

Drugs used in anaesthesia

This section describes drugs used in anaesthesia. The reader is referred to WHO. *Model Prescribing Information . Drugs used in Anaesthesia* . Geneva: WHO; 1989 for more detailed information.

To produce a state of prolonged full surgical anaesthesia reliably and safely, a variety of drugs is needed. Special precautions and close monitoring of the patient are required. These drugs may be fatal if used inappropriately and should be used by non-specialized personnel only as a last resort. Irrespective of whether a general or conduction (regional or local) anaesthetic technique is used, it is essential that facilities for intubation and mechanically assisted ventilation are available. A full preoperative assessment is required including, if necessary, appropriate fluid replacement.

Anaesthesia may be induced with an intravenous barbiturate, parenteral ketamine, or a volatile agent. Maintenance is with inhalational agents often supplemented by other drugs given intravenously. Specific drugs may be used to produce muscle relaxation. Various drugs may be needed to modify normal physiological functions or otherwise to maintain the patient in a satisfactory condition during surgery.

LONG-TERM MEDICATION

The risk of stopping long-term medication before surgery may be greater than the risk of continuing it. It is essential that the anaesthetist is told of **all** drugs that the patient is (or has been) taking; for further advice see section 10.2 (oral anticoagulants), section 18.1 (corticosteroids), section 18.3.1 (hormonal contraceptives), and section 18.7 (diabetic patients).

General anaesthetics and oxygen

Intravenous agents

Intravenous anaesthetics may be used alone to produce anaesthesia for short surgical procedures but are more commonly used for induction only. They can produce apnoea and hypotension and thus facilities for adequate resuscitation must be available. They are contraindicated if the anaesthetist is not confident of being able to maintain an airway. Before intubation is attempted, a muscle relaxant must be given. Individual requirements vary considerably; lesser dosage is indicated in the elderly, debilitated or hypovolaemic patients.

Intravenous induction using **thiopental** is rapid and excitement does not usually occur. Anaesthesia persists for about 4–7 minutes; large or repeated doses severely depress respiration and delay recovery.

Anaesthesia with **ketamine** persists for up to 15 minutes after a single intravenous injection and is characterized by profound analgesia. It may be used as the sole agent for diagnostic and minor surgical interventions. Subanaesthetic concentrations of ketamine may be used to provide analgesia for painful procedures of short duration such as the dressing of burns, radiotherapeutic procedures, marrow sampling and

minor orthopaedic procedures. Recovery from ketamine anaesthesia is associated with a high incidence of hallucinations and other emergence reactions. Ketamine is of particular value in children, in whom hallucinations are believed to be less significant.

Thiopental sodium

Thiopental is a representative intravenous anaesthetic. Various drugs can serve as alternatives

Injection (Powder for solution for injection), thiopental sodium, 0.5-g and 1-g ampoules

Uses:

induction of anaesthesia prior to administration of inhalational anaesthetic; anaesthesia of short duration

Contraindications:

inability to maintain airway; hypersensitivity to barbiturates; cardiovascular disease; dyspnoea or obstructive respiratory disease; porphyria

Precautions:

local extravasation can result in extensive tissue necrosis and sloughing; intra-arterial injection causes intense pain and may result in arteriospasm; hepatic impairment (Appendix 5); pregnancy (Appendix 2); **interactions:** Appendix 1

SKILLED TASKS. Warn patient not to perform skilled tasks, for example operating machinery, driving, for 24 hours and also to avoid alcohol for 24 hours

Dosage:

Induction, *by intravenous injection* as a 2.5% (25 mg/ml) solution over 10–15 seconds, **Adult** 100–150 mg (reduced in elderly or debilitated patients), followed by a further 100–150 mg if necessary according to response after 60 seconds; *or* up to 4 mg/kg; **Child** 2–7 mg/kg repeated if necessary according to response after 60 seconds

RECONSTITUTION. Solutions containing 25 mg/ml should be freshly prepared by mixing 20 ml of water for injections with the contents of the 0.5-g ampoule or 40 ml with the 1-g ampoule. Any solution made up over 24 hours previously or in which cloudiness, precipitation or crystallization is evident should be discarded

Adverse effects:

rapid injection may result in severe hypotension and hiccup; cough, laryngeal spasm, allergic reactions

Ketamine

Injection (Solution for injection), ketamine (as hydrochloride) 50 mg/ml, 10-ml vial

Uses:

induction and maintenance of anaesthesia; analgesia for painful procedures of short duration

Contraindications:

thyrotoxicosis; hypertension (including pre-eclampsia); history of cerebrovascular accident, cerebral trauma, intracerebral mass or haemorrhage or other cause of raised intracranial pressure; eye injury and increased intraocular pressure; psychiatric disorders, particularly hallucinations

Precautions:

supplementary analgesia often required in surgical procedures involving visceral pain pathways (morphine may be used but addition of nitrous oxide will often suffice); during recovery, patient must remain undisturbed but under observation; pregnancy (Appendix 2); **interactions:** Appendix 1

SKILLED TASKS. Warn patient not to perform skilled tasks, for example operating machinery or driving, for 24 hours and also to avoid alcohol for 24 hours

Dosage:

Induction, *by intramuscular injection*, **Adult** and **Child** 6.5–13 mg/kg (10 mg/kg usually produces 12–25 minutes of anaesthesia)

Induction, *by intravenous injection* over at least 1 minute, **Adult** and **Child** 1–4.5 mg/kg (2 mg/kg usually produces 5–10 minutes of anaesthesia)

Induction, *by intravenous infusion* of a solution containing 1 mg/ml, **Adult** and **Child** total induction dose 0.5–2 mg/kg; maintenance (using microdrip infusion), 10–45 micrograms/kg/minute, rate adjusted according to response

Analgesia, *by intramuscular injection*, **Adult** and **Child** initially 4 mg/kg

DILUTION AND ADMINISTRATION. According to manufacturer's directions

Adverse effects:

hallucinations and other emergence reactions during recovery possibly accompanied by irrational behaviour (effects rarely persist for more than few hours but can recur at any time within 24 hours); transient elevation of pulse rate and blood pressure common, arrhythmias have occurred; hypotension and bradycardia occasionally reported

Volatile inhalational agents

One of the volatile anaesthetics, ether, halothane (with or without nitrous oxide), must be used for induction when intravenous agents are contraindicated and particularly when intubation is likely to be difficult.

Full muscle relaxation is achieved in deep anaesthesia with **ether** . Excess bronchial and salivary secretion can be avoided by premedication with atropine. Laryngeal spasm may occur during induction and intubation. Localized capillary bleeding can be troublesome and postoperative nausea and vomiting are frequent; recovery time is slow particularly after prolonged administration.

If intubation is likely to be difficult, **halothane** is preferred. It does not augment salivary or bronchial secretions and the incidence of postoperative nausea and vomiting is low. Severe hepatitis, which may be fatal, sometimes occurs; it is more likely in patients who are repeatedly anaesthetized with halothane within a short period of time.

Ether, anaesthetic

Drug subject to international control under the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988)

Volatile liquid

Uses:

induction and maintenance of anaesthesia (administered from many types of vaporizers)

Contraindications:

severe liver disease; diabetes mellitus; impaired kidney function; raised cerebrospinal fluid pressure

Precautions:

risk of potentially fatal convulsions in febrile patients; pregnancy (Appendix 2);

interactions: Appendix 1

FIRE Diathermy must not be used when ether/oxygen mixtures in use and operating theatre and its equipment should be designed to minimize risk of static discharge, particularly in hot, dry climates
HAZARD.

Dosage:

Induction, **Adult** and **Child** , up to 15% in inspired gases

Maintenance of light anaesthesia, **Adult** and **Child** 3–5% in air (with or without muscle relaxants); up to 10% for deep anaesthesia

Adverse effects:

transient postoperative effects include impairment of liver function and leukocytosis; nausea and vomiting; capillary bleeding

Halothane

Volatile liquid

Uses:

induction and maintenance of anaesthesia

Contraindications:

history of unexplained jaundice or pyrexia following previous exposure to halothane; family history of malignant hyperthermia; raised cerebrospinal fluid pressure; porphyria

Precautions:

anaesthetic history should be carefully taken to determine previous exposure and previous reactions to halothane (at least 3 months should be allowed to elapse between each re-exposure); avoid for dental procedures in patients under 18 years unless treated in hospital (high risk of arrhythmias); pregnancy and breastfeeding (Appendices 2 and 3); **interactions:** Appendix 1

Dosage:

Induction, using specifically calibrated vaporizer, gradually increase inspired gas concentration to 2–4% (**ADULT**) or 1.5–2% (**CHILD**) in oxygen or nitrous oxide–oxygen

Maintenance, **ADULT** and **CHILD** 0.5–2%

Adverse effects:

arrhythmias; bradycardia; respiratory depression; hepatic damage

Inhalational gases

Nitrous oxide is used for the maintenance of anaesthesia. It is too weak to be used alone, but it allows the dosage of other anaesthetic agents to be reduced. It has a strong analgesic action.

Oxygen should be added routinely during anaesthesia with inhalational agents, even when air is used as the carrier gas, to protect against hypoxia.

Oxygen is also used in the management of anaphylaxis (section 3.1), myocardial infarction (section 12.5), and severe acute asthma (section 25.1).

Identification of cylinders for inhalation gases

An ISO standard (International Standard 32, Gas cylinders for medical use, 1977) requires that cylinders containing nitrous oxide should bear the name of the contents in legible and permanent characters and, preferably, also the chemical symbol N_2O . The neck, from the valve to the shoulder, should be coloured blue. Cylinders containing oxygen intended for medical use should bear the name of the contents in legible and permanent characters and, preferably, also the chemical symbol O_2 . The neck, from the valve to the shoulder, should be coloured white. Cylinders containing nitrous oxide and oxygen mixtures should be similarly labelled, and the neck coloured white and blue.

Nitrous oxide

Inhalation gas

Uses:

maintenance of anaesthesia in combination with other anaesthetic agents (halothane, ether, or ketamine) and muscle relaxants; analgesia for obstetric practice, for emergency management of injuries, during postoperative physiotherapy and for refractory pain in terminal illness

Contraindications:

demonstrable collection of air in pleural, pericardial or peritoneal space; intestinal obstruction; occlusion of middle ear; arterial air embolism; decompression sickness; chronic obstructive airway disease, emphysema

Precautions:

minimize exposure of staff; pregnancy (Appendix 2); **interactions:** Appendix 1

Dosage:

Anaesthesia, **Adult** and **Child** nitrous oxide mixed with 25–30% oxygen

Analgesia, 50% nitrous oxide mixed with 50% oxygen

Adverse effects:

nausea and vomiting; after prolonged administration megaloblastic anaemia, depressed white cell formation; peripheral neuropathy

Oxygen

Inhalation gas

Uses:

to maintain an adequate oxygen tension in inhalational anaesthesia

FIRE HAZARD. Avoid use of cautery when oxygen is used with ether; reducing valves on oxygen cylinders **must not** be greased (risk of explosion)

Precautions:

interactions: Appendix 1

Dosage:

Concentration of oxygen in inspired anaesthetic gases should never be less than 21%

Adverse effects:

concentrations greater than 80% have a toxic effect on the lungs leading to pulmonary congestion, exudation and atelectasis

Local anaesthetics

Drugs used for conduction anaesthesia (also termed local or regional anaesthesia) act by causing a reversible block to conduction along nerve fibres. Local anaesthetics are used very widely in dental practice, for brief and superficial interventions, for obstetric procedures, and for specialized techniques of regional anaesthesia calling for highly developed skills. Where patient cooperation is required the patient must be psychologically prepared to accept the proposed procedure. Facilities and equipment for resuscitation should be readily available at all times. Local anaesthetic injections should be given slowly in order to detect inadvertent intravascular injection.

LOCAL INFILTRATION

Many simple surgical procedures that neither involve the body cavities nor require muscle relaxation can be performed under local infiltration anaesthesia. Lower-segment caesarean section can also be performed under local infiltration anaesthesia. The local anaesthetic drug of choice is **lidocaine** 0.5% with or without epinephrine. No more than 4 mg/kg of plain lidocaine or 7 mg/kg of lidocaine with epinephrine should be administered on any one occasion. The addition of **epinephrine** (adrenaline) diminishes local blood flow, slows the rate of absorption of the local anaesthetic, and prolongs its effect. Care is necessary when using epinephrine for this purpose since, in excess, it may produce ischaemic necrosis. It should **not** be added to injections used in digits or appendages.

SURFACE ANAESTHESIA

Topical preparations of **lidocaine** are available and topical eye drop solutions of **tetracaine** (section 21.3) are used for local anaesthesia of the cornea and conjunctiva.

REGIONAL BLOCK

A regional nerve block can provide safe and effective anaesthesia but its execution requires considerable training and practice. Nevertheless, where the necessary skills are available, techniques such as axillary or ankle blocks can be invaluable. Either **lidocaine** 1% or **bupivacaine** 0.5% is suitable. Bupivacaine has the advantage of a longer duration of action.

SPINAL ANAESTHESIA

This is one of the most useful of all anaesthetic techniques and can be used widely for surgery of the abdomen and the lower limbs. It is a major procedure requiring considerable training and practice. Either **lidocaine** 5% in glucose or **bupivacaine** 0.5% in glucose can be used but the latter is often chosen because of its longer duration of action.

Bupivacaine hydrochloride

Bupivacaine is a representative local anaesthetic. Various drugs can serve as alternatives

Injection (Solution for injection), bupivacaine hydrochloride 2.5 mg/ml (0.25%), 10-ml ampoule; 5 mg/ml (0.5%), 10-ml ampoule; 5 mg/ml (0.5%) with glucose 75 mg/ml (7.5%), 4-ml ampoule

Uses:

infiltration anaesthesia; peripheral and sympathetic nerve block; spinal anaesthesia; postoperative pain relief

Contraindications:

adjacent skin infection, inflamed skin; concomitant anticoagulant therapy; severe anaemia or heart disease; spinal or epidural anaesthesia in dehydrated or hypovolaemic patient

Precautions:

respiratory impairment; hepatic impairment (Appendix 5); epilepsy; porphyria; myasthenia gravis; pregnancy and breastfeeding (Appendices 2 and 3); **interactions:** Appendix 1

Dosage:

Local infiltration, using 0.25% solution, **ADULT** up to 150 mg (up to 60 ml)

Peripheral nerve block, using 0.5% solution, **ADULT** up to 150 mg (up to 30 ml)

Dental anaesthesia, using 0.5% solution, **ADULT** 9–18 mg (1.8–3.6 ml)

Lumbar epidural block in surgery, using 0.5% solution, **ADULT** 50–100 mg (10–20 ml)

Lumbar epidural block in labour, using 0.25–0.5% solution, **ADULT** (female) up to 60 mg (maximum 12 ml)

Caudal block in surgery, using 0.25–0.5% solution, **ADULT** up to 150 mg (maximum 30 ml)

Caudal block in labour, using 0.25–0.5% solution, **ADULT** (female) up to 100 mg (maximum 20 ml)

Note. Maximum cumulative safe dose for adults and children of a 0.25% solution of bupivacaine is 1.5 mg/kg

Use lower doses for debilitated, elderly, epileptic, or acutely ill patients

Do not use solutions containing preservatives for spinal, epidural, caudal or intravenous regional anaesthesia

Adverse effects:

with excessive dosage or following intravascular injection, light-headedness, dizziness, blurred vision, restlessness, tremors and, occasionally, convulsions rapidly followed by drowsiness, unconsciousness and respiratory failure; cardiovascular toxicity includes hypotension, heart block and cardiac arrest; hypersensitivity and allergic reactions also occur; epidural anaesthesia occasionally complicated by urinary retention, faecal incontinence, headache, backache or loss of perineal sensation; transient paraesthesia and paraplegia very rare

Lidocaine hydrochloride

Lidocaine is a representative local anaesthetic. Various drugs can serve as alternatives

Injection (Solution for injection), lidocaine hydrochloride 5 mg/ml (0.5%), 20-ml ampoule; 10 mg/ml (1%), 20-ml ampoule; 50 mg/ml (5%), 2-ml ampoule to be mixed with glucose 75 mg/ml (7.5%)

Injection (Solution for injection) with epinephrine, lidocaine hydrochloride 10 mg/ml (1%) with epinephrine 5 micrograms/ml (1 in 200 000), 20-ml ampoule

Injection (Solution for injection) with epinephrine (dental use), lidocaine hydrochloride 20 mg/ml (2%) with epinephrine 12.5 micrograms/ml (1 in 80 000), 2.2-ml dental cartridge

Topical gel or solution , lidocaine hydrochloride 20–40 mg/ml (2–4%)

Uses:

surface anaesthesia of mucous membranes; infiltration anaesthesia; peripheral and sympathetic nerve block; dental anaesthesia; spinal anaesthesia; intravenous regional anaesthesia; arrhythmias (section 12.2)

Contraindications:

adjacent skin infection, inflamed skin; concomitant anticoagulant therapy; severe anaemia or heart disease; spinal or epidural anaesthesia in dehydrated or hypovolaemic patient

Precautions:

respiratory impairment; hepatic impairment (Appendix 5); epilepsy; porphyria; myasthenia gravis; avoid (or use with great care) solutions containing epinephrine (adrenaline) for ring block of digits or appendages (risk of ischaemic necrosis); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions:** Appendix 1

Dosage:

Plain Solutions

Local infiltration and peripheral nerve block, using 0.5% solution, **ADULT** up to 250 mg (up to 50 ml)

Local infiltration and peripheral nerve block, using 1% solution, **ADULT** up to 250 mg (up to 25 ml)

Surface anaesthesia of pharynx, larynx, trachea, using 4% solution, **ADULT** 40–200 mg (1–5 ml)

Surface anaesthesia of urethra, using 4% solution, **ADULT** 400 mg (10 ml)

Spinal anaesthesia, using 5% solution (with glucose 7.5%), **ADULT** 50–75 mg (1–1.5 ml)

Solutions containing epinephrine

Local infiltration and peripheral nerve block, using 0.5% solution with epinephrine, **ADULT** up to 400 mg (up to 80 ml)

Local infiltration and peripheral nerve block, using 1% solution with epinephrine, **ADULT** up to 400 mg (up to 40 ml)

Dental anaesthesia, using 2% solution with epinephrine, **ADULT** 20–100 mg (1–5 ml)

NOTE. Maximum safe doses of lidocaine for **adult** and **child** are: 0.5% or 1% lidocaine, 4 mg/kg; 0.5% or 1% lidocaine + epinephrine 5 micrograms/ml (1 in 200 000), 7 mg/kg

Use lower doses for debilitated, elderly, epileptic, or acutely ill patients

Do not use solutions containing preservatives for spinal, epidural, caudal or intravenous regional anaesthesia

Adverse effects:

with excessive dosage or following intravascular injection, light-headedness, dizziness, blurred vision, restlessness, tremors and, occasionally, convulsions rapidly followed by drowsiness, unconsciousness and respiratory failure; cardiovascular toxicity includes hypotension, heart block and cardiac arrest; hypersensitivity and allergic reactions also occur; epidural anaesthesia occasionally complicated by urinary retention, faecal incontinence, headache, backache or loss of perineal sensation; transient paraesthesia and paraplegia very rare

Vasoconstrictors

The sympathetic block from spinal or epidural anaesthesia may cause hypotension. Such hypotension is managed by giving intravenous fluids (usually prophylactically) and oxygen, and elevating legs and giving a pressor drug such as ephedrine. In addition to vasoconstriction, ephedrine also accelerates the heart rate and can therefore counter bradycardia (but atropine sulfate is used to reverse persistent bradycardia).

Ephedrine hydrochloride

Ephedrine hydrochloride is a complementary drug

Injection (Solution for injection), ephedrine hydrochloride 30 mg/ml, 1-ml ampoule

Uses:

prevention of hypotension during delivery under spinal or epidural anaesthesia

Precautions:

hyperthyroidism; diabetes mellitus; ischaemic heart disease, hypertension; angle-closure glaucoma; renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions:** Appendix 1

Dosage:

To prevent hypotension during delivery under spinal anaesthesia, *by slow intravenous injection* of solution containing 3 mg/ml, **ADULT** (female) 3–6 mg (maximum single dose 9 mg), repeated if necessary every 3–4 minutes; maximum cumulative dose 30 mg

Adverse effects:

anorexia, hypersalivation, nausea, vomiting; tachycardia (also in fetus), arrhythmias, anginal pain, vasoconstriction with hypertension, vasodilation with hypotension; dyspnoea; headache, dizziness, anxiety, restlessness, confusion, tremor; difficulty in micturition; sweating, flushing; changes in blood-glucose concentration

Epinephrine (adrenaline)**Uses:**

vasoconstrictor to retard systemic absorption of infiltrated local anaesthetics

Contraindications:

ring block of digits, penis or other situations where there is risk of local ischaemia

Precautions:

hypertension, atherosclerotic heart disease, cerebral vascular insufficiency, heart block; thyrotoxicosis or diabetes mellitus; **interactions:** Appendix 1

Dosage:

Final concentration 5 micrograms/ml (1 in 200 000); in dental surgery, in which small volumes are injected, concentrations of up to 12.5 micrograms/ml (1 in 80 000) commonly used; total dose should not exceed 500 micrograms

Preoperative medication and sedation

Pre-anaesthetic medication is often advisable prior to both conduction and general anaesthetic procedures.

Sedatives improve the course of subsequent anaesthesia in apprehensive patients. Diazepam and promethazine are effective. **Diazepam** can be administered by mouth, by rectum, or by intravenous injection. **Promethazine**, which has antihistaminic and antiemetic properties as well as a sedative effect, is of particular value in children.

A potent analgesic such as **morphine** (section 1.5) should be administered preoperatively to patients in severe pain or for analgesia during and after surgery.

Anticholinergic (more correctly antimuscarinic) drugs such as **atropine** are also used before general anaesthesia. They inhibit excessive bronchial and salivary secretions induced, in particular, by ether and ketamine. Intramuscular administration is most effective, but oral administration is more convenient in children. Lower doses should be used in cardiovascular disease or hyperthyroidism.

Atropine sulfate

Injection (Solution for injection), atropine sulfate 600 micrograms/ml, 1-ml ampoule

Uses:

to inhibit salivary secretions; to inhibit arrhythmias resulting from excessive vagal stimulation; to block the parasympathomimetic effects of anticholinesterases such as neostigmine; organophosphate poisoning (section 4.2.3); antispasmodic (section 17.5); mydriasis and cycloplegia (section 21.5)

Contraindications:

angle-closure glaucoma; myasthenia gravis; paralytic ileus, pyloric stenosis; prostatic enlargement

Precautions:

Down syndrome, children, elderly; ulcerative colitis, diarrhoea; hyperthyroidism; heart failure, hypertension; pregnancy and breastfeeding (Appendices 2 and 3);

interactions: Appendix 1

Duration of action. Since atropine has a shorter duration of action than neostigmine, late unopposed bradycardia may result; close monitoring of the patient is necessary

Dosage:

Premedication, *by intramuscular injection* 30–60 minutes before induction, **ADULT** and **Child** 20 micrograms/kg; *by intravenous injection* immediately before induction, **ADULT** up to maximum 500 micrograms

Inhibition of bradycardia, *by intravenous injection*, **ADULT** 0.4–1 mg, **CHILD** 10–30 micrograms/kg

Reversal of neuromuscular block, *by intravenous injection* 2–3 minutes before anticholinesterase, **ADULT** 0.6–1.2 mg, **CHILD** 20 micrograms/kg

Adverse effects:

dry mouth; blurred vision, photophobia; flushing and dryness of skin, rash; difficulty in micturition; less commonly arrhythmias, tachycardia, palpitations; confusion (particularly in elderly); heat prostration and convulsions, especially in febrile children

Diazepam

Drug subject to international control under the Convention on Psychotropic

Substances (1971)

Diazepam is a representative benzodiazepine. Various drugs can serve as alternatives

Tablets, diazepam 2 mg, 5 mg

Injection (Solution for injection), diazepam 5 mg/ml, 2-ml ampoule

Uses:

premedication before major or minor surgery; sedation with amnesia for endoscopic procedures and surgery under local anaesthesia; in combination with pethidine [not included on WHO Model List], when anaesthetic not available, for emergency reduction of fractures; epilepsy (section 5.1); anxiety disorders (section 24.3)

Contraindications:

central nervous system depression or coma; shock; respiratory depression; acute pulmonary insufficiency; sleep apnoea; acute alcohol intoxication; severe hepatic impairment; myasthenia gravis

Precautions:

respiratory disease; muscle weakness; history of alcohol or drug abuse; marked personality disorder; elderly or debilitated patients (adverse effects more common in these groups); hepatic impairment (Appendix 5) or renal failure (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); porphyria; **interactions:** Appendix 1

SKILLED TASKS. Warn patient not to perform skilled tasks, for example operating machinery, driving, for 24 hours

Dosage:

Premedication, *by mouth* 2 hours before surgery, **ADULT** and **CHILD** over 12 years, 5–10 mg

Sedation, *by slow intravenous injection* immediately before procedure, **ADULT** and **CHILD** over 12 years, 200 micrograms/kg

ADMINISTRATION. Absorption following intramuscular injection slow and erratic; route should only be used if oral or intravenous administration not possible

Slow intravenous injection into large vein reduces risk of thrombophlebitis

Resuscitation equipment must be available

Adverse effects:

central nervous system effects common and include drowsiness, sedation, confusion, amnesia, vertigo, and ataxia; hypotension, bradycardia, or cardiac arrest, particularly in elderly or severely ill patients; also paradoxical reactions, including irritability, excitability, hallucinations, sleep disturbances; pain and thromboembolism on intravenous injection

Promethazine hydrochloride

Tablets, promethazine hydrochloride 10 mg, 25 mg

Elixir (Oral solution), promethazine hydrochloride 5 mg/5 ml

Injection, (Solution for injection), promethazine hydrochloride 25 mg/ml, 2-ml ampoule

Uses:

premedication prior to surgery; antiemetic (section 17.2)

Contraindications:

child under 1 year; impaired consciousness due to cerebral depressants or of other origin; porphyria

Precautions:

prostatic hypertrophy, urinary retention; glaucoma; epilepsy; hepatic impairment (Appendix 5); pregnancy and breastfeeding (Appendices 2 and 3); **interactions:** Appendix 1

SKILLED TASKS. Warn patient not to perform skilled tasks, for example operating machinery, driving, for 24 hours

Dosage:

Premedication, *by mouth* 1 hour before surgery, **CHILD** over 1 year 0.5–1 mg/kg

Premedication, *by deep intramuscular injection* 1 hour before surgery, **ADULT** 25 mg

Adverse effects:

drowsiness (rarely paradoxical stimulation in children); headache; anticholinergic effects such as dry mouth, blurred vision, urinary retention

Muscle relaxants and cholinesterase inhibitors

Muscle relaxants used in surgery are classified according to their mode of action as depolarizing or non-depolarizing neuromuscular blocking drugs. Their use allows

abdominal surgery to be carried out under light anaesthesia. They should never be given until it is certain that general anaesthesia has been established and ventilation must be mechanically assisted until they have been completely inactivated.

Suxamethonium is the only widely used depolarizing muscle relaxant. It produces rapid, complete paralysis, which is very short-lasting in most patients and is of particular value for laryngoscopy and intubation. Should paralysis be prolonged, ventilation must be assisted until muscle function is fully restored. Suxamethonium normally produces a phase I (depolarizing) neuromuscular block. After high doses or prolonged use, the nature of the block changes to a phase II (non-depolarizing) block; this phase II block (also known as dual block) is associated with prolonged neuromuscular blockade and apnoea.

Alcuronium is a non-depolarizing muscle relaxant with a duration of action of about 30 minutes. Its effects may be rapidly reversed after surgery by the anticholinesterase neostigmine, provided atropine is given to prevent excessive autonomic activity.

Vecuronium, a relatively new and expensive non-depolarizing muscle relaxant, has a shorter duration of action (20–30 minutes); it causes minimal adverse cardiovascular effects

REVERSAL OF BLOCK

Cholinesterase inhibitors, such as **neostigmine**, are used at the end of an operation to reverse the muscle paralysis produced by non-depolarizing blocking drugs, such as alcuronium and vecuronium. Neostigmine must not be used with depolarizing blocking drugs, such as suxamethonium, since neostigmine will prolong the muscle paralysis. Neostigmine is also used to treat postoperative non-obstructive urinary retention.

For use of cholinesterase inhibitors in myasthenia gravis, see section 20.2.

Muscle relaxants

Alcuronium chloride

Alcuronium is a representative non-depolarizing muscle relaxant. Various drugs can serve as alternatives

Injection (Solution for injection), alcuronium chloride 5 mg/ml, 2-ml ampoule

Uses:

muscle relaxation during surgery

Contraindications:

respiratory insufficiency or pulmonary disease; dehydrated or severely ill patients; myasthenia gravis or other neuromuscular disorders

Precautions:

renal or hepatic impairment (see Appendices 4 and 5); possibly increase dose in patient with burns; electrolyte disturbances; possibly decrease dose in respiratory acidosis or hypokalemia; history of asthma; pregnancy and breastfeeding (Appendices 2 and 3); **interactions:** Appendix 1

Dosage:

Muscle relaxation, *by intravenous injection*, **ADULT** initially 200–250 micrograms/kg, then 50 micrograms/kg as required for maintenance; **CHILD** initially 125–200 micrograms/kg, then 50 micrograms/kg for maintenance

Adverse effects:

histamine release, causing allergic reactions, such as wheal and flare effects at site of injection, flushing, bronchospasm (anaphylactoid reactions reported); transient hypotension, slight increase in heart rate or decreased pulse rate

Vecuronium bromide

Vecuronium is a complementary non-depolarizing muscle relaxant

Injection (Powder for solution for injection), vecuronium chloride, 10-mg vial

Uses:

muscle relaxation during surgery

Contraindications:

respiratory insufficiency or pulmonary disease; dehydrated or severely ill patients; myasthenia gravis or other neuromuscular disorders

Precautions:

renal impairment (Appendix 4); hepatic impairment; possibly increase dose in patient with burns; electrolyte disturbances; possibly decrease dose in respiratory acidosis or hypokalemia; history of asthma; severe obesity (maintenance of adequate airway and ventilation support); pregnancy and breastfeeding (Appendices 2 and 3); **interactions:** Appendix 1

Dosage:

Intubation, *by intravenous injection*, **ADULT** and **CHILD** over 5 months, 80–100 micrograms/kg; maintenance of relaxation 20–30 micrograms/kg; **CHILD** under 4 months, initially 10–20 micrograms/kg, followed by increments according to response

Muscle relaxation, *by intravenous infusion*, **ADULT**, initial bolus 40–100 micrograms/kg then 0.8–1.4 micrograms/kg/minute

Adverse effects:

minimal release of histamine (rarely hypersensitivity reactions including bronchospasm, hypotension, tachycardia, oedema, erythema, pruritus)

Suxamethonium chloride

Injection (Solution for injection), suxamethonium chloride 50 mg/ml, 2-ml ampoule

Injection (Powder for solution for injection), suxamethonium chloride

Note. Powder formulation recommended; liquid requires refrigerated storage

Uses:

brief muscular paralysis during endotracheal intubation, endoscopy and electroconvulsive therapy

Contraindications:

inability to maintain clear airway; personal or family history of malignant hyperthermia; neurological disease involving acute wasting of major muscle, prolonged immobilization (risk of hyperkalaemia); personal or family history of congenital myotonic disease; Duchenne muscular dystrophy; myasthenia gravis; glaucoma, ocular surgery; liver disease; burns; low plasma cholinesterase activity (including severe liver disease); hyperkalaemia

Precautions:

digitalis toxicity or recent digitalization; cardiac, respiratory or neuromuscular disease; paraplegia, spinal cord injury, or severe trauma; severe sepsis (risk of hyperkalaemia); prolonged apnoea on repeated injection (infusion preferred for long surgical procedures); hepatic impairment (Appendix 5); renal impairment; pregnancy (Appendix 2); children; **interactions:** Appendix 1

Dosage:

Muscle relaxation, *by intramuscular injection*, **INFANT** up to 4–5 mg/kg; **CHILD** up to 4 mg/kg; maximum 150 mg

Muscle relaxation, *by intravenous injection*, **ADULT** and **CHILD** 1 mg/kg, followed if necessary by supplements of 0.5–1 mg/kg at 5–10 minute intervals; **INFANT** 2 mg/kg

Muscle relaxation (prolonged procedures), *by intravenous infusion*, **ADULT** 2.5–4 mg/minute of solution containing 1–2 mg/ml; maximum 500 mg/hour; **child** reduce infusion rate according to body weight

Adverse effects:

postoperative muscle pain, particularly in patients ambulant after operation, and more common in females; myoglobinuria; myoglobinaemia; prolonged apnoea; increased

intra-ocular pressure; hyperkalaemia; bradycardia, hypotension, arrhythmias, particularly with halothane (however, with repeated doses tachycardia, hypertension); increased salivary, bronchial and gastric secretions; transient rise in intragastric pressure; hypersensitivity reactions including flushing, rash, urticaria, bronchospasm, and shock (more common in women, in history of allergy, or in asthmatics); rarely, malignant hyperthermia (often fatal)

Cholinesterase inhibitor

Neostigmine metilsulfate

Injection (Solution for injection), neostigmine metilsulfate 500 micrograms/ml, 1-ml ampoule; 2.5 mg/ml, 1-ml ampoule

Uses:

counteract effect of non-depolarizing muscle relaxants administered during surgery; postoperative non-obstructive urinary retention; myasthenia gravis (section 20.2)

Contraindications:

recent intestinal or bladder surgery; mechanical intestinal or urinary tract obstruction; after suxamethonium; pneumonia; peritonitis

Precautions:

asthma; urinary tract infections; cardiovascular disease, including arrhythmias (especially bradycardia or atrioventricular block); vagotonia; hypotension; peptic ulcer; epilepsy; parkinsonism; hyperthyroidism; avoid before halothane administration has been stopped; maintain adequate ventilation (respiratory acidosis predisposes to arrhythmias); renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions:** Appendix 1

Dosage:

Reversal of non-depolarizing block, *by intravenous injection* over 1 minute, **ADULT** 2.5 mg, followed if necessary by supplements of 500 micrograms to maximum total dose of 5 mg; **CHILD** 40 micrograms/kg (titrated using peripheral nerve stimulator)

Note. To reduce muscarinic effects atropine sulfate *by intravenous injection* (**ADULT** 0.6–1.2 mg, **CHILD** 20 micrograms/kg) with or before neostigmine

Postoperative urinary retention, *by subcutaneous or intramuscular injection*, **ADULT** 500 micrograms (catheterization required if urine not passed within 1 hour)

Adverse effects:

increased salivation and bronchial secretions, nausea and vomiting, abdominal cramps, diarrhoea; allergic reactions, hypotension

Analgesics and opioid antagonists

Opioid analgesics, such as **morphine**, may be used to supplement general anaesthesia, usually in combination with nitrous oxide–oxygen and a muscle relaxant. Repeated doses of intra-operative analgesics should be given with care, since respiratory depression may persist into the postoperative period.

The specific opioid antagonist **naloxone** will immediately reverse this respiratory depression but the dose may need to be repeated. Other resuscitative measures must also be available. It is important to remember that naloxone will also antagonize the *analgesic* effect of opioids.

Paracetamol and **nonsteroidal anti-inflammatory drugs** may be useful alternatives (or adjuncts) for the relief of postoperative pain; they do not affect respiration and gastrointestinal motility.

For further information on opioid analgesics, see section 2.2; for paracetamol and nonsteroidal anti-inflammatory drugs, see section 2.1.

Opioid analgesics

Morphine

Drug subject to international control under the Single Convention on Narcotic Drugs (1961)

Injection (Solution for injection), morphine (as hydrochloride or sulfate) 10 mg/ml, 1-ml ampoule

Uses:

adjunct during major surgery; postoperative analgesia; pain, myocardial infarction, acute pulmonary oedema (section 2.2)

Contraindications:

acute respiratory depression; increased intracranial pressure, head injury or brain tumour; severe hepatic impairment (Appendix 5); adrenocortical insufficiency; hypothyroidism; convulsive disorders; acute alcoholism, delirium tremens; diverticulitis and other spastic conditions of colon; recent surgery on biliary tract; diarrhoea due to toxins

Precautions:

asthma, emphysema, or heart failure secondary to chronic lung disease; ability to maintain airway; if used in biliary colic, antispasmodic needed; renal impairment (Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3); **overdosage:** section 4.2.2; **interactions:** Appendix 1

Dosage:

Premedication, *by subcutaneous or intramuscular injection* 1 hour before surgery, **ADULT** 150–200 micrograms/kg; *by intramuscular injection* 1 hour before surgery, **CHILD** 50–100 micrograms/kg

Intra-operative analgesia, *by intravenous injection*, **ADULT** and **CHILD** 100 micrograms/kg, repeated every 40–60 minutes as required

Postoperative analgesia, *by intramuscular injection*, **ADULT** 150–300 micrograms/kg every 4 hours, **CHILD** 100–200 micrograms/kg; or *by intravenous infusion* **ADULT** 8–10 mg over 30 minutes, then 2–2.5 mg/hour

Adverse effects:

respiratory depression; anorexia, nausea, vomiting, constipation; euphoria, dizziness, drowsiness, confusion, headache; dry mouth; spasm of urinary and biliary tract; circulatory depression, hypotension, bradycardia, palpitations; miosis; allergic reactions; physical dependence

Opioid antagonists**Naloxone hydrochloride**

Injection (Solution for injection), naloxone hydrochloride 400 micrograms/ml, 1-ml ampoule

Uses:

to counteract respiratory depression induced by opioids during anaesthesia; opioid overdose (see also section 4.2.2)

Precautions:

dependence on opioids; cardiovascular disease

Dosage:

Opioid-induced respiratory depression, *by intravenous injection*, **ADULT** 100–200 micrograms, repeated every 2–3 minutes to obtain required response; **CHILD** initially 10 micrograms/kg, if no response followed by 100 micrograms/kg

Opioid-induced respiratory depression at birth, by *subcutaneous, intramuscular, or intravenous injection*, **NEONATE** 10 micrograms/kg immediately after delivery

Adverse effects:

nausea and vomiting; hypertension and hypotension reported; left ventricular failure; pulmonary oedema; seizures; arrhythmias such as ventricular tachycardia or fibrillation, particularly in pre-existing cardiac disease

Blood substitutes and solutions for correcting fluid imbalance

Fluid requirements must be assessed before, during and after major surgery. Replacement fluids should correspond as nearly as possible in volume and composition to those lost. Blood transfusion is essential to restore oxygen-carrying capacity when more than 15% of the circulating blood volume is lost but should be avoided whenever screening for human immunodeficiency viruses and hepatitis B virus is impracticable. Isotonic sodium chloride solution may be used for short-term volume replacement. Plasma expanders such as dextran 70 or polygeline may be useful. Provided renal function is maintained, fluid is most simply replaced by intravenous administration of **sodium chloride solution** (sodium chloride 9 mg/ml, 0.9%) or the more physiologically appropriate **compound solution of sodium lactate**. In emergency cases, there is usually an existing fluid deficit, which must be assessed and corrected before surgery. Isotonic **glucose/sodium chloride** mixtures (most commonly glucose 4%/ sodium chloride 0.18%) are preferred in children to avoid the danger of sodium overload and hypoglycaemia. When fluids are administered intravenously for more than 24 hours, potassium chloride is required to prevent potassium depletion. In order to avoid serious arrhythmias, especially in patients with impaired renal function, the required dose of potassium should be determined, whenever possible, by monitoring plasma concentrations of potassium.

See also sections 11.1 (plasma substitutes) and 26.2 (solutions correcting water, electrolyte, and acid-base disturbances).