by Barbiturates

A number of otherwise pharmacologically inactive compounds are known to prolong sleep induced by barbiturates in mammals[1]. The most widely investigated of these is '*SKF 525A*' (2-diethylaminoethyl 2,2-diphenylpentanoate), which prolongs the action of barbiturates and other drugs by inhibiting liver microsomal enzymes which degrade a wide variety of drugs[1]. When applied to insects, '*SKF 525A*' synergizes pyrethroid insecticides and antagonizes the toxicity of the organophosphorus poison, malathion[2]. In these respects, '*SKF 525A*' mimics the action of commonly used insecticide synergists such as piperonyl butoxide[2]. Although piperonyl butoxide and other chemically related synergists have been included in insecticide formulations for many years, their effects on drug activity in mammals have not been examined. In this communication the effects of two insecticide synergists on the hypnotic action of barbiturates are described.

The synergists (Fig. 1) examined were: (1) technical piperonyl butoxide containing 80 per cent 3,4-methylenedioxy-6-propylbenzyl butyldiethylene glycol ether and 20 per cent related compounds; (2) 96–98 per cent pure sesoxane (2-(2-ethoxy ethoxy)-ethyl 3,4-methylenedioxyphenyl acetal of acetaldehyde). The synergists were administered by intraperitoneal injection to 15–20 g female mice. Initially it was established that the synergists themselves (emulsified with 'Tween 20' in physiological saline) injected at dosages as high as 75 mg/kg did