have minimal cardiovascular and histamine-releasing effects. High doses (greater than 900 micrograms/kg of rocuronium bromide) have mild vagolytic activity. It should be used with caution in patients with biliary disease or hepatic or renal impairment.

Hepatic impairment. There have been conflicting reports of the pharmacokinetics and pharmacodynamics of rocuronium in patients with hepatic impairment. In contrast to earlier studies[1,2] one group of workers[3] found a significant reduction in the plasma clearance of rocuronium in patients with cirrhosis. The elimination half-life has been variously reported to be unchanged[1] or prolonged[2,3] with delayed recovery.[3] Some studies[2,3] found that the onset of action was not affected while one group of workers[1] reported a delay.

Licensed product information recommends that care should be taken when giving rocuronium to patients with clinically significant hepatic impairment (see also under Uses and Administration, below).

1. Khalil M, *et al.* Pharmacokinetics and pharmacodynamics of rocuronium in patients with cirrhosis. *Anesthesiology* 1994; **80:** 1241–7.
2. Magorian T, *et al.* The pharmacokinetics and neuromuscular effects of rocuronium bromide in patients with liver disease. *Anesth Analg* 1995; **80:** 754–9.
3. van Miert MM, *et al.* The pharmacokinetics and pharmacodynamics of rocuronium in patients with hepatic cirrhosis. *Br J Clin Pharmacol* 1997; **44:** 139–44.

Hypersensitivity. Although rocuronium is considered to have minimal histamine-releasing effects, histaminoid reactions have been reported[1] on induction of anaesthesia in 3 patients who had been given rocuronium. An increased incidence of severe hypersensitivity reactions (particularly anaphylactic shock) has been reported with rocuronium compared with other neuromuscular blockers available in France.[2] Fatalities have occurred.[3]

See also the discussion of the relative risks of hypersensitivity associated with neuromuscular blockers, under Suxamethonium Chloride, p.1910.

1. Neal SM, *et al.* Histaminoid reactions associated with rocuronium. *Br J Anaesth* 2000; **84:** 108–11.
2. Mayer M. Information importante de pharmacovigilance: Esméron et manifestations allergiques. Available at: http://agmed.sante.gouv.fr/htm/10/filltrpsc/letesmer.pdf (accessed 28/05/04)
3. Baillard C, *et al.* Anaphylaxis to rocuronium. *Br J Anaesth* 2002; **88:** 600–602.

Pain on administration. Severe transient burning pain associated with injection of rocuronium was considered[1] to be responsible for the spontaneous movement sometimes seen in the arm or wrist into which rocuronium is given. It is recommended that rocuronium should be given only when a deep stage of unconsciousness has been achieved.

1. Borgeat A, Kwiatkowski D. Spontaneous movements associated with rocuronium: is pain on injection the cause? *Br J Anaesth* 1997; **79:** 382–3.

Renal impairment. In a study[1] of the pharmacokinetics and neuromuscular effects of rocuronium, the clearance of rocuronium was reduced in patients with renal failure when compared with healthy patients, but the accompanying increase in duration of clinical relaxation did not reach statistical significance. However, it was recommended that rocuronium should be used with caution in the presence of renal failure as there were large interpatient variations in both clinical response and pharmacokinetic parameters. It has been suggested[2] that chronic renal failure may have played a role in the prolongation of neuromuscular blockade in a 47-year-old woman given rocuronium 1 mg/kg. Although this dose is within the recommended adult dose range, it was criticised[3] as being excessive for a patient with renal impairment.

For recommendation that care should be taken when giving rocuronium to patients with renal failure, see under Uses and Administration, below.

1. Cooper RA, *et al.* Time course of neuromuscular effects and pharmacokinetics of rocuronium bromide (ORG 9426) during isoflurane anaesthesia in patients with and without renal failure. *Br J Anaesth* 1993; **71:** 222–6.
2. Lewis KS, *et al.* Prolonged neuromuscular blockade associated with rocuronium. *Am J Health-Syst Pharm* 1999; **56:** 1114–18.
3. Cozanitis DA, Booij HD. Muscle relaxants and renal failure. *Am J Health-Syst Pharm* 2000; **57:** 1713–14.

Interactions

For interactions associated with competitive neuromuscular blockers, see Atracurium, p.1903.

Pharmacokinetics

On intravenous use plasma concentrations of rocuronium follow a three-compartment open model. There is an initial distribution phase with a half-life of 1 to 2 minutes followed by a slower distribution phase with a half-life of 14 to 18 minutes. It is reported to be about 30% bound to plasma proteins. The elimination half-life is about 1.2 to 1.4 hours. Up to 40% of a dose may be excreted in the urine within 24 hours; rocuronium is also excreted in the bile. The main metabolite of rocuronium, 17-desacetylrocuronium, is reported to have a weak neuromuscular blocking effect.

◊ References.

1. Khuenl-Brady KS, Sparr H. Clinical pharmacokinetics of rocuronium bromide. *Clin Pharmacokinet* 1996; **31:** 174–83.
2. McCoy EP, *et al.* Pharmacokinetics of rocuronium after bolus and continuous infusion during halothane anaesthesia. *Br J Anaesth* 1996: **76:** 29–33.
3. Wierda JMKH, *et al.* Pharmacokinetics and pharmacokinetic-dynamic modelling of rocuronium in infants and children. *Br J Anaesth* 1997; **78:** 690–5.
4. Atherton DPL, Hunter JM. Clinical pharmacokinetics of the newer neuromuscular blocking drugs. *Clin Pharmacokinet* 1999; **36:** 169–89.
5. Proost JH, *et al.* Urinary, biliary and faecal excretion of rocuronium in humans. *Br J Anaesth* 2000; **85:** 717–23.

Intensive care. The pharmacokinetics of rocuronium appear to differ between intensive care patients given prolonged dosage and surgical patients.[1] The volume of distribution at steady state may be increased, the plasma clearance decreased, and the terminal half-life prolonged. Recovery time on stopping may also be longer.

1. Sparr HJ, *et al.* Pharmacodynamics and pharmacokinetics of rocuronium in intensive care patients. *Br J Anaesth* 1997; **78:** 267–73.

Pregnancy. The mean concentration of rocuronium in venous plasma of 32 patients given a dose of 600 micrograms/kg before undergoing caesarean section was 2412 nanograms/mL at delivery;[1] the ratio of mean concentrations of rocuronium in umbilical venous plasma to maternal venous plasma at this time was 0.16. In 12 of these patients the mean concentration of rocuronium in umbilical arterial plasma was 271 nanograms/mL giving a ratio of 0.62 for the mean concentration of rocuronium in arterial to venous umbilical plasma. The concentration of 17-desacetylrocuronium in maternal venous plasma was 178 nanograms/mL and was less than 25 nanograms/mL in umbilical plasma.

1. Abouleish E, *et al.* Rocuronium (Org 9426) for Caesarean section. *Br J Anaesth* 1994; **73:** 336–41.

Uses and Administration

Rocuronium bromide is an aminosteroidal competitive neuromuscular blocker (see Atracurium, p.1905). After intravenous injection it produces muscle relaxation within 1 to 2 minutes with a duration of about 30 to 50 minutes. Rocuronium bromide is used for endotracheal intubation and to provide muscle relaxation in general anaesthesia for surgical procedures (see Anaesthesia, p.1900) and to aid controlled ventilation (see Intensive Care, p.1901).

Doses of neuromuscular blockers need to be carefully titrated for individual patients according to response, and may vary with the procedure, the other drugs given, and the state of the patient; monitoring of the degree of block is recommended in order to reduce the risk of overdosage. A usual initial dose is 600 micrograms/kg by intravenous injection; however, higher doses of 1 mg/kg are recommended for intubation during rapid sequence induction of anaesthesia. Usual maintenance doses are 150 micrograms/kg by injection, although these should be reduced to 75 to 100 micrograms/kg if prolonged inhalational anaesthesia is planned. Maintenance may also be by infusion at a rate of 300 to 600 micrograms/kg per hour although higher rates have been used in the USA. Similar doses to those used in adults have been used in the UK in infants and children older than one month but maintenance doses may be required more frequently. In the USA, rocuronium is licensed for use in children aged 3 months and over; again doses are similar to those used in adults.

For obese patients weighing more than 30% over their ideal body-weight UK licensed product information recommends that doses should be calculated according to lean body-mass; in the USA it is recommended that dosage should be based on actual body-weight. UK product information also recommends reduced maintenance doses of 75 to 100 micrograms/kg by injection in the elderly. For doses in hepatic or renal impairment, see below.

◊ Reviews and discussions.

1. Mirakhur RK. Newer neuromuscular blocking drugs: an overview of their clinical pharmacology and therapeutic use. *Drugs* 1992; **44:** 182–9.
2. Hunter JM. Rocuronium: the newest aminosteroid neuromuscular blocking drug. *Br J Anaesth* 1996; **76:** 481–3.

Administration in children. In a study involving 70 children, conditions for intubation were judged to be good to excellent within one minute of intravenous doses of rocuronium 600 or 900 micrograms/kg, with a trend to better conditions with the higher dose.[1]

1. Fuchs-Buder T, Tassonyi E. Intubating conditions and time course of rocuronium-induced neuromuscular block in children. *Br J Anaesth* 1996; **77:** 335–8.

INTRAMUSCULAR ROUTE. Intramuscular injection of rocuronium 1 mg/kg into the deltoid muscle permitted tracheal intubation to be carried out in lightly anaesthetised infants after 2.5 minutes.[1] In children a dose of 1.8 mg/kg enabled tracheal intubation after 3 minutes. However, the mean time to initial recovery after these large doses was 57 minutes in infants and 70 minutes in children. This prolonged duration of action may limit intramuscular use for brief procedures, particularly in children.

1. Reynolds LM, *et al.* Intramuscular rocuronium in infants and children: dose-ranging and tracheal intubating conditions. *Anesthesiology* 1996; **85:** 231–9.

Administration in hepatic or renal impairment. UK licensed product information recommends a reduced maintenance dose of 75 to 100 micrograms/kg in patients with hepatic or biliary-tract disease, or renal failure. Initial doses remain unaltered.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Zemuron†; ***Austral.:*** Esmeron; ***Austria:*** Esmeron; ***Belg.:*** Esmeron; ***Braz.:*** Esmeron; Rocuron; ***Canad.:*** Zemuron; ***Chile:*** Esmeron; ***Cz.:*** Esmeron; ***Denm.:*** Esmeron; ***Fin.:*** Esmeron; ***Fr.:*** Esmeron; ***Ger.:*** Esmeron; ***Gr.:*** Esmeron; ***Hong Kong:*** Esmeron; ***Hung.:*** Esmeron; ***Indon.:*** Esmeron; Roculax; ***Irl.:*** Esmeron; ***Israel:*** Esmeron; ***Ital.:*** Esmeron; ***Jpn:*** Eslax; ***Malaysia:*** Esmeron; ***Mex.:*** Esmeron; ***Neth.:*** Esmeron; ***Norw.:*** Esmeron; ***NZ:*** Esmeron; ***Philipp.:*** Esmeron; ***Pol.:*** Esmeron; ***Port.:*** Esmeron; ***Rus.:*** Esmeron (Эсмерон); ***S.Afr.:*** Esmeron; ***Singapore:*** Esmeron; ***Spain:*** Esmeron; ***Swed.:*** Esmeron; ***Switz.:*** Esmeron; ***Thai.:*** Esmeron; ***Turk.:*** Esmeron; ***UK:*** Esmeron; ***USA:*** Zemuron; ***Venez.:*** Esmeron.

Suxamethonium Chloride *(BAN, pINN)*

Choline Chloride Succinate; Cloruro de suxametonio; Succicurarium Chloride; Succinylcholine Chloride; Suksametonio chloridas; Suksametoniowy chlorek; Suksametoniumkloridi; Süksinilkolin Klorür; Suxamethonii chloridum; Suxamethonii Chloridum Dihydricum; Suxamethonium chlorid dihydrát; Suxaméthonium, chlorure de; Suxametoniumklorid; Suxametonklorid; Szuxametóniumklorid. 2,2′-Succinyldioxybis(ethyltrimethylammonium) dichloride dihydrate.

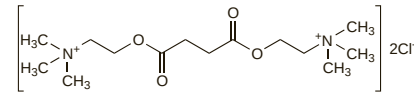
Суксаметония Хлорид

$C_{14}H_{30}Cl_2N_2O_4,2H_2O$ = 397.3.

CAS — 306-40-1 (suxamethonium); 55-94-7 (suxamethonium bromide); 71-27-2 (anhydrous suxamethonium chloride); 6101-15-1 (suxamethonium chloride dihydrate); 541-19-5 (suxamethonium iodide).

ATC — M03AB01.

ATC Vet — QM03AB01.



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

Ph. Eur. 6.2 (Suxamethonium Chloride). A white or almost white, hygroscopic, crystalline powder. Freely soluble in water; slightly soluble in alcohol. A 0.5% solution in water has a pH of 4.0 to 5.0. Protect from light.

USP 31 (Succinylcholine Chloride). A white, odourless, crystalline powder. The anhydrous form is hygroscopic. Soluble 1 in 1 of water and 1 in 350 of alcohol; slightly soluble in chloroform; practically insoluble in ether. Its solutions in water have a pH of about 4. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Incompatibility. Incompatibilities of neuromuscular blockers are discussed under Atracurium, p.1902.

Stability. A study of the loss of potency of suxamethonium chloride 20 mg/mL in water indicated that decomposition occurred at a considerably higher rate at 40° than at 25° and that the pH range of maximum stability was 3.75 to 4.50 for unbuffered solutions.[1] Assuming the usual conditions of manufacturing, transit, and storage the total loss of potency was estimated to be 7% and 9% respectively for injections kept at room temperature for 4 and 6 weeks. If unbuffered, suxamethonium chloride injection complying with USP 31 pH limits (3.0 to 4.5) must be stored at room temperature; it should not be kept for longer than 4 weeks.

1. Boehm JJ, *et al.* Shelf life of unrefrigerated succinylcholine chloride injection. *Am J Hosp Pharm* 1984; **41:** 300–2.

Adverse Effects

The neuromuscular blocking action of suxamethonium chloride is terminated by the enzyme plasma cholinesterase and prolonged apnoea may occur in patients with an atypical enzyme or with low enzyme activity. Apnoea may also occur following development of phase II block (see Uses and Administration, below) after high or repeated doses of suxamethonium chloride, although tachyphylaxis may also occur with repeated doses.

Transient fasciculations occur during the onset of depolarising block. Rhabdomyolysis, myoglobinae-

mia, and myoglobinuria have been reported and may be associated with muscle damage following fasciculations. Postoperative muscle pain occurs in some patients but is not directly related to the degree of fasciculation. A transient rise in intra-gastric pressure may occur secondary to fasciculation of abdominal muscles. A transient increase in intra-ocular pressure often occurs. Depolarisation of skeletal muscle produces an immediate increase in plasma-potassium concentration and this can have serious consequences in some patients (see below).

Stimulation of the vagus nerve and parasympathetic ganglia by suxamethonium chloride may be followed by bradycardia, other arrhythmias, and hypotension, and may be exacerbated by the raised plasma-potassium concentration; cardiac arrest has been reported. Tachycardia and an increase in blood pressure due to stimulation of sympathetic ganglia have also been reported.

Suxamethonium chloride may cause an increase in salivary, bronchial, and gastric secretion and other muscarinic effects. Salivary gland enlargement has occurred.

Direct release of histamine from mast cells occurs but this is not the main mechanism of hypersensitivity reactions (see Hypersensitivity, below). Flushing, skin rash, bronchospasm, and shock have been reported.

Other reported effects include prolonged respiratory depression and apnoea.

Suxamethonium chloride is implicated in the development of malignant hyperthermia (p.1896) in those patients with a genetic predisposition to the syndrome.

◊ Reviews.

1. Book WJ, *et al.* Adverse effects of depolarising neuromuscular blocking agents: incidence, prevention and management. *Drug Safety* 1994; **10:** 331–49.
2. Orebaugh SL. Succinylcholine: adverse effects and alternatives in emergency medicine. *Am J Emerg Med* 1999; **17:** 715–21.

Effects on intra-ocular pressure. Doses of suxamethonium are often followed 20 to 30 seconds later by a transient increase in intra-ocular pressure, which may be due in part to contracture of extra-ocular muscles. If suxamethonium is used during eye surgery after incision of the eyeball or in patients with a penetrating eye injury, there is a theoretical risk that any increase in intra-ocular pressure may result in extrusion of ocular contents and loss of sight. However, there appear to be few reports of vitreous extrusion associated with suxamethonium,[1] and a large retrospective study[2] has failed to find any evidence that suxamethonium caused additional eye damage in patients with penetrating eye injuries. Furthermore, the procedure of intubation itself is associated with a greater increase in intra-ocular pressure than that seen with suxamethonium. Nonetheless, some suggest that a rapid competitive neuromuscular blocker would be preferable to aid intubation in patients with penetrating eye injuries, after incision of the eyeball, and in glaucoma, although others consider that the risk of a transient rise of intra-ocular pressure in these situations should be weighed against the need for rapid intubation.[1,3] For a discussion on the use of various drugs to counteract the rise in intra-ocular pressure associated with suxamethonium and intubation in general, see under Anaesthesia, p.1900.

1. Book WJ, *et al.* Adverse effects of depolarising neuromuscular blocking agents: incidence, prevention and management. *Drug Safety* 1994; **5:** 331–49.
2. Libonati MM, *et al.* The use of succinylcholine in open eye surgery. *Anesthesiology* 1985; **62:** 637–40.
3. Edmondson L. Intraocular pressure and suxamethonium. *Br J Anaesth* 1997; **79:** 146.

Effects on the muscles. Muscle fasciculations and postoperative muscle pain commonly follow use of suxamethonium. **Fasciculations** (generalised and desynchronised contractions of skeletal muscle fibres) occur during the onset of depolarising block in almost all patients given suxamethonium and may cause muscle damage. They are seen especially in the 'fine' muscles of the hands and face, and can be useful as an indication that suxamethonium is working. Attempts have been made to prevent their development with the aim of reducing postoperative muscle pain. However, there appears to be no direct correlation between the extent of visible fasciculations and muscle pain.[1,2] Slow infusion of suxamethonium[3] or giving divided doses[4] reduces fasciculations but not muscle pain.

Postoperative **muscle pain** is one of the most common adverse effects of suxamethonium and has been noted in about 50% of patients, although the reported incidence varies widely from around 1.5 to about 90%.[2] It usually occurs on the first postoperative day and lasts for 2 or 3 days, and most often affects muscles of the neck, shoulders, and upper abdomen.[2] The incidence and severity of muscle pain is increased in patients who are mobile soon after surgery and in females, but it occurs less often in children, pregnant women, and the elderly.[2]

The mechanism of suxamethonium-induced muscle pain is not fully understood; there have been many attempts to prevent it. Pretreatment with a small dose of a competitive neuromuscular blocker reduces both visible fasciculations and the incidence and severity of muscle pain,[1,2,5-8] but may delay the onset and alter the intensity of subsequent suxamethonium block[9] and impair conditions for intubation[1,9] (see Neuromuscular Blockers, under Interactions in Atracurium, p.1905). In addition, larger doses of suxamethonium are required;[10] consequently the practice is considered controversial by some authors.[10,11] Pretreatment with a small dose (10 mg) of suxamethonium in a 'self-taming' technique appears to offer no protection against muscle pain.[1,2] The choice of anaesthetic induction agent has been suggested to be significant, as has the timing of doses, but despite claims for benefit with, for example, propofol, this remains questionable.[2] Pretreatment with benzodiazepines or NSAIDs has produced conflicting results.[2] Other drugs that have been tried include lidocaine, calcium gluconate, and vitamin C; there is some evidence that lidocaine may be the most effective pretreatment.[2] Not all methods have concentrated on drug treatment. A simple regimen of stretching exercises before premedication has reduced the incidence of both fasciculations and postoperative muscle pain.[12]

Suxamethonium may also produce an increase in **jaw tension** (masseter spasm or trismus)[13] in both adults[14] and children[15,16] during the onset of neuromuscular blockade. Tracheal intubation is greatly hindered in affected patients. It is not possible to predict which patients will show this response and the mechanism is unknown, although in about 50% of patients it may indicate the onset of malignant hyperthermia. Pretreatment with a paralysing dose of a competitive neuromuscular blocker prevents the response[16] but it is not known whether this is clinically useful.

1. O'Sullivan EP, *et al.* Differential effects of neuromuscular blocking agents on suxamethonium-induced fasciculations and myalgia. *Br J Anaesth* 1988; **60:** 367–71.
2. Wong SF, Chung F. Succinylcholine-associated postoperative myalgia. *Anaesthesia* 2000; **55:** 144–52.
3. Feingold A, Velazquez JL. Suxamethonium infusion rate and observed fasciculations: a dose-response study. *Br J Anaesth* 1979; **51:** 241–5.
4. Wilson DB, Dundee JW. Failure of divided doses of succinylcholine to reduce the incidence of muscle pains. *Anesthesiology* 1980; **52:** 273–5.
5. Bennetts FE, Khalil KI. Reduction of post-suxamethonium pains by pretreatment with four non-depolarising agents. *Br J Anaesth* 1981; **53:** 531–6.
6. Erkola O, *et al.* Five non-depolarizing muscle relaxants in precurarization. *Acta Anaesthesiol Scand* 1983; **27:** 427–32.
7. Sosis M, *et al.* Comparison of atracurium and d-tubocurarine for prevention of succinylcholine myalgia. *Anesth Analg* 1987; **66:** 657–9.
8. Findlay GP, Spittal MJ. Rocuronium pretreatment reduces suxamethonium-induced myalgia: comparison with vecuronium. *Br J Anaesth* 1996; **76:** 526–9.
9. Pauca AL, *et al.* Inhibition of suxamethonium relaxation by tubocurarine and gallamine pretreatment during induction of anaesthesia in man. *Br J Anaesth* 1975; **47:** 1067–73.
10. McManus CM. Neuromuscular blockers in surgery and intensive care, part 2. *Am J Health-Syst Pharm* 2001; **58:** 2381–99.
11. Mencke T, *et al.* Pretreatment before succinylcholine for outpatient anesthesia? *Anesth Analg* 2002; **94:** 573–6.
12. Magee DA, Robinson RJS. Effect of stretch exercises on suxamethonium induced fasciculations and myalgia. *Br J Anaesth* 1987; **59:** 596–601.
13. Saddler JM. Jaw stiffness—an ill understood condition. *Br J Anaesth* 1991; **67**: 515–16.
14. Leary NP, Ellis FR. Masseteric muscle spasm as a normal response to suxamethonium. *Br J Anaesth* 1990; **64:** 488–92.
15. Van Der Spek AFL, *et al.* Changes in resistance to mouth opening induced by depolarizing and non-depolarizing neuromuscular relaxants. *Br J Anaesth* 1990; **64:** 21–7.
16. Smith CE, *et al.* Pretreatment with non-depolarizing neuromuscular blocking agents and suxamethonium-induced increases in resting jaw tension in children. *Br J Anaesth* 1990; **64:** 577–81.

Effects on plasma-potassium concentration. Suxamethonium causes depolarisation of motor end-plates in skeletal muscle, resulting in an immediate increase in plasma-potassium concentration. The rise is usually small, being about 0.5 mmol or less per litre, but suxamethonium is best avoided in patients whose plasma-potassium concentration is already high, such as those with renal impairment. An exaggerated response, with severe hyperkalaemia resulting in ventricular fibrillation and cardiac arrest, has been reported in patients with burns,[1,2] massive trauma, closed head injury, neuromuscular disease (see Neuromuscular Disorders, under Precautions, below), and severe long-lasting sepsis.[3] See also Children, under Precautions, below for reference to fatal cardiac arrest associated with hyperkalaemia in children. With burns or trauma the period of greatest risk is from about 10 to 90 days after the injury, but may be further prolonged if there is delayed healing or persistent infection. These patients may still react abnormally to suxamethonium 2 years after the injury. In neuromuscular disease the greatest risk period is usually from 3 weeks to 6 months after onset, but severe hyperkalaemia may occur after 24 to 48 hours or later than 6 months. Patients with severe sepsis for more than a week should be considered at risk of hyperkalaemia and suxamethonium should not be given until the infection has cleared. The mechanism of this hyperkalaemic response appears to be a supersensitivity of acetylcholine receptors in which the entire muscle fibre membrane, rather than discrete motor end-plate sites, becomes directly excitable by depolarising drugs. Depolarisation by suxamethonium thus results in release of potassium over the entire muscle fibre membrane and hyperkalaemia results.

Various methods have been tried to attenuate the hyperkalaemia, including pretreatment with a small dose of a competitive neuromuscular blocker[3,4] or with suxamethonium itself.[5,6] No method is reliable enough to be used clinically.

Anaesthetics such as thiopental and halothane can increase the hyperkalaemic response.[4]

1. Martyn J, *et al.* Clinical pharmacology of muscle relaxants in patients with burns. *J Clin Pharmacol* 1986; **26:** 680–5.
2. Anonymous. Neuromuscular blockers in patients with burns. *Lancet* 1988; **ii:** 1003–4.
3. Kohlschütter B, *et al.* Suxamethonium-induced hyperkalaemia in patients with severe intra-abdominal infections. *Br J Anaesth* 1976; **48:** 557–62.
4. Dhanaraj VJ, *et al.* A study of the changes in serum potassium concentration with suxamethonium using different anaesthetic agents. *Br J Anaesth* 1975; **47:** 516–19.
5. Magee DA, Gallagher EG. "Self-taming" of suxamethonium and serum potassium concentration. *Br J Anaesth* 1984; **56:** 977–9.
6. Plötz J, Schreiber W. Side effects induced by suxamethonium on the skeletal muscle and their prevention. *Br J Anaesth* 1985; **57:** 1044–5.

Hypersensitivity. Hypersensitivity reactions to neuromuscular blockers are more common in women than in men,[1,2] in atopic patients and those who have a history of asthma or allergy,[2] and in patients who have had a previous reaction to anaesthetic drugs.[2] Circulatory collapse, flushing, skin rash, urticaria, and bronchospasm have occurred in hypersensitivity reactions associated with suxamethonium;[1,3,4] deaths have been reported.[3,5]

Data from intradermal testing has been used to qualify the **risk** of allergic reactions associated with the neuromuscular blockers:[6]

- benzylisoquinolinium blockers *alcuronium* and *tubocurarine* and the depolarising blocker *suxamethonium* were considered to be associated with the highest risk
- benzylisoquinolinium blockers *atracurium*, *cisatracurium*, *gallamine*, and *mivacurium* and the aminosteroid *rocuronium* presented an intermediate risk
- the aminosteroids *pancuronium* and *vecuronium* were considered to have the lowest risk

A type I immediate hypersensitivity reaction involving IgE antibodies is considered to be the **mechanism** of most hypersensitivity reactions associated with neuromuscular blockers.[2,5,7,8] Antibodies reacting with neuromuscular blockers, including suxamethonium, have been demonstrated.[5,8] The antibodies appear to be directed against quaternary or tertiary ammonium-ion groups which are present in neuromuscular blockers; such groups are also found in other drugs, cosmetics, disinfectants, and foods. This may help explain the cross-reactivity reported between different neuromuscular blockers[1,2,5,8,9] and how sensitisation occurs without prior exposure to any neuromuscular blocker.[2,5] At least 50% of patients sensitive to one neuromuscular blocker will react to one or more others[10] with some patients sensitive to most.[1] Intradermal skin tests are used to investigate and predict sensitivity to neuromuscular blockers, but their interpretation is controversial and it cannot be concluded that all patients with positive skin tests will have clinical sensitivity.[1,10] Although radioallergosorbent tests can detect antibodies to suxamethonium, alcuronium, and thiopental[3,11] some consider that their routine use is not justified as reactions could be avoided by taking an adequate patient history.[12]

However, neuromuscular blockers also have a direct effect on mast cells, releasing histamine without immunological involvement, and could cause anaphylactoid reactions. Histamine release associated with use of aminosteroidal blockers is rare compared with the benzylisoquinolinium blockers.[13] Tubocurarine is considered to be the most potent releaser of histamine, with pancuronium and vecuronium having only very weak activity. Suxamethonium is considered to have only 1% of the histamine-releasing activity of tubocurarine but is more likely to produce serious hypersensitivity reactions.

1. Youngmen PR, *et al.* Anaphylactoid reactions to neuromuscular blocking agents: a commonly undiagnosed condition? *Lancet* 1983; **ii:** 597–9.
2. Fisher MM, Munro I. Life-threatening anaphylactoid reactions to muscle relaxants. *Anesth Analg* 1983; **62:** 559–64.
3. Brahams D. Fatal reaction to suxamethonium: case for screening by radioallergosorbent test? *Lancet* 1989; **i:** 1400–1.
4. 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.
5. Fisher M, Baldo B. Adverse reactions to alcuronium: an Australian disease? *Med J Aust* 1983; **1:** 630–2.
6. Rose M, Fisher M. Rocuronium: high risk for anaphylaxis? *Br J Anaesth* 2001; **86:** 678–82.
7. Vervloet D. Anaphylactoid reactions to suxamethonium. *Lancet* 1983; **ii:** 1197.
8. Harle DG, *et al.* Detection of IgE antibodies to suxamethonium after anaphylactoid reactions during anaesthesia. *Lancet* 1984; **I:** 930–2.
9. Harle DG, *et al.* Cross-reactivity of metocurine, atracurium, vecuronium and fazadinium with IgE antibodies from patients unexposed to these drugs but allergic to other myoneural blocking drugs. *Br J Anaesth* 1985; **57:** 1073–6.
10. Withington DE. Relevance of histamine to the anaesthetist. *Br J Hosp Med* 1988; **40:** 264–70.
11. Assem ESK. Anaphylactic anaesthetic reactions: the value of paper radioallergosorbent tests for IgE antibodies to muscle relaxants and thiopentone. *Anaesthesia* 1990; **45:** 1032–8.
12. Noble DW, Yap PL. Screening for antibodies to anaesthetics. *BMJ* 1989; **299:** 2.
13. Naguib M, *et al.* Histamine-release haemodynamic changes produced by rocuronium, vecuronium, mivacurium, atracurium and tubocurarine. *Br J Anaesth* 1995; **75:** 588–92.

Treatment of Adverse Effects

Once suxamethonium chloride has been given assisted respiration should be maintained until spontaneous respiration has been fully restored. Transfusion of fresh frozen plasma or other source of plasma cholinesterase will help the destruction of the suxamethonium when

prolonged paralysis is a result of atypical or low serum concentrations of plasma cholinesterase. Anticholinesterases should not normally be used since they potentiate the usual phase I block (see Uses and Administration, below). If the neuromuscular block ceases to be depolarising in type and acquires some features of a competitive block (phase II block) the cautious use of an anticholinesterase may be considered. A short-acting anticholinesterase such as edrophonium may be given intravenously and if an obvious improvement is maintained for several minutes, neostigmine may be given with atropine.

Severe hypersensitivity reactions should be treated promptly with supportive and symptomatic measures.

If malignant hyperthermia develops, it may be treated as described on p.1896.

The muscarinic effects of suxamethonium chloride, such as bradycardia and excessive salivary secretion, may be reduced by giving an antimuscarinic such as atropine before suxamethonium. A small dose of a competitive neuromuscular blocker given before suxamethonium has been used to reduce some of the adverse effects of suxamethonium on the muscles (see Effects on the Muscles, above).

Precautions

Patients given a neuromuscular blocker should always have their respiration assisted or controlled until the drug has been inactivated or antagonised.

Suxamethonium chloride is contra-indicated in patients with atypical plasma cholinesterase and should be used with caution in patients with reduced plasma cholinesterase activity (see below), which may occur in certain disease states and following exposure to certain drugs. Plasma cholinesterase concentrations fall during pregnancy and the puerperium and therefore maternal paralysis may be mildly prolonged. Suxamethonium is contra-indicated in patients with burns, massive trauma, renal impairment with a raised plasma-potassium concentration, severe long-lasting sepsis, and severe hyperkalaemia, since suxamethonium-induced rises in plasma-potassium concentration can have serious consequences in such patients; patients who have been immobilised for prolonged periods may be at similar risk. It is contra-indicated in patients with a history of hypersensitivity to the drug and, because high rates of cross-sensitivity have been reported (see above), should be used with caution when hypersensitivity to any neuromuscular blocker has previously occurred. Suxamethonium should be avoided in patients with a penetrating eye injury, raised intra-ocular pressure or glaucoma, or those about to undergo incision of the eyeball in eye surgery, because of the risks from increased intra-ocular pressure (although see under Adverse Effects, above). Suxamethonium chloride produces muscle contractions before relaxation and should therefore be used with caution in patients with bone fractures. It is contra-indicated in patients with a personal or family history of malignant hyperthermia.

The response to suxamethonium chloride is often unpredictable in patients with neuromuscular disorders and it should be used with great caution in these patients (see below). Caution is also needed if it is given to a patient with cardiac or respiratory disease. Children may be at special risk from cardiac arrest associated with hyperkalaemia (see below).

Hypothermia may enhance the neuromuscular blocking effects of suxamethonium chloride and an increase in body temperature may reduce them.

Children. Reports of fatal cardiac arrests[1,2] in apparently healthy children and adolescents, who were subsequently found to have had undiagnosed myopathies, led to restrictions in the USA on the use of suxamethonium in this age group. Suxamethonium was contra-indicated except for emergency tracheal intubation or where an immediate securing of an airway was essential. Many anaesthetists disagreed[2] with this contra-indication and an FDA Committee advised[3] that it should be replaced by a warning about the possibility of cardiac arrest associated with hyperkalaemia with special attention being paid to male children who are considered to be at the highest risk. One British anaesthetist who questioned the rationale behind restricting the elective use of suxamethonium pointed out that alternatives to suxamethonium had not been shown to be as safe or effective for airway management.[4] The rare occurrence of cardiac arrest in children might be further reduced by taking a careful family history to exclude undiagnosed myopathies and by using an intravenous as opposed to inhalation induction when suxamethonium is to be used.[4] A survey had found that most cases of cardiac arrest in children in the UK associated with the use of suxamethonium had been caused by vagal overactivity in non-atropinised patients.

1. Rosenberg H, Gronert GA. Intractable cardiac arrest in children given succinylcholine. *Anesthesiology* 1992; **77:** 1054.
2. Book WJ, *et al.* Adverse effects of depolarising neuromuscular blocking agents: incidence, prevention and management. *Drug Safety* 1994; **10:** 331–49.
3. *FDC Reports Pink Sheet* 1994; June 13: 16.
4. Hopkins PM. Use of suxamethonium in children. *Br J Anaesth* 1995; **75:** 675–7.

Neuromuscular disorders. Caution is needed if suxamethonium is to be given to patients with neuromuscular disease, since severe complications have been reported.[1] Hyperkalaemia and cardiac arrhythmias or cardiac arrest have been reported after use of suxamethonium in patients with hemiplegia, diffuse intracranial lesions (head injury, encephalitis, ruptured cerebral aneurysm), tetanus, paraplegia, acute anterior horn cell disease, and muscular dystrophies. An exaggerated response to suxamethonium has been reported in the myasthenic syndrome but resistance may occur in patients with neurofibromatosis. Resistance may also occur in patients with myasthenia gravis, but uneventful use has also been reported, although early onset of phase II block is possible in these patients. Muscle contractures and hyperkalaemia may be expected in amyotrophic lateral sclerosis and muscular denervation. Suxamethonium should be avoided in patients with myotonias, as response is unpredictable. It is recommended that suxamethonium is also avoided in hemiplegia, paraplegia, muscular denervation, and muscular dystrophies.

1. Azar I. The response of patients with neuromuscular disorders to muscle relaxants: a review. *Anesthesiology* 1984; **61:** 173–87.

Plasma cholinesterase deficiency. Suxamethonium is normally rapidly hydrolysed by plasma cholinesterase and the clinical effects usually last for only several minutes. Activity of the enzyme varies between individuals and prolonged paralysis following suxamethonium is commonly due to a hereditary or acquired reduction in plasma cholinesterase activity. The genes involved in the control of plasma cholinesterase production are termed usual, atypical (dibucaine-resistant), fluoride-resistant, and silent. About 96% of the population are homozygous for the usual gene. The commonest variant in western populations is the atypical form with about 3 to 4% of the population being heterozygous for this variant. They exhibit a slightly prolonged response to suxamethonium. Homozygotes for the atypical variant have a frequency of about 0.04%. They exhibit markedly prolonged apnoea following a standard dose of suxamethonium but can be readily identified by biochemical tests. The fluoride-resistant and silent variants occur very rarely. A measure of plasma cholinesterase activity can be obtained from the percentage inhibition of the enzyme by the local anaesthetic cinchocaine (commonly known in this context by its American name, dibucaine) to give the **dibucaine number**. Most normal people have a dibucaine number of about 80.

Acquired plasma cholinesterase deficiency is clinically less important than genetically determined deficiency. The enzyme is synthesised in the liver and **severe liver impairment** or malnutrition may cause abnormally low enzyme levels with some prolongation of suxamethonium activity. Reduced enzyme activity may also be found in severe anaemia, burns, cancer, collagen diseases, severe dehydration, severe infections, malnutrition, myocardial infarction, myxoedema, and renal impairment; plasmapheresis or plasma exchange removes significant amounts of plasma cholinesterase.

During **pregnancy** there is a rapid fall in plasma cholinesterase concentration that persists throughout pregnancy and for up to several weeks into the puerperium. The concentration of atypical plasma cholinesterase is also reduced in pregnancy and the puerperium. A number of **drugs** reduce plasma cholinesterase synthesis or activity and may prolong suxamethonium paralysis as discussed under Interactions, below.

References.

1. Wood GJ, Hall GM. Plasmapheresis and plasma cholinesterase. *Br J Anaesth* 1978; **50:** 945–9.
2. Evans RT, Wroe JM. Plasma cholinesterase changes during pregnancy: their interpretation as a cause of suxamethonium-induced apnoea. *Anaesthesia* 1980; **35:** 651–4.
3. Lumley J. Prolongation of suxamethonium following plasma exchange. *Br J Anaesth* 1980; **52:** 1149–50.
4. Williams FM. Clinical significance of esterases in man. *Clin Pharmacokinet* 1985; **10:** 392–403.
5. Robson N, *et al.* Plasma cholinesterase changes during the puerperium. *Anaesthesia* 1986; **41:** 243–9.
6. Cherala SR, *et al.* Placental transfer of succinylcholine causing transient respiratory depression in the newborn. *Anaesth Intensive Care* 1989; **17:** 202–4.

Renal impairment. Suxamethonium chloride may be given in usual doses to patients with renal failure[1,2] although it is usually recommended that it should be avoided if hyperkalaemia is also present (see Effects on Plasma-potassium Concentration above). However, in a retrospective review[3] of 38 patients with serum potassium levels greater than 5.5 mmol/litre given a standard intubation dose of suxamethonium, there were no reports of dysrhythmias or unexpected admissions to the intensive care unit.

Patients with renal failure given repeated doses of suxamethonium did not show an excessive increase in serum potassium; however sinus bradycardia commonly occurred and it was recommended that repeated injections should be avoided in such patients.[2] If necessary, pretreatment with glycopyrrolate or atropine to protect against bradycardia should be considered.

1. Ryan DW. Preoperative serum cholinesterase concentration in chronic renal failure. *Br J Anaesth* 1977; **49:** 945–9.
2. Thapa S, Brull SJ. Succinylcholine-induced hyperkalemia in patients with renal failure: an old question revisited. *Anesth Analg* 2000; **91:** 237–41.
3. Schow AJ, *et al.* Can succinylcholine be used safely in hyperkalemic patients? *Anesth Analg* 2002; **95:** 119–22.

Interactions

A number of drugs may interact with depolarising neuromuscular blockers such as suxamethonium. The mechanisms of interaction can include a direct effect on neuromuscular transmission or an alteration of enzyme activity and may result in potentiation or antagonism of neuromuscular block. In general, such interactions are potentially more serious in patients with impaired neuromuscular function or reduced activity of plasma cholinesterase, who are more sensitive to suxamethonium's effects.

Interactions common to competitive and depolarising neuromuscular blockers are covered under Atracurium, p.1903 whereas those specific for depolarising blockers are discussed below.

Antiarrhythmics. See under Atracurium, p.1903.

Antibacterials. See under Atracurium, p.1903.

Anticholinesterases. The action of suxamethonium may be markedly prolonged in patients using eye drops containing *ecothiopate*, a long-acting anticholinesterase that inhibits both acetylcholinesterase and plasma cholinesterase. After systemic absorption of ecothiopate, plasma cholinesterase activity may rapidly be reduced to 5% or less of normal and prolonged apnoea after use of suxamethonium has occurred. On stopping ecothiopate, enzyme activity remains depressed for 1 to 2 months. If a patient has used ecothiopate eye drops in the previous 2 months, suxamethonium should not be given unless normal plasma cholinesterase activity can be demonstrated; a competitive neuromuscular blocker is preferable. Exposure to *organophosphorus insecticides* may also reduce plasma cholinesterase activity resulting in prolonged paralysis after use of suxamethonium; enzyme activity may be totally abolished. Anticholinesterases including *edrophonium*, *neostigmine*, *pyridostigmine*, *rivastigmine*, *tacrine*, and possibly *donepezil* enhance the action of suxamethonium, although suxamethonium-induced phase II block can be reversed with an anticholinesterase. Care should be taken if there is a need to use suxamethonium for urgent short procedures after a competitive-neuromuscular-induced block has been antagonised with an anticholinesterase, as the resulting block may be greatly prolonged.[1]

1. Fleming NW, *et al.* Neuromuscular blocking action of suxamethonium after antagonism of vecuronium by edrophonium, pyridostigmine or neostigmine. *Br J Anaesth* 1996; **77:** 492–5.

Antiepileptics. The mean time to recovery from suxamethonium-induced neuromuscular block was 14.3 minutes in 9 patients receiving chronic treatment with *phenytoin* and/or *carbamazepine* compared with 10.0 minutes in 9 patients not receiving antiepileptics.[1]

1. Melton AT, *et al.* Prolonged duration of succinylcholine in patients receiving anticonvulsants: evidence for mild upregulation of acetylcholine receptors? *Can J Anaesth* 1993; **40:** 939–42.

Antineoplastics. *Cyclophosphamide* has been reported to prolong the neuromuscular block produced by suxamethonium through reduction of plasma cholinesterase activity, possibly by alkylation of the enzyme.[1] Since enzyme activity may be reduced by up to 70% for several days to several weeks, it was suggested[2] that suxamethonium should be avoided if possible in patients receiving cyclophosphamide. A more recent case report[3] would also support this suggestion. Other alkylating agents also reported to reduce plasma cholinesterase activity include *chlormethine*, *thiotepa*, and *tretamine*.[2]

1. Walker IR, *et al.* Cyclophosphamide, cholinesterase and anaesthesia. *Aust N Z J Med* 1972; **3:** 247–51.
2. Zsigmond EK, Robins G. The effect of a series of anti-cancer drugs on plasma cholinesterase activity. *Can Anaesth Soc J* 1972; **19:** 75–82.
3. Koseoglu V, *et al.* Acquired pseudocholinesterase deficiency after high-dose cyclophosphamide. *Bone Marrow Transplant* 1999; **24:** 1367–8.

Aprotinin. See under Atracurium, p.1904.

Benzodiazepines. See under Atracurium, p.1904.

Beta blockers. See under Atracurium, p.1904.

Cardiac inotropes. See under Atracurium, p.1904.

Ganglion blockers. See under Atracurium, p.1904.

General anaesthetics. Tachyphylaxis and phase II block (see Uses and Administration, below) develop earlier, and after smaller total doses of suxamethonium, when inhalation anaesthetics are used. *Halothane* may increase the incidence of arrhythmias associated with suxamethonium and can potentiate suxamethonium-induced muscle damage.[1] Suxamethonium should be used with caution with other drugs that might produce additive cardiovascular effects. Severe bradycardia and asystole

have occurred when used in anaesthetic regimens with *propofol* and opioids such as *fentanyl*.
See also under Interactions of Atracurium, p.1904.
1. Laurence AS, Henderson P. Serum myoglobin after suxamethonium administration to children: effect of pretreatment before iv and inhalation induction. *Br J Anaesth* 1986; **58:** 126P.

Histamine H_2 antagonists. See under Atracurium, p.1904.

Lithium. See under Atracurium, p.1904.

Local anaesthetics. *Procaine*, *cocaine*, and *chloroprocaine* are ester-type local anaesthetics which are hydrolysed by plasma cholinesterase and may competitively enhance the neuromuscular blocking activity of suxamethonium. See also Antiarrhythmics under Atracurium, p.1903.

Magnesium salts. See under Atracurium, p.1904.

MAOIs. Reduction of plasma cholinesterase activity by *phenelzine* has been reported[1] to cause significant prolongation of suxamethonium paralysis. Enzyme activity may be reduced to 10% of normal and recovery can take up to a month. The dosage of suxamethonium may need to be substantially reduced or a competitive neuromuscular blocker used.
1. Bodley PO, *et al.* Low serum pseudocholinesterase levels complicating treatment with phenelzine. *BMJ* 1969; **3:** 510–12.

Metoclopramide. Dose-dependent prolongation of suxamethonium-induced neuromuscular blockade has been reported in patients given metoclopramide.[1,2] The potent inhibitory effect of metoclopramide on plasma cholinesterase may account for this interaction.
1. Turner DR, *et al.* Neuromuscular block by suxamethonium following treatment with histamine type 2 antagonists or metoclopramide. *Br J Anaesth* 1989; **63:** 348–50.
2. Kao YJ, *et al.* Dose-dependent effect of metoclopramide on cholinesterases and suxamethonium metabolism. *Br J Anaesth* 1990; **65:** 220–4.

Neuromuscular blockers. See under Atracurium, p.1905.

Sex hormones. *Oestrogens* and oestrogen-containing *oral contraceptives* reduce plasma cholinesterase activity[1] possibly due to suppression of hepatic synthesis of the enzyme, but little prolongation of suxamethonium paralysis may be expected since activity is reduced by only about 20%. See also under Atracurium, p.1905.
1. Robertson GS, Aberd MB. Serum protein and cholinesterase changes in association with contraceptive pills. *Lancet* 1967; **i:** 232–5.

Sympathomimetics. *Bambuterol* can inhibit plasma cholinesterase activity and so prolong the activity of suxamethonium.[1] Phase II block has been reported in some patients with abnormal plasma cholinesterase.[2]
1. Staun P, *et al.* The influence of 10 mg and 20 mg bambuterol on the duration of succinylcholine-induced neuromuscular blockade. *Acta Anaesthesiol Scand* 1990; **34:** 498–500.
2. Bang U, *et al.* The effect of bambuterol on plasma cholinesterase activity and suxamethonium-induced neuromuscular blockade in subjects heterozygous for abnormal plasma cholinesterase. *Acta Anaesthesiol Scand* 1990; **34:** 600–604.

Pharmacokinetics

After injection, suxamethonium is rapidly hydrolysed by plasma cholinesterase. One molecule of choline is split off rapidly to form succinylmonocholine which is then slowly hydrolysed to succinic acid and choline. About 10% of suxamethonium is excreted unchanged in the urine. Succinylmonocholine has weak muscle-relaxant properties mainly of a competitive nature.

The gene responsible for the expression of plasma cholinesterase exhibits polymorphism and enzyme activity varies between individuals (see under Precautions, above).

Small amounts of suxamethonium cross the placenta.

◊ Reviews.
1. Booij LHDJ, Vree TB. Skeletal muscle relaxants: pharmacodynamics and pharmacokinetics in different patient groups. *Int J Clin Pract* 2000; **54:** 526–34.

Uses and Administration

Suxamethonium is a depolarising neuromuscular blocker used to produce muscle relaxation. It combines with cholinergic receptors of the motor end-plate to produce depolarisation but is resistant to breakdown by acetylcholinesterase. This prevents repolarisation and subsequent depolarisation, and a flaccid muscle paralysis occurs. This initial depolarisation block is commonly known as a **phase I block.** The muscles that produce fine rapid movements such as those of the face are the first to be affected followed by those of the limbs, abdomen, and chest; the diaphragm is affected last. Recovery occurs in reverse order. When excessive amounts of suxamethonium accumulate at the neuromuscular junction, for example after high or prolonged dosage, the nature of the block may change to one with characteristics similar to competitive block. This is commonly termed **phase II block** or **dual block** and may be associated with prolonged neuromuscular blockade and apnoea.

After intravenous injection suxamethonium chloride acts in about 30 to 60 seconds and has a duration of action of about 2 to 6 minutes. After intramuscular injection it acts in 2 to 3 minutes and has a duration of action of about 10 to 30 minutes.

Suxamethonium is used in surgical and other procedures in which a rapid onset and brief duration of muscle relaxation is needed (see Anaesthesia, p.1900), including intubation, endoscopies, and ECT. It is used as suxamethonium chloride, and is normally given by intravenous injection. The content of preparations of suxamethonium chloride may be described in terms of either the dihydrate or the anhydrous form, depending on the country of origin, and this should be borne in mind when evaluating the literature although the differences are small (anhydrous suxamethonium chloride 1 mg is equivalent to about 1.1 mg of the dihydrate).

Suxamethonium should be given after induction of general anaesthesia because paralysis is usually preceded by painful muscle fasciculations. A competitive neuromuscular blocker may sometimes be given before suxamethonium to try to reduce some of the adverse effects on the muscles (see Effects on the Muscles, above). Premedication with an antimuscarinic may be of value in reducing bradycardia and excessive salivation. Assisted ventilation is necessary.

An initial test dose of 100 micrograms/kg, or 5 to 10 mg, of suxamethonium chloride may be given intravenously if increased sensitivity is suspected. Doses of neuromuscular blockers need to be carefully titrated for individual patients according to response, and may vary with the procedure, the other drugs given, and the state of the patient; monitoring of the degree of block is recommended in order to reduce the risk of overdosage. The response to suxamethonium varies considerably and the usual single dose of suxamethonium chloride for an adult is 0.3 to 1.1 mg/kg by intravenous injection. Supplementary doses of 50 to 100% of the initial dose may be given at 5 to 10 minute intervals if required but the total dose given by repeated intravenous injection or continuous infusion (see below) should not exceed 500 mg/hour. Infants and children are more resistant to suxamethonium than adults. A recommended intravenous dose for infants under one year of age is 2 mg/kg; a dose of 1 mg/kg is recommended for children 1 to 12 years old.

When a suitable vein is inaccessible suxamethonium chloride has been given by intramuscular injection in a dose of 3 to 4 mg/kg to a maximum total dose of 150 mg. The intramuscular dose for infants is up to 4 to 5 mg/kg and for older children up to 4 mg/kg to a maximum total dose of 150 mg.

For prolonged procedures in adults sustained relaxation may be obtained by continuous intravenous infusion of a 0.1 to 0.2% solution. A rate of 2.5 to 4 mg/minute is usually adequate but may be adjusted as necessary. The total dose given by repeated intravenous injection (see above) or continuous infusion should not exceed 500 mg/hour.

Suxamethonium bromide and suxamethonium iodide have also been used.

ECT. Suxamethonium chloride is used to decrease the muscular contractions associated with electrically induced convulsions. It temporarily paralyses muscles during ECT, preventing violent muscle contractions which can potentially result in broken bones and fractures.

Suxamethonium chloride remains the most commonly used neuromuscular blocker in ECT. However, patients with a history of malignant hyperthermia, neuroleptic malignant syndrome, catatonic schizophrenia, and organophosphate poisoning are more susceptible to adverse effects.[1] Mivacurium has been used, with satisfactory results, in at-risk-patients, although histamine release and hypotension may be a problem. Other competitive neuromuscular blockers tried include atracurium and vecuronium.

1. Ding Z, White PF. Anesthesia for electroconvulsive therapy. *Anesth Analg* 2002; **94:** 1351–64.

Preparations

BP 2008: Suxamethonium Chloride Injection;
USP 31: Succinylcholine Chloride for Injection; Succinylcholine Chloride Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Actirelax; Fosfitone; Succi†; ***Austral.:*** Scoline; ***Austria:*** Lysthenon; ***Belg.:*** Myoplegine†; ***Braz.:*** Quelicin; Succitrat; Succnil Colin; ***Canad.:*** Quelicin; ***Fin.:*** Sukolin; ***Fr.:*** Celocurine†; ***Ger.:*** Lysthenon; Pantolax; ***Gr.:*** Lycitrope; ***India:*** Midarine; ***Indon.:*** Quelicin; ***Irl.:*** Anectine; ***Israel:*** Succinyl; ***Ital.:*** Midarine; Myotenlis†; ***Malaysia:*** Ethicoline; Succinyl†; ***Mex.:*** Anectine; Uxicolin; ***Neth.:*** Curalest; ***Norw.:*** Curacit; ***NZ:*** Ethicholine†; ***Pol.:*** Chlorsuccillin; ***Port.:*** Mioflex; ***Rus.:*** Lysthenon (Листенон); ***S.Afr.:*** Scoline; ***Singapore:*** Ethicholine; ***Spain:*** Anectine; Mioflex; ***Swed.:*** Celocurin; ***Switz.:*** Lysthenon; Midarine; Succinolin; ***Thai.:*** Succinyl; ***Turk.:*** Lysthenon; ***UK:*** Anectine; ***USA:*** Anectine; Quelicin.

Tubocurarine Chloride *(BAN, rINN)*

Cloruro de tubocurarina; *d*-Tubocurarine Chloride; (+)-Tubocurarine Chloride Hydrochloride Pentahydrate; Tubocurarine, chlorure de; Tubocurarini chloridum; Tubocurarinii Chloridum Pentahydricum; Tubokurariinikloridi; Tubokurarinium-chlorid pentahydrát; Tubokurarinklorid; Tubokurarin-klorid; Tubokurarino chloridas. (+)-7′,12′-Dihydroxy-6,6′-dimethoxy-2,2′,2′-trimethyltubocuraranium dichloride pentahydrate.

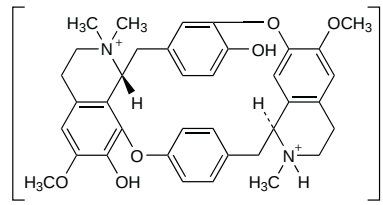
Тубокурарина Хлорид

$C_{37}H_{42}Cl_2N_2O_6,5H_2O$ = 771.7.

CAS — 57-95-4 (tubocurarine); 57-94-3 (anhydrous tubocurarine chloride); 6989-98-6 (tubocurarine chloride, pentahydrate).

ATC — M03AA02.

ATC Vet — QM03AA02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Tubocurarine Chloride). A white or slightly yellowish crystalline powder. Soluble in water and in alcohol; practically insoluble in acetone; dissolves in solutions of alkali hydroxides. A 1% solution in water has a pH of 4.0 to 6.0. Store in airtight containers.
USP 31 (Tubocurarine Chloride). A white or yellowish-white to greyish-white, crystalline powder. Soluble 1 in 20 of water and 1 in 45 of alcohol. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for competitive neuromuscular blockers in general (see Atracurium, p.1902). A transient fall in blood pressure commonly occurs, due in part to ganglionic blockade and the release of histamine; there may be an increase in heart rate. Tubocurarine has a greater propensity to cause histamine release than other competitive neuromuscular blockers in clinical use. Tubocurarine should be used with caution in patients with renal impairment. Resistance to the effect of tubocurarine may occur in patients with hepatic impairment.

Interactions

For interactions associated with competitive neuromuscular blockers, see Atracurium, p.1903.

Pharmacokinetics

Tubocurarine chloride is a quaternary ammonium compound and absorption from the gastrointestinal tract is extremely poor. Absorption is slow and irregular when given intramuscularly. After intravenous injection tubocurarine is widely distributed throughout body tissues; less than 50% is bound to plasma proteins. After a single dose extensive redistribution to tissues is responsible for the termination of activity, but after a large single dose or repeated small doses tissue saturation occurs and renal excretion becomes the main determinant of duration. When given in usual doses it does not pass the blood-brain barrier, and does not appear to cross the placenta in significant amounts. Up to 75% of a dose is excreted unchanged in the urine in 24 hours, and up to 12% in bile. Biliary excretion is increased in renal impairment. A small proportion of a dose is metabolised in the liver.

Uses and Administration

Tubocurarine is a benzylisoquinolinium competitive neuromuscular blocker (see Atracurium, p.1905). It may be obtained from extracts of the stems of *Chondodendron tomentosum* (Menispermaceae) and is one of the active principles of curare, by which name it is sometimes referred to in anaesthetic literature. Tubocurarine chloride is the chloride of (+)-tubocurarine. After intravenous injection of tubocurarine chloride neuromuscular block appears within 1 minute and lasts for about 30 minutes; the maximum effect is attained within 2 to 5 minutes.

Tubocurarine chloride has been used similarly to other competitive neuromuscular blockers to produce muscle relaxation in various procedures but has largely been replaced by other drugs with fewer cardiovascular effects and a lower potential for histamine release.