A study comparing the effects of etomidate with those of methohexital on the adrenocortical function of neonates borne by mothers who received these agents for induction of anaesthesia before caesarean section indicated that there was no evidence to preclude the use of etomidate in such patients. However, regardless of which anaesthetic agent was used, early feeding was recommended to avoid neonatal hypoglycaemia.[3]

1. Ledingham IM, Watt I. Influence of sedation on mortality in critically ill multiple trauma patients. *Lancet* 1983; **i:** 1270.
2. Goldberg A. Etomidate. *Lancet* 1983; **ii:** 60.
3. Crozier TA, *et al.* Effects of etomidate on the adrenocortical and metabolic adaptation of the neonate. *Br J Anaesth* 1993; **70:** 47–53.

Hypersensitivity. Reactions involving immediate widespread cutaneous flushing or urticaria attributed to etomidate have been described.[1] There have also been reports[2,3] of anaphylactic reactions after injection of etomidate.

1. Watkins J. Etomidate: an 'immunologically safe' anaesthetic agent. *Anaesthesia* 1983; **38** (suppl): 34–8.
2. Sold M, Rothhammer A. Lebensbedrohliche anaphylaktoide reaktion nach etomidat. *Anaesthesist* 1985; **34:** 208–10.
3. Krumholz W, *et al.* Ein fall von anaphylaktoider reaktion nach gabe von etomidat. *Anaesthesist* 1984; **33:** 161–2.

Porphyria. Etomidate is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Interactions

A reduced dose of etomidate may be necessary in patients who have received antipsychotics, sedatives, or opioids. The hypnotic effect of etomidate has been potentiated by other sedative drugs.

See also Interactions of General Anaesthetics, p.1779.

Calcium-channel blockers. Prolonged anaesthesia and Cheyne-Stokes respiration following etomidate injection has been reported in 2 patients also given *verapamil*.[1]

1. Moore CA, *et al.* Potentiation of etomidate anesthesia by verapamil: a report of two cases. *Hosp Pharm* 1989; **24:** 24–5.

General anaesthetics. For a report of synergy between *propofol* and etomidate, see p.1792.

Pharmacokinetics

After injection, etomidate is rapidly redistributed from the CNS to other body tissues, and undergoes rapid metabolism in the liver and plasma. Pharmacokinetics are complex and have been described by both 2- and 3-compartment models. Etomidate is about 76% bound to plasma proteins. It is mainly excreted in the urine, but some is excreted in the bile. It may cross the placenta and is distributed into breast milk.

◊ References.

1. Levron JC, Assoune P. Pharmacocinétique de l'étomidate. *Ann Fr Anesth Reanim* 1990; **9:** 123–6.
2. Sfez M, *et al.* Comparaison de la pharmacocinétique de l'étomidate chez l'enfant et chez l'adulte. *Ann Fr Anesth Reanim* 1990; **9:** 127–31.
3. Esener Z, *et al.* Thiopentone and etomidate concentrations in maternal and umbilical plasma, and in colostrum. *Br J Anaesth* 1992; **69:** 586–8.

Uses and Administration

Etomidate is an intravenous anaesthetic used for the induction of general anaesthesia (p.1780). Anaesthesia is rapidly induced and may last for 6 to 10 minutes with a single usual dose. Recovery is usually rapid without hangover effect. Etomidate has no analgesic activity.

For the induction of anaesthesia, etomidate is available as a conventional or an emulsion injection formulation. The usual dose is 300 micrograms/kg of etomidate given slowly, preferably into a large vein in the arm, although a lower dose of 150 micrograms/kg of the emulsion formulation may be sufficient. An initial dose of 150 to 200 micrograms/kg is recommended in the elderly, subsequently adjusted according to effects. Dosage should also be reduced in hepatic cirrhosis. Children may require up to 30% more than the usual adult dose of the emulsion formulation. Opioid analgesics or benzodiazepines as premedication reduce myoclonic muscle movements; opioids also reduce injection site pain. A neuromuscular blocker is necessary if intubation is required.

Administration in the elderly. A study[1] in elderly patients has demonstrated that although reducing the rate of intravenous injection of etomidate reduces the speed of induction, the dosage required is also reduced. Giving etomidate 0.2% solution at a rate of 10 mg/minute induced anaesthesia in a mean of 89.6 seconds and required a mean dose of 0.11 mg/kg. Corresponding values for a rate of 40 mg/minute were 47.7 seconds and 0.26 mg/kg, respectively.

1. Berthoud MC, *et al.* Comparison of infusion rates of three i.v. anaesthetic agents for induction in elderly patients. *Br J Anaesth* 1993; **70:** 423–7.

Anaesthesia. Etomidate might be useful for induction if rapid tracheal intubation is required with a competitive neuromuscular blocker as it has been shown to reduce the time to onset of block with vecuronium.[1,2]

1. Gill RS, Scott RPF. Etomidate shortens the onset time of neuromuscular block. *Br J Anaesth* 1992; **69:** 444–6.
2. Bergen JM, Smith DC. A review of etomidate for rapid sequence intubation in the emergency department. *J Emerg Med* 1997; **15:** 221–30.

Status epilepticus. General anaesthesia may be used to control refractory tonic-clonic status epilepticus (p.469). A short-acting barbiturate such as thiopental is usually used, but other anaesthetics including etomidate have also been tried[1] for intractable convulsive status epilepticus. However, like a number of other anaesthetics there have been reports of seizures associated with its use in anaesthesia,[2] especially in patients with epilepsy.

1. Yeoman P, *et al.* Etomidate infusions for the control of refractory status epilepticus. *Intensive Care Med* 1989; **15:** 255–9.
2. Nicoll K, Callender J. Etomidate-induced convulsion prior to electroconvulsive therapy. *Br J Psychiatry* 2000; **177:** 373.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Hypnomidate; ***Belg.:*** Hypnomidate; ***Braz.:*** Hypnomidate; ***Chile:*** Hypnomidate†; ***Cz.:*** Hypnomidate; ***Fr.:*** Hypnomidate; ***Ger.:*** Hypnomidate; ***Gr.:*** Hypnomidate; ***Mex.:*** Hypnomidate; ***Neth.:*** Hypnomidate; ***Pol.:*** Hypnomidate; ***Port.:*** Hypnomidato; ***S.Afr.:*** Hypnomidate; ***Spain:*** Hypnomidate; ***Turk.:*** Hypnomidate; ***UK:*** Hypnomidate; ***USA:*** Amidate.

Halothane *(BAN, rINN)*

Alotano; Halotaani; Halotán; Halotan; Halotanas; Halotano; Halothan; Halothanum; Phthorothanum. *(RS)*-2-Bromo-2-chloro-1,1,1-trifluoroethane.

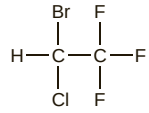
Галотан

$CHBrCl.CF_3$ = 197.4.

CAS — 151-67-7.

ATC — N01AB01.

ATC Vet — QN01AB01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Halothane). A clear, colourless, mobile, dense, non-flammable liquid. Distillation range 49° to 51°. Slightly soluble in water; miscible with dehydrated alcohol and with trichloroethylene. Halothane contains 0.01% w/w of thymol. Store at a temperature not greater than 25° in airtight containers. Protect from light.
USP 31 (Halothane). A colourless, mobile, non-flammable, heavy liquid having a characteristic odour resembling that of chloroform. It contains not less than 0.008% and not more than 0.012% of thymol, by weight, as a stabiliser. It should contain not more than 0.03% of water. Distillation range 49° to 51°.
Slightly soluble in water; miscible with alcohol, with chloroform, with ether, and with fixed oils. Store in airtight containers at a temperature not greater than 40°. Protect from light. Dispense only in the original container.

Incompatibility. In the presence of moisture, halothane reacts with many metals. Rubber and some plastics deteriorate when in contact with halothane vapour or liquid.

Stability. Halothane contains 0.01% w/w of thymol as a stabiliser; some commercial preparations may also contain up to 0.00025% w/w of ammonia. Thymol does not volatilise with halothane and therefore accumulates in the vaporiser. It may give a yellow colour to any remaining liquid; halothane that has discoloured should be discarded.

Adverse Effects

As with other halogenated anaesthetics, halothane has a depressant action on the cardiovascular system and reduces blood pressure; signs of overdosage are bradycardia and profound hypotension. It is also a respiratory depressant and can cause cardiac arrhythmias; there have been instances of cardiac arrest. The sensitivity of the heart to sympathomimetic amines is increased.

Adverse effects on the liver have limited its use in recent years (see below); these effects range from liver dysfunction to fatal hepatitis and necrosis and are more frequent following repeated use.

Halothane can produce nausea, vomiting, and shivering. Malignant hyperthermia has been reported.

See also Adverse Effects of General Anaesthetics, p.1779.

Effects on the cardiovascular system. The incidence of cardiac arrhythmias is higher with halothane than with enflurane or isoflurane; also the arrhythmogenic threshold with injected adrenaline is lower with halothane than isoflurane or enflurane.

Arrhythmias are considered to be very common in children anaesthetised with halothane and in the UK it is recommended that it should not be used for dental procedures outside hospital in those under 18 years old.

Effects on the kidneys. Renal failure has been reported after halothane anaesthesia,[1,2] sometimes with concurrent liver failure.[2]

1. Cotton JR, *et al.* Acute renal failure following halothane anesthesia. *Arch Pathol Lab Med* 1976; **100:** 628–9.
2. Gelman ML, Lichtenstein NS. Halothane-induced nephrotoxicity. *Urology* 1981; **17:** 323–7.

Effects on the liver. Liver damage has been recognised as an adverse effect of halothane for many years.[1-3] It may be severe, and associated with a high mortality.

Two types of hepatotoxicity are recognised; in **type I** there is a minor disturbance in liver function shown by increases in liver enzyme values; this may occur in up to 30% of patients given halothane,[4] or more if activity is measured by glutathione S-transferase rather than serum aminotransferase.[5] Subsequent re-exposure to halothane is not necessarily associated with liver damage.[2,6]

Type II hepatotoxicity, which is rarer, involves massive liver cell necrosis; reported incidences[2] range from 1 in 2500 to 1 in 36 000. Type II liver toxicity is characterised by several clinical features: non-specific gastrointestinal upset, delayed pyrexia, jaundice, eosinophilia, serum autoantibodies, rash, and arthralgia.[1,3] Biochemical tests of liver function show changes typical of hepatocellular damage; histological features are typified by centrilobular necrosis.[1] Several **risk factors** for development of serious toxicity have become apparent;[1-3] they include repeated exposure, previous adverse reactions to halothane (jaundice, pyrexia), female gender, obesity, middle age, genetic predisposition, enzyme induction, and a history of drug allergy.

The **causes** of halothane hepatotoxicity have been debated. Type I reactions may result from toxic products of halothane metabolism, possibly influenced by genetic factors or from an imbalance between hepatic oxygen supply and demand. Changes in cellular calcium homoeostasis may also be involved. Type II reactions are most likely immune-mediated.[1,2] It has been suggested[4] that metabolism of halothane produces a reactive metabolite which binds covalently to proteins in the endoplasmic reticulum of hepatocytes. In susceptible patients it is believed that these metabolite-modified proteins provoke an immune response which is responsible for the liver damage. Findings[7,8] have implicated the cytochrome P450 isoenzyme CYP2E1 as having a major role in the metabolism of halothane and patients with high levels of this isoenzyme may be predisposed to developing immune-medicated liver damage after halothane exposure.

The UK CSM,[9] after receiving 84 further reports of hepatotoxicity between 1978 and 1985, issued the following **guidelines** on **precautions** to be taken before using halothane:

- a careful anaesthetic history should be taken to determine previous exposure and previous reactions to halothane
- repeated exposure to halothane within a period of at least 3 months should be avoided unless there are overriding clinical circumstances. An opinion has been expressed that the 3-month interval between exposures would be unlikely to prevent hepatotoxicity[2]
- a history of unexplained jaundice or pyrexia in a patient following exposure to halothane is an absolute contra-indication to its future use in that patient

These guidelines were reiterated in 1997 after the CSM were notified of a further 15 cases of acute liver failure all requiring transplantation.[10]

The problem of patients sensitised to halothane who require **subsequent anaesthesia** with a volatile anaesthetic has been discussed.[4] Although the incidence of hepatotoxicity produced by *enflurane* appears to be less than with halothane it is of a similar nature and there have been reports of several patients who apparently had cross-sensitivity to both. Hepatotoxicity with *isoflurane* appears to be rare and it was suggested that for the majority of patients sensitised to halothane, isoflurane would be likely to be free from hepatotoxic effects. However, there has been a report[11] of a patient who had had two previous exposures to isoflurane and subsequently developed liver function abnormalities after receiving halothane. Hepatotoxicity with *desflurane* (see p.1781) might also be associated with sensitisation to halothane.

1. Ray DC, Drummond GB. Halothane hepatitis. *Br J Anaesth* 1991; **67:** 84–99.
2. Neuberger JM. Halothane and hepatitis: incidence, predisposing factors and exposure guidelines. *Drug Safety* 1990; **5:** 28–38.
3. Rosenak D, *et al.* Halothane and liver damage. *Postgrad Med J* 1989; **65:** 129–35.
4. Kenna JG, Neuberger JM. Immunopathogenesis and treatment of halothane hepatitis. *Clin Immunother* 1995; **3:** 108–24.

5. Allan LG, *et al.* Hepatic glutathione S-transferase release after halothane anaesthesia: open randomised comparison with isoflurane. *Lancet* 1987; **i:** 771–4.
6. Neuberger J, Williams R. Halothane anaesthesia and liver damage. *BMJ* 1984; **289:** 1136–9.
7. Kharasch ED, *et al.* Identification of the enzyme responsible for oxidative halothane metabolism: implications for prevention of halothane hepatitis. *Lancet* 1996; **347:** 1367–71.
8. Kenna JC, *et al.* Formation of the C[F] CO-protein antigens implicated in the pathogenesis of halothane hepatitis is catalyzed in human liver microsomes in vitro by CYP 2E1. *Br J Clin Pharmacol* 1997; **43:** 209.
9. CSM. Halothane hepatotoxicity. *Current Problems 18* 1986. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024425&RevisionSelectionMethod=LatestReleased (accessed 25/07/08)
10. CSM/MCA. Safety issues in anaesthesia: reminder: hepatotoxicity with halothane. *Current Problems* 1997; **23:** 7. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023230&RevisionSelectionMethod=LatestReleased (accessed 16/05/06)
11. Slayter KL, *et al.* Halothane hepatitis in a renal transplant patient previously exposed to isoflurane. *Ann Pharmacother* 1993; **27:** 101.

Precautions

The risk of halothane hepatitis led the UK CSM to issue guidelines on its use (see Effects on the Liver, under Adverse Effects, above). It is also recommended that patients be informed of any reactions and that this be done in addition to the updating of the patients' medical records.

It is recommended in the UK that halothane should not be used for dental procedures outside hospital in patients under 18 years old.

Halothane reduces uterine muscle tone during pregnancy and generally its use is not recommended in obstetrics because of the increased risk of postpartum haemorrhage.

Premedication with atropine has been recommended to reduce vagal tone and to prevent bradycardia and severe hypotension.

Allowance may need to be made for any increase in CSF pressure or in cerebral blood flow. Halothane should be used with caution in patients with phaeochromocytoma.

As with other halogenated anaesthetics, patients with known or suspected susceptibility to malignant hyperthermia should not be anaesthetised with halothane.

See also Precautions for General Anaesthetics, p.1779.

Abuse. A brief review[1] of abuse of volatile anaesthetics found that of 14 patients who had ingested or sniffed halothane 10 had died. Another patient who had injected halothane intravenously also died. There has also been another report[2] of fatalities resulting from acute pulmonary oedema after intravenous injection of halothane.

1. Yamashita M, *et al.* Illicit use of modern volatile anaesthetics. *Can Anaesth Soc J* 1984; **31:** 76–9.
2. Berman P, Tattersal M. Self-poisoning with intravenous halothane. *Lancet* 1982; **i:** 340.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving halothane, and the American Academy of Pediatrics[1] considers that it is therefore usually compatible with breast feeding.

Trace amounts of halothane have been detected in the breast milk of an anaesthetist exposed to environmental halothane in the operating theatre.[2]

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 25/05/04)
2. Coté CJ, *et al.* Trace concentrations of halothane in human breast milk. *Br J Anaesth* 1976; **48:** 541–3.

Porphyria. Halothane has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

Adrenaline and most other sympathomimetics, and theophylline should be avoided during halothane anaesthesia since they can produce cardiac arrhythmias; the risk of arrhythmias is also increased if halothane is used in patients receiving dopaminergics. The effects of competitive neuromuscular blockers such as atracurium, and of ganglion blockers such as trimetaphan are enhanced by halothane and if required they should be given in reduced dosage. Morphine increases the depressant effects of halothane on respiration. Chlorpromazine also enhances the respiratory depressant effect of halothane. The effects of both ergometrine and oxytocin on the parturient uterus are diminished by halothane.

See also Interactions of General Anaesthetics, p.1779.

Antiepileptics. For a case of *phenytoin* intoxication associated with halothane anaesthesia, see p.497.

Benzodiazepines. *Midazolam* has been reported to potentiate the anaesthetic action of halothane.[1]

1. Inagaki Y, *et al.* Anesthetic interaction between midazolam and halothane in humans. *Anesth Analg* 1993; **76:** 613–17.

General anaesthetics. For a report that halothane increases serum concentrations of *propofol*, see p.1792.

Neuromuscular blockers. For the potentiation of the neuromuscular blockade of neuromuscular blockers such as *atracurium* by halothane, see p.1904. For increased toxicity during halothane anaesthesia, see *suxamethonium* p.1911.

Trichloroethane. A report[1] of 2 patients showing evidence of chronic cardiac toxicity after repeated exposure to trichloroethane. In both cases there was circumstantial evidence of a deterioration after routine anaesthetic use of halothane.

1. McLeod AA, *et al.* Chronic cardiac toxicity after inhalation of 1,1,1-trichloroethane. *BMJ* 1987; **294:** 727–9.

Xanthines. For references to increased cardiotoxicity when patients taking *theophylline* were anaesthetised with halothane, see p.1145.

Pharmacokinetics

Halothane is absorbed on inhalation. It has a relatively low solubility in blood and is more soluble in the neutral fats of adipose tissue than in the phospholipids of brain cells. Up to 80% of inhaled halothane is excreted unchanged through the lungs. Up to 20% is metabolised by the liver by oxidative and, under hypoxic conditions, reductive pathways. Urinary metabolites include trifluoroacetic acid and bromide and chloride salts (oxidative pathway) and fluoride salts (reductive pathway). Halothane diffuses across the placenta and has been detected in breast milk.

Uses and Administration

Halothane is a volatile halogenated anaesthetic given by inhalation. It has a minimum alveolar concentration (MAC) value (see Uses of General Anaesthetics, p.1779) ranging from 0.64% in the elderly to 1.08% in infants. It is non-flammable and is not explosive when mixed with oxygen at normal atmospheric pressure. It is not irritant to the skin and mucous membranes and does not produce necrosis when spilt on tissues. It suppresses salivary, bronchial, and gastric secretions and dilates the bronchioles. However, its use has diminished due to the risk of hepatotoxicity; in the UK, it is only available on a named-patient basis and in other countries, such as the USA, it has been withdrawn from the market.

Halothane is used for the induction and maintenance of general anaesthesia (p.1780) and is given using a calibrated vaporiser to provide close control over the concentration of inhaled vapour.

Anaesthesia may be induced with 2 to 4% v/v of halothane in oxygen or mixtures of nitrous oxide and oxygen; induction may also be started at a concentration of 0.5% v/v and increased gradually to the required level. For induction in children a concentration of 1.5 to 2% v/v has been used. It takes up to about 5 minutes to attain surgical anaesthesia and halothane produces little or no excitement in the induction period. The more usual practice is to induce anaesthesia with an intravenous agent. Anaesthesia is maintained with concentrations of 0.5 to 2% v/v depending on the flow rate used; the lower concentration is usually suitable for the elderly.

Adequate muscle relaxation is only achieved with deep anaesthesia so a neuromuscular blocker is given to increase muscular relaxation if necessary.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Ineltano; ***Austral.:*** Fluothane; ***Austria:*** Fluothane†; ***Braz.:*** Fluothane; ***Chile:*** Fluothane†; ***Cz.:*** Narcotan; ***Fr.:*** Fluothane†; ***Ger.:*** Fluothane†; ***Gr.:*** Fluothane†; ***Hung.:*** Narcotan; ***India:*** Fluothane; ***Indon.:*** Fluothane; ***Israel:*** Fluothane†; ***Malaysia:*** Fluothane†; ***NZ:*** Fluothane; ***Pol.:*** Narcotan; ***S.Afr.:*** Fluothane†; ***Spain:*** Fluothane; ***Swed.:*** Fluothane†; ***Turk.:*** Fluothane; ***USA:*** Fluothane†.

Isoflurane *(BAN, USAN, rINN)*

Compound 469; Isofluraani; Isofluran; Isoflurano; Isofluranum; Izoflurán; Izofluran; Izofluranas. 1-Chloro-2,2,2-trifluoroethyl difluoromethyl ether; 2-Chloro-2-(difluoromethoxy)-1,1,1-trifluoroethane.

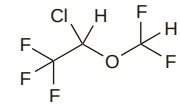
Изофлуран

$C_3H_2ClF_5O$ = 184.5.

CAS — 26675-46-7.

ATC — N01AB06.

ATC Vet — QN01AB06.



Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.

Ph. Eur. 6.2 (Isoflurane). A clear, colourless, mobile, heavy liquid. B.p. about 48°. It is non-flammable. Practically insoluble in water; miscible with dehydrated alcohol and with trichloroethylene. Store in airtight containers. Protect from light.

USP 31 (Isoflurane). A clear, colourless, volatile liquid having a slight odour. B.p. about 49°. Insoluble in water; miscible with common organic solvents and with fats and oils. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects and Precautions

As with other halogenated anaesthetics, respiratory depression, hypotension, arrhythmias, and malignant hyperthermia have been reported; patients with known or suspected susceptibility to malignant hyperthermia should not be anaesthetised with isoflurane. Isoflurane differs from halothane and enflurane in that it produces less cardiac depression than either drug and heart rate may be increased. Also isoflurane sensitises the myocardium to sympathomimetics to a lesser extent than halothane and enflurane. The incidence of cardiac arrhythmias is lower with isoflurane than with halothane. Shivering, nausea, and vomiting have been reported in the postoperative period.

Induction with isoflurane is not as smooth as with halothane and this may be connected with its pungency; breath holding, coughing, and laryngospasm may occur. It has been reported to increase the cerebrospinal pressure and should be used with caution in patients with raised intracranial pressure. Isoflurane relaxes the uterine muscle; increased blood loss may occur after curettage or termination of pregnancy.

In order to minimise the risk of developing elevated carboxyhaemoglobin levels, carbon dioxide absorbents in anaesthetic apparatus should not be allowed to dry out when delivering volatile anaesthetics such as isoflurane (see below).

See also Adverse Effects and Precautions of General Anaesthetics, p.1779.

◊ A comparison[1] of isoflurane and halothane for outpatient dental anaesthesia in children considered that isoflurane would produce fewer arrhythmias than halothane, but that the ease of induction and the quality of anaesthesia was inferior to that with halothane. Others[2] also found a higher incidence of coughing, salivation, and laryngospasm with isoflurane than halothane, but felt that it could be used as an alternative.

Further information on the adverse effects profile of isoflurane can be obtained from the report of and commentaries on an extensive multicentre study of patients undergoing anaesthesia with this agent.[3,4]

1. Cattermole RW, *et al.* Isoflurane and halothane for outpatient dental anaesthesia in children. *Br J Anaesth* 1986; **58:** 385–9.
2. McAteer PM, *et al.* Comparison of isoflurane and halothane in outpatient paediatric dental anaesthesia. *Br J Anaesth* 1986; **58:** 390–3.
3. Forrest JB, *et al.* A multi-centre clinical evaluation of isoflurane. *Can Anaesth Soc J* 1982; **29** (suppl): S1–S69.
4. Levy WJ. Clinical anaesthesia with isoflurane: a review of the multicentre study. *Br J Anaesth* 1984; **56:** 101S–112S.

Carbon dioxide absorbents. Significant carboxyhaemoglobinaemia may develop rarely during anaesthesia with volatile anaesthetics given by circle breathing systems containing carbon dioxide absorbents.[1] The effect is only seen when the absorbent has become excessively dried out. The use of barium hydroxide lime (which is not available in the UK) as an absorbent produces more carbon monoxide than soda lime, particularly at low water