in incidence in Britain (in the manner demonstrated in diverticulosis), then remain stationary or even fall (as occurred in diabetes²) during rationing? A full list of these peculiar diseases, which included diverticulosis, derived from the observations of workers in Africa, was suggested some 12 years ago.³ To this list varicose veins and osteoarthritis should be added. Even blood pressure may remain stationary throughout life⁴ and serum cholesterol may fall.⁵

From 1955 and now spreading to some 16 of the most developed countries⁶ there has been a definite but slight decreased expectation of life in adults, to which atheroma makes the major contribution. In Britain all cohorts aged 15-75 had a decreased expectation of life in 1969, only those over 75 had increased expectation.⁷ I suggest that the latter group were born largely before major changes of feeding infants and adults occurred towards the end of the last century.

The pioneer studies of Cleave⁸ have suggested that we should look on chronic diseases of unknown aetiology in terms of poor adaptation to new environmental factors—new in the time-scale of evolution. Caries—a failure to starch and sugar, diverticulosis—a failure to low fibre. To these I now add kwashiorkor—a failure of the weanling to adapt to protein-poor diets, and lung cancer—a failure to adapt to cigarette smoke. Weaklings go to the wall; the species survives.

This brilliant new perspective opens up fundamental insights. We must consider how our children are adapting to evolutionary recent changes in their upbringing: seldom breast milk, often cows' milk (3½ times as much protein) at all ages; optimal diets containing much sugar and refined cereals. Fed thus they mature rapidly; the menarche has fallen 5-6 years in little over a century. Western-fed children and adults have a *milieu intérieur* statistically different in many respects from that of those reared in the ancient manner.³

Might not the traditional African blood cholesterol at 40 years 147 mg/100 ml and fasting blood sugar 106 mg/100 ml be the human normal, and explain partially the low incidence of atheroma and diabetes, until nowadays diets and disease incidence change into the Western pattern?—I am, etc.,

HUGH TROWELL

Fordingbridge,
Hants

- 1 Cohen, A. M., Kaufmann, N. A., Poznanski, R., Blondheim, S. H., and Stein, Y., *British Medical Journal*, 1966, 1, 339.
- 2 Himsworth, H. P., *Proceedings of the Royal Society Medicine*, 1949, 42, 323.
- 3 Trowell, H. C., *Non-Infective Disease in Africa*, pp. 465 and 467. London: Arnold, 1960.
- 4 Pickering, G., *High Blood Pressure*, 2nd edn., p. 226. London: Churchill, 1968.
- 5 Shaper, A. G., and Jones, K. W., *Lancet*, 1959, 2, 534.
- 6 *Medical News Tribune*, 1970, 2, No. 46.
- 7 *The Times*, 20 May 1971, p. from *The Registrar's General Statistical Review of England and Wales for 1969, Part 1. Tables, Medical*. London: H.M.S.O., 1971.
- 8 Cleave, T. L., Campbell, G. D., and Painter, N. S., *Diabetes, Coronary Thrombosis, and the Saccharine Disease*, 2nd edn. Wright, Bristol, 1969.

Humidity in Hospitals

SIR,—This letter is stimulated by the article on mucolytic agents (5 June, p. 581) which mentions the value of steam inhalations. I wonder whether medical advisory committees

to hospitals are aware of the importance to chest patients of maintaining an adequate degree of relative humidity in the air of wards?

My limited experience of hospitals is that in winter the air becomes much too dry, so making the sputum of patients suffering from chest infections much more viscid. Not so many years ago, in the old Nightingale-type of wards, an electric sterilizer kept steaming away, so keeping the air moist. Nowadays, even the windows are kept shut, to save on the heating bills.

My own experience of a new centrally-heated house is that for two winters running I suffered from acute sinusitis, until I discovered the cure was adequate humidification of the air. I found this out only after buying a sensitive and accurate hygrometer, which showed that last winter the percentage relative humidity inside the house was only 30%, although in the outside air it quickly registered 65%. The optimum relative humidity at 70°F (21°C) is about 50%. One year previously I had bought an inexpensive hygrometer which registered much the same winter and summer, indoors and outdoors, so it is false economy to buy a cheap instrument.—I am, etc.,

JOHN R. WRAY

Municipal Offices,
Boroughs of Calne, Chippenham, and Malmesbury,
Wilts

Sniffing Syndrome

SIR,—Your leading article on the "Sniffing Syndrome" (24 April, p. 183) issue draws attention to an important social and medical problem which, fortunately for the majority of your readers, does not appear to be as widespread in Europe as in the United States.

I would, however, take issue with your apparently uncritical acceptance of the conclusion of the report by Taylor and Harris¹ and draw your attention to two publications from this laboratory^{2,3} that show firstly, that the results obtained by Taylor and Harris can be explained on the grounds of anoxia alone and, secondly, that the ability to sensitize the heart to sympathomimetic agents is a property shared by many hydrocarbons and halocarbons. As with many questions dealing with toxicity, it is the dose necessary to produce a particular effect that is important and in this regard there is no evidence that cardiac sensitization occurs at inspired air concentrations of the various agents that are associated with normal use conditions. The teenagers that have died have been inhaling exceedingly high concentrations of the compounds under conditions of gross abuse of the intended use of the product. The asthma inhalers present a different problem since there appears to be no evidence from countries other than the U.K. for an increase in asthma deaths, and I believe that this increase has now ceased and that asthma deaths have declined to the levels prevailing prior to the introduction of the pressurized aerosol inhalers containing fluorocarbons. The fact that under conditions of gross overdosage Professor C. T. Dollery⁴ was able to detect fluorocarbon levels in the blood is not in itself surprising or an indictment of the safety of the propellants. What is needed is quantitative information on the levels of halocarbon in the blood that are associated with a serious risk of cardiac arrhythmias.

This information is now being gathered by several organizations. Since it has been shown by Reinhardt *et al.*² that the fluorocarbon propellants vary in their ability to cause sensitization of the heart to epinephrine, it may be that for certain purposes, such as the medicated aerosols that are intended to be inhaled, the substitution of propellants having a very small potential for causing the sensitization phenomenon would further enhance the safety factor in this type of application—I am, etc.,

G. J. STOPPS

Haskell Laboratory for Toxicology and Industrial Medicine, du Pont de Nemours and Co., Wilmington, Del., U.S.A.

- ¹ Taylor, G. J., and Harris, W. S., *Journal of the American Medical Association*, 1970, 214, 81.
- ² Reinhardt, C. F., Azar, A., Mayfield, M. E., Smith, P. E., jun., and Mullin, L. S., *Archives of Environmental Health*, 1971, 22, 265.
- ³ Azar, A., Zapp, J. A., Reinhardt, C. F., and Stopps, G. J., *Journal of the American Medical Association*, 1971, 215, 1501.
- ⁴ Dollery, C. T., Draffan, G. M., Davies, D. S., Williams, F., and Connolly, M. E., *Lancet*, 1970, 2, 1164.

SIR,—Your recent leading article on the "Sniffing Syndrome" (24 April, p. 183) has prompted me to offer a brief account of experiments we have recently carried out to assess the potential danger of aerosol propellants to asthmatic patients. The starting points of our work were the report by Taylor and Harris,¹ which seemed to show that propellants like Freons 11 and 12 were highly toxic to heart muscle in anaesthetized, hypoxic mice, and the report by Reinhardt *et al.*,² which showed that aerosol propellants, like many other organic solvents, could sensitize the heart of conscious dogs to large intravenous challenges with adrenaline.

Our first experiments were obviously directed to checking the surprising results reported by Taylor and Harris. We quickly found that this work could not be repeated by us; this has also been the experience of Azar *et al.*³ and of Silverglade.⁴ The apparent cardiotoxic effect found by Taylor and Harris depended on their finding that control animals, which received no propellants, could be totally deprived of air for three to four minutes with only minor changes in cardiac performance. There can be few, if any, mammalian species for which this is true. Our mice responded to asphyxiation with brief tachycardia which was followed by bradycardia and then by major arrhythmias as the degree of hypoxia increased. The hearts of animals which received propellant gases or nitrogen before being asphyxiated behaved in essentially the same way but, not surprisingly, the symptoms occurred a little earlier because most of the oxygen in their lungs had been removed by the pretreatment.

The work of Reinhardt *et al.* is different and gives rise to these questions: What concentrations of aerosol propellants are necessary to sensitize heart muscle to adrenaline? Do these concentrations adversely affect cardiac performance in hypoxic, anxious individuals? Can such concentrations be achieved in the blood of asthmatic patients who abuse inhalers?

We have found that blood concentrations of about 20-25 µg/ml of Freon 11 and about twice this amount of Freon 12 are the limiting levels for cardiac sensitization to adrenaline challenge in conscious dogs. These or

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.—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 µl/litres/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 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 Hanburys Ltd.

Ware, Herts

- 1 Taylor, G. J., and Harris, W. S., *Journal of the American Medical Association*, 1970, 214, 81.
- 2 Reinhardt, C. F., Azar, A., Maxfield, M. E., Smith, P. E. jun., and Mullin, L. S., *Archives of Environmental Health*, 1971, 22, 265.
- 3 Azar, A., Zapp, J. A., Reinhardt, C. F., and Stopps, G. J., *Journal of the American Medical Association*, 1971, 215, 1501.
- 4 Silverglade, A., *Journal of the American Medical Association*, 1971, 215, 1502.
- 5 Collins, J. M., McDevitt, D. G., Shanks, R. G., Swanton, J. G., *British Journal of Pharmacology*, 1969, 36, 35.
- 6 Dollery, C. T., Draffan, G. H., Davies, D. S., Williams, F., and Conolly, M. E., *Lancet*, 1970, 2, 1164.

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