with raised intracranial pressure has not been established and therefore sevoflurane should be used with caution. As emergence and recovery are particularly rapid with sevoflurane patients may require early postoperative pain relief.

See also Precautions for General Anaesthetics, p.1779.

Carbon dioxide absorbents. The breakdown of sevoflurane by carbon dioxide absorbents (such as soda lime) results in the formation of pentafluoroisopropenyl fluoromethyl ether (PIFE; compound A), and trace amounts of pentafluoromethoxy isopropyl fluoromethyl ether (PMFE; Compound B). Compound A has been shown to be nephrotoxic in *rats* (see under Effects on the Kidneys, above). Even during short exposure times, as required for induction of anaesthesia, use of moist soda lime is important to minimise sevoflurane degradation, which is aggravated by a high potassium hydroxide content of the soda lime.[1]

Licensed product information states that increased amounts of compound A may be formed if barium hydroxide lime is used as a carbon dioxide absorbent rather than soda lime.

The use of desiccated carbon dioxide absorbents with sevoflurane has also been associated with rare cases of extreme heat and smoke or fire developing in the anaesthetic apparatus.[2]

1. Funk W, *et al*. Dry soda lime markedly degrades sevoflurane during simulated inhalation induction. *Br J Anaesth* 1999; **82:** 193–8.
2. Abbott Laboratories, Canada. Important safety information regarding the use of Sevorane AF (sevoflurane) in conjunction with anesthesia machines. Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/sevorane_hpc-cps-eng.pdf (accessed 08/08/08)

Interactions

Care is advised if adrenaline or other sympathomimetics are given during sevoflurane anaesthesia. The effects of competitive neuromuscular blockers such as atracurium are enhanced by sevoflurane (see p.1904). The metabolism, and hence toxicity, of sevoflurane may be increased by drugs or compounds that induce cytochrome P450 isoenzyme CYP2E1 including isoniazid and alcohol.

See also Interactions of General Anaesthetics, p.1779.

◊ References.

1. Dale O. Drug interactions in anaesthesia: focus on desflurane and sevoflurane. *Baillieres Clin Anaesthesiol* 1995; **9:** 105–17.

Pharmacokinetics

Sevoflurane is absorbed on inhalation. The blood/gas partition coefficient is low. Up to 5% of the absorbed dose of sevoflurane is metabolised in the liver by the cytochrome P450 isoenzyme CYP2E1 and defluorinated to its major metabolites hexafluoroisopropanol (HFIP), inorganic fluoride, and carbon dioxide. HFIP is rapidly conjugated with glucuronic acid and eliminated in the urine. Sevoflurane crosses the placenta.

◊ References.

1. Behne M, *et al*. Clinical pharmacokinetics of sevoflurane. *Clin Pharmacokinet* 1999; **36:** 13–26.

Uses and Administration

Sevoflurane 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 1.4% in the elderly to 3.3% in neonates. It is used for the induction and maintenance of general anaesthesia (p.1780). It is non-flammable. Sevoflurane has a nonpungent odour and does not cause respiratory irritation. It also has muscle relaxant properties which may be sufficient for some surgical procedures to be performed without a neuromuscular blocker. However, it possesses no analgesic properties.

Sevoflurane is given using a calibrated vaporiser. For induction, sevoflurane is given in concentrations of up to 5% v/v in adults, with oxygen or a mixture of oxygen and nitrous oxide. Concentrations of up to 7% v/v may be used in children. A short-acting barbiturate or other intravenous induction agent may be given before inhaling sevoflurane. Induction with sevoflurane is rapid (surgical anaesthesia in less than 2 minutes) and smooth because of its nonpungent odour. Maintenance of anaesthesia is achieved with a concentration of 0.5 to 3% v/v with or without nitrous oxide.

◊ Reviews.

1. Patel SS, Goa KL. Sevoflurane: a review of its pharmacodynamic and pharmacokinetic properties and its clinical use in general anaesthesia. *Drugs* 1996; **51:** 658–700.
2. Smith I, *et al*. Sevoflurane—a long-awaited volatile anaesthetic. *Br J Anaesth* 1996; **76:** 435–45.
3. Grounds RM, Newman PJ. Sevoflurane. *Br J Hosp Med* 1997; **57:** 43–6.
4. Goa KL, *et al*. Sevoflurane in paediatric anaesthesia: a review. *Paediatr Drugs* 1999; **1:** 127–53.
5. Ghatge S, *et al*. Sevoflurane: an ideal agent for adult day-case anesthesia? *Acta Anaesthesiol Scand* 2003; **47:** 917–31.
6. Sakai EM, *et al*. Inhalation anesthesiology and volatile liquid anesthetics: focus on isoflurane, desflurane, and sevoflurane. *Pharmacotherapy* 2005; **25:** 1773–88.

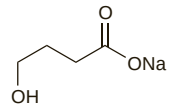
Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Eraldin; Sevorane; ***Austral.:*** Sevorane; ***Austria:*** Sevorane; ***Belg.:*** Sevoranet†; ***Braz.:*** Sevocris; Sevorane; ***Canad.:*** Sevorane; ***Chile:*** Sevorane; ***Cz.:*** Sevorane; ***Denm.:*** Sevorane; ***Fin.:*** Sevorane; ***Fr.:*** Sevorane; ***Ger.:*** Sevorane; ***Gr.:*** Sevorane; ***Hong Kong:*** Sevorane; ***Hung.:*** Sevorane; ***Indon.:*** Sevorane; ***Irl.:*** Sevorane; ***Israel:*** Sevorane; ***Ital.:*** Sevorane; ***Malaysia:*** Sevorane; ***Mex.:*** Sevorane; ***Neth.:*** Sevorane; ***Norw.:*** Sevorane; ***NZ:*** Sevorane; ***Philipp.:*** Sevorane; ***Pol.:*** Sevorane; ***Port.:*** Sevorane; ***Rus.:*** Sevoran (Севоран); ***S.Afr.:*** Ultane; ***Singapore:*** Sevorane; ***Spain:*** Sevorane; ***Swed.:*** Sevorane; ***Switz.:*** Sevorane; ***Thai.:*** Sevorane; ***Turk.:*** Sevorane; ***USA:*** Sojourn; Ultane; ***Venez.:*** Sevorane.

Sodium Oxybate *(USAN)*

NSC-84223; Oxibato sódico; Sodium Gamma-hydroxybutyrate; Wy-3478. Sodium 4-hydroxybutyrate.

$C_4H_7NaO_3$ = 126.1.
CAS — 502-85-2.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of sodium oxybate or gamma-hydroxybutyrate:
Blue nitro; Blue verve; Caps; Cherry Meth; Date rape drug; Drogue Du Cambriolage Sexuel Parfait; Easy lay; Everclear; EZLay; Fantasy; G; Gamma Oh; Gamma-OH; GBH; Georgia home boy; GHB; Goop; Great hormones at bedtime; Grievous bodily harm; G-riffic; Jib; Liquid E; Liquid ecstacy; Liquid ecstasy; Liquid G; Liquid X; Organic quaalude; Salty water; Scoop; Sleep; Sleep-500; Soap; Somatomax; Somatomax PM; Vita-G; Water.

Pharmacopoeias. In *Chin.*

Adverse Effects

When used in general anaesthesia adverse effects with sodium oxybate include abnormal muscle movements during the induction period and nausea and vomiting. Occasional emergence delirium has been reported. Bradycardia frequently occurs. Respiration may be slowed and hypokalaemia has been reported.

The most common adverse reactions seen in patients taking sodium oxybate orally for the management of narcolepsy are dizziness, headache, and, particularly in women, nausea. Other common reactions include anorexia, vomiting, diarrhoea, peripheral oedema, abnormal dreams and nightmares, sleepwalking, confusion, depression, anxiety, insomnia, paraesthesia, somnolence, tremor, amnesia, blurred vision, sweating, muscle cramps, nocturnal enuresis, urinary incontinence, asthenia, and fatigue. Blood pressure may also be increased. Psychosis, convulsions, hallucinations, agitation, hypersensitivity, and faecal incontinence are less common; rarely, respiratory depression has been reported.

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

Effects on electrolyte balance. A report of severe metabolic disorders occurring during therapy with sodium oxybate and tetracosactide in 4 patients with severe head injuries.[1] The disorders consisted of hypernatraemia, hypokalaemia, and metabolic acidosis.

1. Béal JL, *et al*. Troubles métaboliques induits par l'association gamma-hydroxy butyrate de sodium et tétracosactide chez le traumatisé crânien. *Therapie* 1983; **38:** 569–71.

Precautions

In general anaesthesia, sodium oxybate should not be given to patients with severe hypertension, bradycardia, conditions associated with defects of cardiac conduction, epilepsy, eclampsia, renal impairment, or alcohol abuse.

Treatment with oral sodium oxybate is contra-indicated in patients with succinic semialdehyde dehydrogenase deficiency, an enzyme involved in its metabolism to succinic acid. Its use is also contra-indicated in patients with epilepsy as safety and efficacy have not been established; convulsions have been reported with sodium oxybate use.

Patients with a history of depression or suicide attempt should be carefully monitored for depressive symptoms while taking sodium oxybate. The high sodium content of sodium oxybate (0.75 g of sodium in a 4.5 g daily dose) should be considered in patients with heart failure, hypertension, or impaired renal function.

Rebound symptoms with an increased frequency of cataplexy may be seen when sodium oxybate is stopped. There has also been rare reports of withdrawal symptoms such as insomnia, headache, dizziness, anxiety, hallucinations, and psychotic disorders following the illicit use of sodium oxybate (see Abuse, below).

See also Precautions for General Anaesthetics, p.1779.

Abuse. Reports[1] of acute poisoning with sodium oxybate following illicit use led the FDA to issue warnings[2] about its potential for abuse. It is usually supplied illicitly as the sodium salt under a variety of names (see above) and has been promoted for body building, weight loss, as a psychedelic substance, and as a sleep aid. Adverse effects include vomiting, drowsiness, amnesia, hypotonia, vertigo, respiratory depression, and involuntary movements. Seizure-like activity, bradycardia, hypotension, and respiratory arrest have also been reported. Resolution of symptoms occurs spontaneously over 2 to 96 hours. However, some patients have required hospitalisation and respiratory support and deaths have been reported in several countries.[3-5] Severity of symptoms depends on the dose of sodium oxybate and the presence of other drugs such as alcohol, benzodiazepines, cannabis, or amfetamines. Prolonged use of large doses may lead to a withdrawal syndrome on discontinuation.[6-8]

There is also a report of CNS depression after ingestion of a chemical derivative, gamma-butyrolactone (GBL).[9] Another derivative, 1,4-butanediol is abused similarly.[7] Withdrawal symptoms have also been associated with discontinuation of these 2 substances in abusers.[8]

1. CDC. Multistate outbreak of poisonings associated with illicit use of gamma hydroxy butyrate. *JAMA* 1991; **265:** 447–8.
2. FDA. Warning about GHB. *JAMA* 1991; **265:** 1802.
3. Anonymous. GBH death indicates increasing problem. *Pharm J* 1996; **256:** 441.
4. CDC. Gamma hydroxy butyrate use—New York and Texas, 1995–1996. *JAMA* 1997; **277:** 1511.
5. Caldicott DGE, *et al*. Fatalities associated with the use of γ-hydroxybutyrate and its analogues in Australasia. *Med J Aust* 2004; **181:** 310–13.
6. Galloway GP, *et al*. Physical dependence on sodium oxybate. *Lancet* 1994; **343:** 57.
7. Rodgers J, *et al*. Liquid ecstasy: a new kid on the dance floor. *Br J Psychiatry* 2004; **184:** 104–6.
8. Wojtowicz JM, *et al*. Withdrawal from gamma-hydroxybutyrate, 1,4-butanediol and gamma-butyrolactone: a case report and systematic review. *CJEM* 2008; **10:** 69–74.
9. LoVecchio F, *et al*. Butyrolactone-induced central nervous system depression after ingestion of RenewTrient, a "dietary supplement". *N Engl J Med* 1998; **339:** 847–8.

Porphyria. Sodium oxybate is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals* or *in-vitro* systems.

Interactions

In anaesthesia, sodium oxybate enhances the effects of opioid analgesics, barbiturates, and competitive neuromuscular blockers. The CNS depressant effects of sodium oxybate may be potentiated by alcohol, sedative-hypnotics, and other CNS depressants. The risk of respiratory depression may also be increased by benzodiazepines.

See also Interactions of General Anaesthetics, p.1779.

Pharmacokinetics

After oral doses sodium oxybate is rapidly but incompletely absorbed from the gastrointestinal tract; absolute bioavailability is about 25%. Peak concentrations are reached within 0.5 to 2 hours. Absorption may be delayed and decreased following a high fat meal. Protein binding is less than 1%. Sodium oxybate is metabolised in the liver via GHB dehydrogenase to succinic semialdehyde, which is then converted to succinic acid via another enzyme, succinic semialdehyde dehydrogenase. Succinic acid enters the Krebs cycle and is metabolised to carbon dioxide, which is expired, and water. Less than 5% of unchanged drug appears in the urine; faecal excretion is also negligible.

◊ References.

1. Palatini P, *et al*. Dose-dependent absorption and elimination of gamma-hydroxybutyric acid in healthy volunteers. *Eur J Clin Pharmacol* 1993; **45:** 353–6.
2. Scharf MB, *et al*. Pharmacokinetics of gammahydroxybutyrate (GHB) in narcoleptic patients. *Sleep* 1998; **21:** 507–14.

Uses and Administration

Sodium oxybate has hypnotic properties and, in its endogenous form, gamma-hydroxybutyrate (a catabolite of gamma-aminobutyric acid), increases dopamine concentrations in the brain. It is given intravenously usually with an opioid analgesic and a neuroleptic to produce general anaesthesia (p.1780). Skeletal muscle relaxants may also be necessary. Sodium oxybate given orally is used in the treatment of cataplexy in patients with narcolepsy; in the USA it is also indicated for the excessive daytime sleepiness associated with narcolepsy.

In general anaesthesia a solution of sodium oxybate equivalent to 20% of the acid is given slowly by intravenous injection, usually in a dose of 60 mg/kg; further smaller doses may be required in long procedures. In children 100 mg/kg may be used.

For the management of narcolepsy in adults, sodium oxybate is given in initial oral doses of 4.5 g daily, as two equally-divided doses. The first dose should be taken at bedtime while in bed and at least 2 to 3 hours after food; the second dose should be taken 2.5 to 4 hours later also while sitting in bed. Both doses should be prepared before going to bed: each dose should be diluted with 60 mL of water. The initial dose may be increased in steps of 1.5 g (0.75 g per dose) every 1 to 2 weeks to a maximum dose of 9 g daily. If therapy has been stopped for more than 14 consecutive days, titration should be restarted at the lowest dose. Reduced doses are recommended in patients with hepatic impairment (see below).

Administration in hepatic impairment. The recommended initial oral dose of sodium oxybate (see above) should be halved in patients with hepatic impairment. Subsequent increases should be monitored against effect.

Alcohol withdrawal syndrome. Gamma-hydroxybutyric acid has been reported[1] to be effective in reducing symptoms of alcohol withdrawal (p.1626) and to be of use as an aid in the maintenance of abstinence.[2,3] However, following reports of CNS toxicity associated with abuse of gamma-hydroxybutyric acid its role in the treatment of substance abuse disorders appears questionable.[4]

1. Gallimberti L, *et al.* Gamma-hydroxybutyric acid for treatment of alcohol withdrawal syndrome. *Lancet* 1989; **ii:** 787–9.
2. Gallimberti L, *et al.* Gamma-hydroxybutyric acid in the treatment of alcohol dependence: a double blind study. *Alcohol Clin Exp Res* 1992; **16:** 673–6.
3. Addolorato G, *et al.* Maintaining abstinence from alcohol with γ-hydroxybutyric acid. *Lancet* 1998; **351:** 38.
4. Quinn DI, *et al.* Pharmacokinetic and pharmacodynamic principles of illicit drug use and treatment of illicit drug users. *Clin Pharmacokinet* 1997; **33:** 344–400.

Narcoleptic syndrome. Sodium oxybate[1-7] given at night is used to improve cataplexy and excessive daytime sleepiness in patients with narcoleptic syndrome (p.2148).

For a reference to the pharmacokinetics of sodium oxybate in narcoleptic patients, see above.

1. Scharf MB, *et al.* The effects and effectiveness of γ-hydroxybutyrate in patients with narcolepsy. *J Clin Psychiatry* 1985; **46:** 222–5.
2. Mamelak M, *et al.* Treatment of narcolepsy with γ-hydroxybutyrate: a review of clinical and sleep laboratory findings. *Sleep* 1986; **9:** 285–9.
3. Scrima L, *et al.* Efficacy of gamma-hydroxybutyrate versus placebo in treating narcolepsy-cataplexy: double-blind subjective measures. *Biol Psychiatry* 1989; **26:** 331–43.
4. US Xyrem Multicenter Study Group. A randomized, double blind, placebo-controlled multicenter trial comparing the effects of three doses of orally administered sodium oxybate with placebo for the treatment of narcolepsy. *Sleep* 2002; **25:** 42–9.
5. US Xyrem Multicenter Study Group. A 12-month, open-label, multicenter extension trial of orally administered sodium oxybate for the treatment of narcolepsy. *Sleep* 2003; **26:** 31–5.
6. Xyrem International Study Group. Further evidence supporting the use of sodium oxybate for the treatment of cataplexy: a double-blind, placebo-controlled study in 228 patients. *Sleep Med* 2005; **6:** 415–21.
7. Lemon MD, *et al.* Sodium oxybate for cataplexy. *Ann Pharmacother* 2006; **40:** 433–40.

Preparations

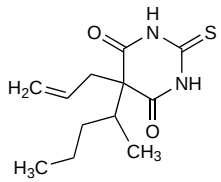
Proprietary Preparations (details are given in Part 3)
Austria: Alcover; ***Cz.:*** Xyrem; ***Fr.:*** Gamma-OH; ***Ger.:*** Somsanit; ***Hung.:*** Alcover†; ***Ital.:*** Alcover; ***Neth.:*** Xyrem; ***Port.:*** Xyrem; ***UK:*** Xyrem; ***USA:*** Xyrem.

Thiamylal Sodium

Tiamilal sódico. Sodium 5-allyl-5-(1-methylbutyl)-2-thiobarbiturate.

$C_{12}H_{17}N_2NaO_2S$ = 276.3.

CAS — 77-27-0 (thiamylal); 337-47-3 (thiamylal sodium).



(thiamylal)

Pharmacopoeias. In *Jpn.*

Profile

Thiamylal sodium is a short-acting intravenous barbiturate anaesthetic. It is possibly slightly more potent than thiopental sodium (p.1796) and has similar actions and uses. It has been used for the production of complete anaesthesia of short duration, for the induction of general anaesthesia, or for inducing a hypnotic state.

Thiopental Sodium *(BANM, rINN)*

Natrium Isopentylaethylthiobarbituricum (cum Natrio Carbonico); Penthiobarbital Sodique; Sodyum Tiopental; Sodyum Tiopenton; Soluble Thiopentone; Thiomebumalnatrium cum Natrii Carbonate; Thiopental et carbonate sodiques; Thiopental Sodique; Thiopental Sodium and Sodium Carbonate; Thiopental sodná sůl a uhličitan sodný; Thiopentalum Natricum; Thiopentalum natricum et natrii carbonas; Thiopentobarbitalum Solubile; Thiopentone Sodium; Tiopentaalinatrium; Tiopentaalinatrium ja natriumkarbonaatti; Tiopental sódico; Tiopentalio natrio druska ir natrio karbonatas; Tiopentalnatrium; Tiopentál-nátrium és nátrium-karbonát; Tiopentalnatrium och natriumkarbonat. Sodium 5-ethyl-5-(1-methylbutyl)-2-thiobarbiturate.

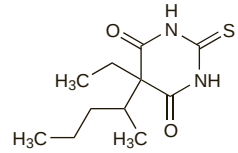
Тиопентал Натрий

$C_{11}H_{17}N_2NaO_2S$ = 264.3.

CAS — 76-75-5 (thiopental); 71-73-8 (thiopental sodium).

ATC — N01AF03; N05CA19.

ATC Vet — QN01AF03; QN05CA19.



(thiopental)

NOTE. The name thiobarbital has been applied to thiopental and has also been used to describe a barbiturate of different composition.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.* Some include thiopental sodium with, some without, anhydrous sodium carbonate; some only include a sterile mixture for injection.

Ph. Eur. 6.2 (Thiopental Sodium and Sodium Carbonate; Thiopental Sodium BP 2008). A yellowish-white hygroscopic powder. It contains 84 to 87% thiopental and 10.2 to 11.2% sodium. Freely soluble in water; partly soluble in dehydrated alcohol. Store in airtight containers. Protect from light.

USP 31 (Thiopental Sodium). A white to off-white crystalline powder, or yellowish-white to pale greenish-yellow hygroscopic powder. May have a disagreeable odour. Its solutions are alkaline to litmus, decompose on standing, and on boiling, precipitation occurs. Soluble in water and in alcohol; insoluble in ether, in petroleum spirit, and in benzene. Store in airtight containers.

Incompatibility. Solutions of thiopental sodium are incompatible with acidic and oxidising substances including some antibacterials, neuromuscular blockers and analgesics. Compounds commonly listed as incompatible include amikacin sulfate, benzylpenicillin salts, cefapirin sodium, codeine phosphate, ephedrine sulfate, fentanyl citrate, glycopyrronium bromide, morphine sulfate, pentazocine lactate, prochlorperazine edisilate, suxamethonium salts, and tubocurarine chloride. Solutions decompose on standing and precipitation occurs on boiling.

Stability. Loss of thiopental in PVC and cellulose propionate delivery systems has been reported,[1,2] but in another study,[3] no loss of potency was noted. Adsorption has been reported[4] not to occur in polyolefin infusion bags.

1. Kowaluk EA, *et al.* Interactions between drugs and polyvinyl chloride infusion bags. *Am J Hosp Pharm* 1981; **38:** 1308–14.
2. Kowaluk EA, *et al.* Interactions between drugs and intravenous delivery systems. *Am J Hosp Pharm* 1982; **39:** 460–7.
3. Martens HJ, *et al.* Sorption of various drugs in polyvinyl chloride, glass, and polyethylene-lined infusion containers. *Am J Hosp Pharm* 1990; **47:** 369–73.
4. Trissel LA, *et al.* Drug compatibility with new polyolefin infusion solution containers. *Am J Health-Syst Pharm* 2006; **63:** 2379–82.

Adverse Effects and Treatment

As for Phenobarbital, p.492.

Excitatory phenomena such as coughing, hiccuping, sneezing, and muscle twitching or jerking may occur with any of the barbiturate anaesthetics, particularly during induction, but they occur more frequently with methohexital than with thiopental. Cough, sneezing, and laryngeal spasm or bronchospasm may also occur during induction. The intravenous injection of concentrated solutions of thiopental sodium such as 5% may result in thrombophlebitis. Extravasation of barbiturate anaesthetics may cause tissue necrosis. Intra-arterial injection causes severe arterial spasm with burning pain and may cause prolonged blanching of the forearm and hand and gangrene of digits. Hypersensitivity reactions have been reported. Barbiturate anaesthetics can cause respiratory depression. They depress cardiac output and often cause an initial fall in blood pressure, and overdosage may result in circulatory failure. Arrhythmias may occur. Postoperative vomiting is infrequent but shivering may occur and there may be persistent drowsiness, confusion, and amnesia. Headache has also been reported.

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

Hypersensitivity. Anaphylactic reactions to thiopental have been reported[1,2] although such reactions are rare. There has also been a report of haemolytic anaemia and renal failure in association with the development of an anti-thiopental antibody in a patient who had undergone general anaesthesia induced by thiopental.[3]

1. Westacott P, *et al.* Anaphylactic reaction to thiopentone: a case report. *Can Anaesth Soc J* 1984; **31:** 434–8.
2. Moneret-Vautrin DA, *et al.* Simultaneous anaphylaxis to thiopentone and a neuromuscular blocker: a study of two cases. *Br J Anaesth* 1990; **64:** 743–5.
3. Habibi B, *et al.* Thiopental-related immune hemolytic anemia and renal failure: specific involvement of red-cell antigen I. *N Engl J Med* 1985; **312:** 353–5. Correction. *ibid.*; 1136.

Intra-arterial injection. Accidental intra-arterial injection of thiopental sodium produces severe arterial spasm with intense burning pain. Anaesthesia, paresis, paralysis, and gangrene may occur. Therapy has concentrated on dilution of injected thiopental, prevention and treatment of arterial spasm, prophylaxis of thrombosis, thrombectomy and other measures to sustain good blood flow. There has been a report[1] of the successful use of urokinase intra-arterially in the management of one patient accidentally given thiopental intra-arterially.

1. Vangerven M, *et al.* A new therapeutic approach to accidental intra-arterial injection of thiopentone. *Br J Anaesth* 1989; **62:** 98–100.

Precautions

Barbiturate anaesthetics are contra-indicated when there is dyspnoea or respiratory obstruction such as in acute severe asthma or when maintenance of an airway cannot be guaranteed.

Barbiturate anaesthetics should be used with caution in shock and dehydration, hypovolaemia, severe anaemia, hyperkalaemia, toxaemia, myasthenia gravis, myxoedema and other metabolic disorders, or in severe renal disease. Caution is also required in patients with cardiovascular disease, muscular dystrophies, adrenocortical insufficiency, or with increased intracranial pressure. Reduced doses are required in the elderly and in severe hepatic disease.

See also Precautions for General Anaesthetics, p.1779.

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

In two groups of 8 women undergoing induction with thiopental, the milk-to-plasma ratio was less than 1 in both groups and it was considered that the effects of thiopental on breast-fed infants would be negligible.[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 26/05/04)
2. Andersen LW, *et al.* Concentrations of thiopentone in mature breast milk and colostrum following an induction dose. *Acta Anaesthesiol Scand* 1987; **31:** 30–2.

Porphyria. Barbiturates including thiopental sodium have been associated with acute attacks of porphyria and are considered unsafe in porphyric patients.

Interactions

Difficulty may be experienced in producing anaesthesia with the usual dose of barbiturate anaesthetics in patients accustomed to taking alcohol or other CNS depressants; additional anaesthetics may be necessary. Patients being treated with phenothiazine antipsychotics may experience increased hypotension. Some phenothiazines, especially promethazine, may also increase the incidence of excitatory phenomena produced by barbiturate anaesthetics; cyclizine may possibly have a similar effect. Opioid analgesics can potentiate the respiratory depressant effect of barbiturate anaesthetics and the dose of the anaesthetic may need to be reduced. Use with nitrous oxide greatly reduces the dose of barbiturate anaesthetics required for