Chapter 8
ANAESTHESIA

The word anaesthesia means absence of sensation. The term 'Anaesthesia' in the first century AD had been used to describe the narcotic like effects of the plant Mandragor. The word anaesthesia is coined from two Greek words "an" meaning without and "aesthsia" meaning sensation: "Anaesthesia" meaning insensible or without feeling. Insensible does not necessary imply loss of consciousness. So general anaesthesia can be defined as a reversible process which results in all of the following effects. 1. Amnesia or loss of awareness 2. Lack of overt muscular response to surgical stimulation 3. Minimal autonomic response to surgical stimulation 4. In addition there may be some muscular relaxation.

8.1 GENERAL ANAESTHESIA

General anaesthesia implies unconsciousness. Only experienced and authorized personnel (anaesthetists) should use the drugs in this section and apply where adequate resuscitative equipment including proper facilities for intubations, close monitoring and mechanically assisted ventilation facilities are available.

It is now common practice to administer several drugs with different actions to produce a state of surgical anaesthesia with minimal risk of toxic effects. An intravenous anaesthetic is usually used for induction, followed by maintenance with inhalation anaesthetics, often supplemented by other drugs administered intravenously. Specific drugs are often used to produce and maintenance of muscle relaxation when positive pressure ventilation is employed.

Various drugs are used before and during anaesthesia to modify physiological functions to maintain the patient in a satisfactory condition during surgery.

PREMEDICATION

Introduction of drugs before the induction of anaesthesia is called **premedication**. The objectives of premedication are: i) to allay anxiety and fear; ii) to reduce secretions; iii) to enhance the hypnotic effect of general anaesthetics; iv) to reduce post operative nausea and vomiting; v) to reduce volume of gastric acid secretion and increase pH; vi) to produce amnesia; vii) to attenuate visual reflexes; viii) to attenuate sympathy ohadrenal response.

Drugs used for premedicarion are:

Atropine/glycopyrolate used as anti-sialogogue; metoclopramide and ondensatron for prevention of vomiting and benzodiazepines for relief of anxiety, morphine and pethidine for relief of pain before surgery.

For certain procedures, controlled hypotension may be required for which

labetalol, sodium nitroprusside, and **glyceryl trinitrate** are used. Glyceryl trinitrate is also used to control hypertension post-operatively.

Beta-blockers *(see section 3.1* (**esmolol), adeno-sine**, **amiodarone** or **verapamil** *(see sec. 3.3.2)* may be used to control perioperative arrhythmias, including tachycardia and hypertension.

Antidepressants need to be stopped at least 2 days before major surgery to avoid withdrawal symptoms, but the normal dose can be continued (with careful monitoring of fluids and electrolytes) for minor surgery.

PROPHYLAXIS OF ACID ASPIRATION: Regurgitation and aspiration of gastric contents is an important complication of general anaesthesia, particularly in obstetrics and emergency surgery. The pH and volume of the aspirate influence the damage to the lungs. Nature of the aspirate whether it is particulate or nonparticulate, has also a role. **H_2-receptor antagonists** *(see sec. 2.3.1),* **omeprazole and metoclopramide-** *(see sec. 2.3.3)* may be used before surgery to increase the pH and reduce the volume of gastric fluid. However, they do not affect the pH of fluid already in the stomach and this limits their value in emergency procedures. Oral H_2-receptor antagonists can be given 1-2 hours before the procedure but omeprazole must be given at least 12 hours earlier.

Antacids *(see section 2.1)* are often used preoperatively to neutralize the acidity of the fluid already in the stomach; for this purpose, 'clear' (i.e. non-particulate) antacids such as sodium citrate are preferred.

Recommended combination should be H_2–receptor antagonists (to increase the pH of the gastric secretions), metoclopramide (to enhance gastric emptying and thus reduce the gastric volume) and non-particulate oral antacids (to increase the pH of the stomach content already in the stomach).

8.1.1 INTRAVENOUS ANAESTHETICS

Intravenous anaesthetics are more commonly used to induce anaesthesia. In some circumstances, such anaesthetics are used also for maintenance either alone or with **nitrous oxide (N_2O).** They may be used as repeated bolus dose or as continuous intravenous infusion. Commonly used intravenous anaesthetics are very rapid in action and can cause apnoea and hypotension; so adequate resuscitative facilities must be available. They are contraindicated if the anaesthetist is not confident of being able to maintain the airway (e.g. in the presence of a tumour in the pharynx or larynx). Extreme care is required in surgery of the mouth, pharynx, or larynx and in patients with acute circulatory failure (shock) or fixed cardiac output.

Individual requirements for the drugs vary considerably and the recommended dosage is only a guide. Smaller dosage is indicated in ill, shocked, or debilitated patients, while robust individuals may require more. To facilitate tracheal intubation, induction is followed by a neuromuscular blocking drug *(see section 8.1.5 on muscle relaxants).*

BARBITURATES

ETOMIDATE

Etomidate is an induction agent having rapid recovery without hangover effect. It is the most cardiovascularly stable of the currently available induction agents, being associated with only a slight fall in blood pressure and little change in heart rate. Cardiac output and myocardial contractility are little changed and this also is the case in patients with ischemic heart disease. There is a high incidence of extraneous muscle movement and of pain on injection; these effects can be minimized by premedication with an opioid analgesic and the use of a larger vein. There is evidence that repeated doses of etomidate may have an undesirable suppressant effect on cortisol output. Preferably, it should be avoided in patients receiving steroid therapy for long time or one who has received such in the recent past

Indications: induction of anaesthesia in patients with an unstable cardiovascular system and is safe to use in patients with prophyria

Cautions: Is best avoided in patients with epilepsy or a history of adrenocortical insufficiency

Dose: Induction 0.2-0.3 mg/kg *by intravenous infusion*

Proprietary Preparation
Etomid *(Popular),* Inj. (IV Infusion), 2mg /ml, Tk. 150.57/amp

KETAMINE[ED]

Ketamine produces dissociative anaesthesia, rather than generalized depression on CNS in which patients may remain conscious, though amnesic and insensible to pain. Onset of action is relatively slow. Unlike other agents analgesia may precede the onset of anaesthesia and persists after the return of consciousness. During this period, bizarre hallucination may occur, associated with the loss of body image and if stimulated react violently and irrationally. It can be given by the intravenous or the intramuscular route, and has good analgesic properties when used in sub-anaesthetic dosage. Muscle tone is increased. There is sympathetic cardiovascular stimulation and arterial pressure may rise with tachycardia

Indications: induction and maintenance of anaesthesia. It is used mainly for paediatric patients when repeated doses are require. Most effective in poor ricks patients and for surgery under adverse circumstances

Cautions: patients with a history of cerebrovascular accidents, myocardial ischemia, hypertension and raised intracranial pressure

Contraindications : airway obstruction, thyrotoxicosis, cerebral trauma, intracranial mass or haemorrhage, penetrating eye injuries, increased intraocular pressure and psychiatric disorders

Interactions: *see Appendix-2*

Side effects: emergence of delirium, nightmares, hypertension, tachycardia, increased salivation, increased ICP, slow recovery, nystagmus, agitation, vomiting, mycholonus and laryngospasm. Nausea and vomiting are common after its sole use

Dose: *By intramuscular injection*, 10 mg/kg usually produce 15-30 minutes of surgical anaesthesia; diagnostic maneuvers and procedures not involving intense pain, initially 4 mg/kg *by intravenous injection* over at least 60 seconds, 2 mg/kg usually produces 5-10 minutes of surgical anaesthesia

By intravenous infusion, for longer procedures, induction, bolus dose of 0.5-2mg/kg; maintenance 10-45 micrograms/kg/min, rate adjusted according to response.

Proprietary Preparations
G-Ketamine *(Gonoshasthaya),* Inj., 50 mg/ml, Tk.100.00/10 ml Vial
Kain *(Renata),* Inj., 50 mg/ml, Tk. 100.00/10ml Vial
Ketalar *(Popular),* Inj., 50 mg/ ml, Tk. 115.43/10 ml Vial
Ketaride *(Incepta),* Inj., 50 mg/ml, Tk. 115.00/10 ml Vial
Pentyl *(ACI),* Inj., 50 mg/ml, Tk. 115.43/10 ml Vial

PROPOFOL

Propofol is a very widely used hindered phenol and virtually insoluble in water is associated with rapid recovery without hangover effect but more rapidly metabolized (rapid induction and recovery). So it is suitable for day case surgery. It has amnesic, anxiolytic, antiemetic and antiepileptic properties. No analgesic effects, while the depression of laryngeal and pharyngeal reflexes yields optimal condition for insertion of LMA

Indications: Induction of anaesthesia, total intravenous anaesthesia, sedation during surgery, diagnostic procedures and in intensive care

Cautions: care must be taken in patients with cardiac diseases or who are hypovolaemic (bradycardia is common). Strict aseptic technique must be taken during use to avoid bacterial

contamination. Avoid with soya or egg with allergies. Monitoring of blood lipid concentrations in patients at risk of fat overload is recommended

Contraindications: history of propofol allergy, airway obstruction, sedation of children and ECT.

Side-effects: profound hypotension and respiratory depression apnoea more common and of longer duration than thiopentone, hypersensitivity reactions; pain on injection.

Dose: induction of anaesthesia, *by intravenous injection* or *by intravenous infusion* 1.5-2.5mg/kg (less in the ELDERLY) at a rate of 20–40 mg every 10 seconds. CHILD over 3 years 2.5 mg/kg adjusted as necessary

Maintenance of anaesthesia, *by intravenous infusion*, 4-12 mg/kg/hour or *by intermittent injection* (25-50 mg repeated according to response); CHILD over 3 years 9-15 mg/kg/hour

Sedation during intensive care (with assisted ventilation), *by intravenous infusion,* 0.3-4 mg/kg/hour for up to 3 days; CHILD not recommended

Sedation for surgical and diagnostic procedures, initially *by intravenous injection* 0.5-1.0mg/kg over 1-5 minutes; maintenance, *by intravenous infusion* 1.5-4.5 mg/kg/hour, those over 55 years may require lower dose; CHILD not recommended

Note. Propofol 2% should not be given by bolus intravenous injection.

Proprietary Preparations

Fresofol[(J)] *(Fresenius)* Inj. (IV Infusion) 1%, Tk. 351.06/20 ml; Tk.779.00/50ml

Pofol *(Popular),* Inj., (IV Infusion), 1%, Tk. 200.75/20 ml

Propofol lipuro [(I)] *(B.Braun)* Inj., (IV Infusion), 1%, Tk. 585.25/50 ml; Tk.278.69/20ml

THIOPENTONE SODIUM [ED]

(Thiopental sodium)

Thiopentone sodium is a widely used, rapid onset, ultrashort acting barbiturates, rapidly reaches the brain and causes unconsciousness within 30-40 seconds but it has no analgesic properties. Induction is generally smooth but owing to its narrow therapeutic margin, cardio respiratory depression may occur with over dosage. The reconstituted solution is highly alkaline and therefore irritant on misplaced injection outside the vein; arterial injection is particularly dangerous.

Awakening from a moderate dose of thiopentone is rapid due to redistribution of the drug in the whole body tissues. Metabolism is, however, slow and some sedative effects may persist for 24 hours. Repeated doses have a cumulative effect.

Indications: Induction of general anaesthesia and in the treatment of status epilepticus

Cautions: Its potency makes it a highly dangerous drug in unexperienced hands. It is very easy to give an over dose to sick and elderly alone. It should never be given patients in the sitting position. Should never be given rapidly to any but fit and robust. Apparatus capable of ventilating should always be readily available. Unsuitable for use in out patients

Contraindications: airway obstruction, hypersensitivity to barbiturate, porphyria, in severe shock, uncompensated heart disease, in status asthamaticus

Interactions: *see Appendix-2*

Side-effects: apnoea, hypotension.

Dose: *By intravenous injection* as a 2.5% solution; the dose required to produce anaesthesia varies, and the response to each patient must be assessed carefully. In adults, initially 3-5 mg/kg (reduced in elderly or debilitated) over 15–20 seconds (longer in elderly or debilitated), followed by further quantity (50–100 mg) as supplementary dose to be given if necessary according to response after 30–60 seconds; CHILD induction 2-4 mg/kg

Proprietary Preparations

Genisia *(Square),* Inj., 500 mg/Vial, Tk. 69.59/Vial

G-Thiopental *(Gonoshasthaya),* Inj., 1 gm/Vial, Tk. 100.00/Vial; 500 mg/Vial, Tk. 64.69/vial

Thiaton *(Techno),* Inj., 1 gm/Vial, Tk. 100.00/Vial ; 500 mg/Vial, Tk. 60.00/Vial

Thiopen *(ACI),* Inj., 1 gm/Vial, Tk. 100.37/Vial; Inj., 500 mg/Vial , Tk. 69.84/Vial

TPS *(Popular),* Inj., 1gm/Vial, Tk. 100.38/Vial; 500 mg/Vial, Tk. 69.85/Vial

8.1.1 INHALATIONAL ANAESTHETICS

Inhalational anaesthetics may be gases or volatile liquids. They can be used both for induction and maintenance of anaesthesia following induction with an intravenous anaesthetic .

Gaseous anaesthetics require suitable equipment for storage and administration. Volatile liquid anaesthetics are administered using calibrated vaporizers, using air, oxygen, or nitrous oxide-oxygen mixture as the carrier gas.

To prevent hypoxia inhalational anaesthetics must be given with concentrations of oxygen (30%) greater than in air.

HALOTHANE[ED]

Halothane is a potent volatile liquid anaesthetic commonly used in clinical practice.. Induction is smooth, the vapour is non-irritant, pleasant to inhale, and seldom induces coughing or breathe holding. Despite these advantages, however, halothane is much less widely used in the developed countries than previously, due mainly to medicolegal fears concerning the risk of hepatitis but also because newer agents are perceived to have advantages. Halothane suppresses salivary or bronchial secretions, sympathetic activity but rapid recovery when the anaesthetic is withdrawn. It causes moderate muscle relaxation but inadequate for major surgery.

Indications: for induction and maintenance of anaesthesia

Cautions: should be used with great caution in patients with intracranial mass lesions,epinephrine administration, while pervious exposure and reaction to halothane

Contraindications: a history of unexplained jaundice or pyrexia in a patient following exposure to halothane is absolute contraindication for its future use in that patient; repeated use of halothane within a period of at least 3 months; severe arrhythmia; hypovolaemic patients with aortic stenosis

Side-effects: respiratory and myocardial depression, hypotension, arrhythmias; post operative shivering.

Dose: using a specifically calibrated vaporizer for induction concentration increased gradually up to 2–4 % in oxygen or nitrous oxide-oxygen; CHILD 1.5–2%. Maintenance 0.5–2 %.

Proprietary Preparation

Halosin *(ACI),* Inhalation anesthetic 250 ml.Tk. 1,656.22 /250ml

ISOFLOURANE

Isoflurane is another volatile anaesthetic similar to halothane but less potent, about twice the concentration being necessary for induction and maintenance. Perhaps the ideal inhalational agent more closely than any other agent. Heart rhythm is generally stable during isoflurane anaesthesia, but heart rate may rise particularly in younger patients. Systemic arterial pressure may fall, owing to a decrease in systemic vascular resistance and with less decrease in cardiac output than occurs with halothane. Respiration is depressed. The marked muscular relaxation, potentiation of muscle relaxant action and stable cardiovascular system are particular advantages of isoflurane. It may also cause hepatotoxic renal toxicity in those sensitized to halogenated anaesthetics but the risk is appreciably smaller than with halothane.

Indication & Cautions: *same as that of halothane*

Contraindications: hepatic and renal impairment

Interaction: *see Appendix-2*

Side-effects: profound respiratory depression

Dose: using a specifically calibrated vaporizer, induction, increased gradually from 0.5% to 3%, in oxygen or nitrous oxide-oxygen *Maintenance*, 1.1 to 1.5% in nitrous oxide-oxygen; an additional 0.5-1% may be required when given with

oxygen alone; caesarean section, 0.5-0.75% in nitrous oxide-oxygen

Proprietary Preparation
Forane [I] *(Abbott)* Inhalation anesthetic Tk.3666.00/100ml

NITROUS OXIDE[ED]

Nitrous oxide (N_2O) a gaseous anaesthetic is supplied in cylinder compressed to a liquid at high-pressure is in wide spared use. Nitrous oxide is unsatisfactory as a sole anaesthetic owing to its lack of potency but is useful as part of a combination of drugs since it allows a significant reduction in dosage. For anaesthesia it is commonly used in a concentration of 50 to 70% in oxygen as part of a balanced technique in association with other inhalational or intravenous agents.

Indications: used for maintenance of anaesthesia and in sub-anaesthetic concentrations for analgesia (changing painful dressings, postoperative physiotherapy, emergency ambulances) and as a sedative in dentistry.A mixture of nitrous oxide and oxygen containing 50% of each gas is used to produce analgesia without loss of consciousness.

Cautions: the most obvious problem with nitrous oxide administration is hypoxia. So oxygen concentration of at least 30 % should be given

Side-effects: hypoxia. Increase pressure in air-containing closed space such as pneumoperitonium, pneumothorax, pneumopericardium, middle ear and obstructed intestine. Exposure for prolonged periods, may result in megaloblastic anemia due to interference with the action of vitamin B_{12}. For the same reason, exposure of theatre staff to nitrous oxide should be minimized. Depression of bone marrow, white cell formation and DNA synthesis may also occur

Dose: for anaesthesia it is commonly used in a concentration of 50 to 70% in oxygen as part of a balanced anaesthetic technique. For analgesia, a mixture with 50% oxygen, according to the patient's needs

SEVOFLURANE

It is non-irritant to the upper airway and bronchi and virtually odourless, induction of anaesthesia is rapid. Unlike isoflurane sevoflurane is not associated with an increase in heart rate. It has less coronary vasodilator properties than isoflurane and does not cause a steal phenomenon in experimental animals with appropriate coronary artery anatomy. It does not potentiate epinephrine induced arrhythmias.
Liver and Kidney blood flow are well preserved under sevoflurane anaesthesia. It has no detrimental effect on overall hepatic function and has a low potential for hepatotoxicity. There is no effect on blood urea and serum creatinine.

Indications: Induction and maintenance of anaesthesia. Sevoflurane has many of the features of an ideal volatile anaesthetic agent which makes it particularly useful in children. It is also suitable for 'vital capacity' induction by inhalation of a single large breath of a high concentration, e.g. 8 per cent in oxygen

Cautions: It is very expensive and should only be used in low flow systems with CO_2 absorption
Contraindications & Side-effects: Same as other volatile anaesthetic.
Dose: It has a MAC value of 1.71-2.05. 2-3% for induction, being higher in children and reduced in the presence of nitrous oxide

Proprietary Preparation
Sevorane[I] *(Abbott)* Inhalation anesthetic Tk.14325.45/250 ml

8.1.2 ANTIMUSCARINIC AND ANXIOLYTIC DRUGS FOR PERI OPERATIVE USE

ANTIMUSCARINIC DRUGS

Antimuscarinic drugs reduce intestinal motility and gastric secretion and may be useful in some forms of dyspepsia, in irritable bowel syndrome, excessive salivation and muscarinic actions of

neostigmine. They are also used to prevent bradycardia and hypotension associated with anaesthesia related drugs such as halothane, propofol and suxamethonium.

Atropine and **hyoscine** (as hydrobromide) are commonly used antimuscarinic drugs in perioperative period.

Glycopyrronium bromide reduces salivary secretions. When given intravenously it produces less tachycardia than atropine.

ATROPINE SULPHATE [ED]

Atropine has an emergency role in the treatment of vagotonic side-effects. It has a definite role in acute arrhythmias after myocardial infarction and during cardiopulmonary resuscitation

Indications: for drying of secretions and reversal of excessive bradycardia; with neostigmine to antagonize its muscarinic action

Cautions: is best avoided where there is marked tachycardia such as may occur in thyrotoxicosis, cardiovascular disease and in cardiac surgery, hyperpyrexial patients and in glaucoma,

Antimuscarinics should be used with caution in Down's syndrome, in children and in the elderly, reflux oesophagitis, diarrhoea, acute myocardial infarction, hypertension, pregnancy and breast-feeding

Contraindications: in angle-closure glaucoma, myasthenia gravis, paralytic ileus, pyloric stenosis and prostatic enlargement

Side-effects: constipation, transient bradycardia (followed by tachycardia,palpitation and arrhythmias), reduced bronchial secretions, urinary urgency and retention, dilatation of the pupils with loss of accommodation, photophobia, dry mouth, flushing and dryness of the skin

Dose: premedication, *by intravenous injection*, 300-600 micrograms immediately before induction of anaesthesia, and in incremental doses of 100micrograms for the treatment of bradycardia

By intramuscular injection, 300-600 micrograms 30–60 minutes before anaesthesia induction; CHILD 20 micrograms/kg.

for control of muscarinic side-effects of neostigmine in reversal of competitive neuromuscular block, *by intravenous injection,* 0.6-1.2 mg usually used in a ratio of 2.5 mg neostigmine to 1mg.

Proprietary Preparations
see section 2.2

GLYCOPYRRONIUM BROMIDE

Indications: to reduce salivary, tracheobronchial, and pharyngeal secretions, as well as decreasing the acidity of gastric secretion. It is also used in conjunction with neostigmine, to prevent muscarinic effects of neostigmine such as bradycardia; treatment of chronic obstructive pulmonary disease, hyperhidrosis

Cautions: thyrotoxicosis, coronary artery disease, cardiac dysarythmias, hypertension, congestive heart failure and cardiac insufficiency, pregnancy

Contraindications: pregnancy, breast-feeding, enlarged prostate, glaucoma

Side-effects: fever and heat stroke in hot environments, dry mouth, difficulty urinating, drowsiness or blurred vision,

Dose: Premedication, *by intramuscular or intravenousinjection*, 200–400 micrograms or 4–5 micrograms/kg(max. 400 micrograms); CHILD 1 month–12 years, 4–8 micrograms/kg (max. 200 micrograms) Intra-operative bradycardia, *by intravenous injection*,200–400 micrograms or 4–5 micrograms/kg (max.400 micrograms), repeated if necessary; CHILD 1month–18 years, 4–8 micrograms/kg (max.200 micrograms), repeated if necessary

Control of muscarinic side-effects of neostigmine in reversal of non-depolarising neuromuscular block, by*intravenous injection,* 200 micrograms per 1mg of neostigmine, or 10–15 micrograms/kg; CHILD 1month–12

years, 10 micrograms/kg (max. 500 micrograms)

Proprietary Preparation
Seebri Breezhaler [I] *(Novartis)* Inhalation Powder Hard Cap., 50 mcg, Tk. 99.50/Cap

HYOSCINE HYDROBROMIDE

(Scopolamine Hydrobromide)

Indications: used as a sedative, amnesic and antisialogogue in premedication, antiemetic and in the treatment of motion sickness

Caution: as atropine sulphate.

Side-effects: As those of atropine sulphate, excitement, ataxia, hallucinations, behavioral abnormalities, and drowsiness

Dose: premedication, *by subcutaneous or intramuscular injection,* 200–600 micrograms 30–60 minutes before induction of anaesthesia (often given with papaveretum)

Proprietary Preparations
Buscon*(Ibn Sina),* Inj., 20 mg/ml , Tk. 7.10/Amp.
Butapan *(Sanofi),*;Inj., 20 mg/ml , Tk. 7.89/Amp.
Colik *(ACI),* Inj., 20 mg/ml , Tk. 7.88/amp
G-Hyoscine *(Gonoshasthaya),* Inj., 20 mg/ml , Tk.7.75/Amp.
Hysomide *(Opsonin),* Inj., 20 mg/ml , Tk. 5.93/Amp.
Spasmoson *(Jayson),* Inj., 20 mg/ml , Tk. 7.88/Amp.

Papaveretum and Hyoscine
Inj. Papaveretum 15.4 mg + hyoscine hydrobromide 400 micrograms/ml, 1 ml amp.

ANXIOLYTICS

(see also section 7.1 & 7.2)

Benzodiazepines (e.g. **diazepam, lorazepam and midazolam)** are widely used.

BENZODIAZEPINES

Short-acting benzodiazepines taken by mouth are the most common premedicants. They have no analgesic effect.Can alleviate anxiety at doses that do not necessarily cause excessive sedation and they are of particular value during short procedures or during operations under local anaesthesia including dentistry. Amnesia reduces the likelihood of any unpleasant memories of the procedure. Benzodiazepines are also used in intensive care units for sedation, particularly in those receiving assisted ventilation.

DIAZEPAM[ED] [CD]

(see also section 7.1)

Diazepam is used to produce mild sedation with amnesia. It is long-acting and its effect and timing of response are unreliable. Diazepam in children is not generally recommended
Indications: for premedication including anxiolysis, sedation and amnesia and regarded as a drug of first choice in the treatment and prevention of all kinds of convulsive states

Cautions: may occasionally cause marked respiratory depression and facilities for its treatment are essential; hepatic and renal impairment particularly the elderly are more sensitive. Diazepam injection cannot be diluted and precipitates when mixed with most other agents

Interactions: *see Appendix-2*

Side-effects: pain, thrombophlebitis, tenderness have occurred following injection of diazepam

Dose: *by mouth,* 5 mg on night before minor or dental surgery then 5 mg 2 hours before procedure

by intravenous injection, into a large vein 10-20 mg over 2-4 minutes as sedative cover for minor surgery or invasive medical procedure; premedication 100-200 micrograms/kg

Note. Diazepam is relatively insoluble in water. Preparations formulated in organic solvents are painful on intravenous injection and may give rise to venous thrombosis. An emulsion preparation is less irritant and safer in respect of venous thrombosis.

Proprietary Preparations
see section 7.1

MIDAZOLAM

Midazolam is a water-soluble, short acting benzodiazepine with general properties similar to those of diazepam except that it has a more profound amnesic action and is often preferred to intravenous diazepam because recovery is faster than from diazepam. It is associated with profound sedation when high doses are given intravenously or when it is used with certain other drugs. Its main differences from thiopentone being the delay in onset of anaesthesia.

Indications: premedication before general anaesthesia, induction of anaesthesia, to provide sedative care for minor surgical or investigative procedures; patients in intensive care who require continuous sedation

Cautions: same as for diazepam
Interactions: *see Appendix-2*

Side-effects: same as diazepam

Dose: premedication, b*y intramuscular injection,* 70-100 micrograms/kg 30-60 minutes before surgery; usual dose 5 mg (ELDERLY 2.5 mg)

Induction of anaesthesia, *by slow intravenous injection,* 200 micrograms/kg (ELDERLY 100-200 microgram/kg; CHILD over 7 years 100 microgram/kg)

Sedation of patients receiving intensive care, *by intravenous infusion,* initially 30-100 micrograms/kg given over 5 minutes, then 30-150 micrograms/kg per hour; reduce dose or omit initial dose in hypovolaemia, vasoconstriction or hypothermia

Sedation for dental, minor surgical and other procedures, *by intravenous injection,* 2 mg initially (half in elderly) over 30 seconds followed after 2 minutes by increments of 0.5-1 mg if sedation not adequate; usual total dose 2.5 to 7.5 mg (~70 micrograms/kg), elderly 1-2 mg.

Proprietary Preparations
Anquil *(General),* Inj., 15 mg/3 ml, Tk.75.00/Amp.
Dormax *(Aristo),* Inj., 15mg/3 ml, Tk.150.00/Amp.
Dormi *(Square),* Inj., 15 mg/3ml, Tk. 120.00/Amp.
Dormicum (I) *(Roche)* Inj. 15mg/3ml, Tk.170.39/3ml Amp.
Dormilat *(ACI),* Inj., 5 mg/5 ml, Tk.55.00/Amp; 15 mg/3 ml, Tk. 75.00/Amp.
Hypnofast *(Incepta),* Inj., 15 mg/3 ml, Tk.90.00/Amp.; 5 mg/5ml, Tk. 50.00/Amp
Midolam *(Opsonin),* Inj., 15 mg/3 ml, Tk.56.60/Amp.
Midzo *(Renata),* Inj., 15mg/3 ml, Tk. 75.00/Amp.
Milam *(Eskayef),* Inj., 15 mg/3 ml, Tk.100.00/Amp.
Sedaquil *(Rangs),* Tab. 7.5 mg, Tk. 8.00/Tab.

8.1.3 ANALGESICS FOR PERI OPERATIVE USE

8.1.3.1 OPIOIDS
8.1.3.2 NON-OPIOIDS

8.1.3.1 OPIOIDS

(see also section 7.5.1)

Preioperative use of opioids is generally limited to those patients who require control of existing pain.

INTRA-OPERATIVE ANALGESIA:
Opioid analgesics given in small doses before or with induction reduce the dose requirement of other drugs used for this purpose. Shorter acting **fentanyl** and **remifentanil** are particularly useful because they act within 1-2 minutes. The initial dose of fentanyl is followed either by successive intravenous injections or by an intravenous infusion; prolonged infusions increase the duration of effect. Repeated intraoperative doses of fentanyl should be given with care since the respiratory depression can persist into the post-operative period *(see below),* and occasionally it may become apparent for the first time postoperatively when monitoring of the patient might be less intensive.

In contrast to other opioids, which are metabolized in the liver, remifentanil undergoes rapid metabolism by non-specific blood and tissue esterases; its short duration of action allows prolonged administration at high dosage, without accumulation, and with little risk of residual postoperative respiratory depression. Remifentanil should not be

given as a bolus injection intra-operatively but it is well suited to continuous infusion; a supplemental analgesic will often be required after stopping the infusion.

POST-OPERATIVE ANALGESIA : The use of any intra-operative opioids affects the prescribing of postoperative analgesics. In many cases, use of intra-operative opioids will delay the need for a postoperative analgesic. A postoperative opioid analgesic should be given with care since it may potentiate any residual respiratory depression.

Morphine and pethidine are still used most widely. Respiratory depression is a major concern with opioid analgesics and it may be treated by artificial ventilation or be reversed by **naloxone**;

FENTANYL[CD]

Fentanyl is chemically related to pethidine, but is not a pethidine derivative. It is a potent narcotic analgesic and shares the share the same properties as other opiates, namely analgesia, sedation, respiratory depression, vagal stimulation, nausea and vomiting, constipation and physical dependence. It is now used mainly on its own as the analgesic component of balanced anaesthesia and is probably the commonest drug used for this purpose.

Indications: for analgesia during operation, enhancement of anaesthesia; epidural anaesthesia and analgesia

Cautions: Analgesic doses of fentanyl will always cause respiratory depression, truncal rigidity and facilities for its treatment must be immediately available.

Contraindications; Side-effects: *see notes above*

Dose: *by intravenous injection*, with spontaneous respiration, 50-200 micro-grams, and then 50 micrograms as required. CHILD 3-5 microgram/kg, and then 1 microgram/kg as required

With assisted ventilation, 0.3–3.5 mg, then 100-200 micrograms as required. CHILD 15 micrograms/kg, then 1–3 micrograms/kg as required

Proprietary Preparations
Durogesic (I) *(Janseen,),* Transdermal Patch, 25micrograms, /h;Tk. 2754.25; 50 micrograms/h;Tk.5456.50
Fentanyl (I), **(***Rotex)* , Inj.,0.1mg/2ml , Tk. 36.76/2mlAmp
Fentanyl HEXAL MAT(I) *(Hexel)* , Transdermal patch (matrix), 25 mcg/h, Tk. 370.00/Patch
Fentyl *(Popular),* Inj., 0.005 gm/100 ml, Tk. 40.15/Amp.
Opifen *(Incepta),* Inj., 0.005 gm/100 ml, Tk. 40.00/Amp

MORPHINE SULPHATE [ED] [CD]

(see section 7.5.1)

Morphine is the oldest analgesic known to man. The main effects of morphine are: on the CNS *Depression, leading to analgesia*, *respiratory depression* (decrease in sensitivity of the respiratory centre to PCO_2), and depression of cough reflex, sleep)
Excitation**,** leading to vomiting, miosis (pupil constriction), convulsions (very rare)

Changes of mood – euphoria
(Sense of well-being) or **dysphoria.**
Tolerance and dependence
(Psychological and physical)
Smooth muscle stimulation
Gastrointestinal muscle spasm
(With constipation) and biliary tract spasm, bronchospasm & retention of urine.
Cardiovascular system
Dilation of resistance and capacitance vessels.
Other effects
Sweating, histamine release, pruritus, piloerection, antidiuretic effect.

Indications: Relief of moderate to severe acute pain , chronic pain often in terminal illness, Brief relief of anxiety in serious and frightening condition, diseases accompanied by pain, relief of dyspnoea in acute left ventricular failure, cardiac ischaemia and in terminal cases, premedication before operation. analgesic component of balanced anaesthesia
Cautions: Depressant action in all level. Concern about overdose and monitoring

Contraindications: adrenocortical insufficiency, severe liver diseases, hypothyroidism, diverticulitis, and other spastic condition of the colon, biliary colic, patients treated with MAOIs, elderly patients, during labour, confusion, vomiting and constipation.
Side effects: Overdoses causes respiratory failure, cardiovascular collapse and coma.
Dose: Usual Adult Dose for Pain
Oral, sublingual, or buccal: 5 to 30 mg every 3 to 4 hours as needed Extended-release capsules: 100 mg and 200 mg for use only in opioid tolerant patients: To be taken *orally* 1 to 2 times daily swallowed whole or opened and sprinkled on a small amount of applesauce immediately prior to ingestion. Maximum dose: 1600 mg orally daily
IM or subcutaneous: 2.5 to 20 mg every 3 to 4 hours as needed
IV: 4 to 15 mg every 3 to 4 hours as needed. Give very slowly over 4 to 5 minutes. Starting doses up to 15 mg every 4 hours have been used. Chest pain: 2 to 4 mg repeat as necessary
Continuous IV: 0.8 to 10 mg/hour. Maintenance dose: 0.8 to 80 mg/hour. Rates up to 440 mg/hour have been used.
IV patient controlled analgesia or subcutaneous patient controlled analgesia: 1 to 2 mg injected 30 minutes after a standard IV dose of 5 to 20 mg. The lockout period is 6 to 15 minutes. The 4 hour limit is 30 mg. *Continuous subcutaneous*: 1 mg/hour after a standard dose of 5 to 20 mg
Epidural: 5 mg one time. May give 1 to 2 mg more after one hour to a maximum of 10 mg. *Intrathecal:* 0.2 to 1 mg one time Intrathecal Continuous: 0.2 mg/24 hours. May be increased up to 20 mg/24 hours.
Rectal: 10 to 30 mg every 4 hours as needed.
Usual Pediatric Dose for Pain
Less than or equal to 4 weeks: Use preservative-free formulation: Initial:0.05mg/kg*IM,IV,or subcutaneously* every 4 to 8 hours titrating carefully to effect Maximum dose: 0.1mg/kg/dose. Continuous Infusion: 0.01 mg/kg/hour continuous IV infusion. Do not exceed infusion rates of 0.015 to 0.02 mg/kg/hour.

Greater than or equal to 1 month but less than 12 years: *Oral*: 0.2 to 0.5 mg /kg / dose every 4 to 6 hours (tablets/solution) or 0.3 to 0.6 mg/kg/dose every 12 hours (extended release)
IM,subcutaneous,IV:0.05 to 0.2mg/kg/ dose (up to 15 mg) every 4 hours as needed.
IV/subcutaneous Continuous: 0.025 to 0.206 mg/kg/hour (sickle cell or cancer pain) or 0.01 to 0.04 mg/kg/hour (postop pain)
Epidural: (use preservative-free formulation): 0.025 mg/kg/dose every 6 to 8 hours (postop pain). Maximum per 24 hours: 5 mg.
Greater than or equal to 12 years: Premedication for anesthesia *IV*: 3 to 4 mg once, may repeat in 5 minutes if necessary. *Oral:* 0.2 to 0.5 mg/kg/dose every 4 to 6 hours (tablets/solution) or 0.3 to 0.6 mg/kg/dose every 12 hours (extended release).*IM,subcutaneous, IV:* 0.05 to 0.2 mg/kg/dose (up to 15 mg) every 4 hours as needed
IV/subcutaneous Continuous: 0.025 to 0.206 mg/kg/hour (sickle cell or cancer pain) or 0.01 to 0.04 mg/kg/hour (postop pain).*Epidural* (use preservative-free formulation): 0.025 mg/kg/dose every 6 to 8 hours (pastor pain). Maximum per 24 hours: 5mg. *IV patient controlled analgesia:* 0.015 mg/kg/dose (postop pain); lockout period of 10 minutes; 4 hour limit of 0.25 mg/kg.
Dose adjustments: Titrate dosage slowly upward, taking into consideration the dosages received for breakthrough pain, to meet the specific needs of a patient.
Factors such as age, disease state, concomitant drug therapy, and tolerance to narcotics can have variable but important effects on dose and response. Women have been reported to require more morphine than men to achieve a similar degree of analgesia.
If a patient is not able to take oral morphine, divide the oral dose by half and give subcutaneously. If the IV route is preferred, the oral dose may be

divided by 3.
The potency ration of oral to rectal morphine is 1:1.

Proprietary Preparations
see also section 7.5.1

PETHIDINE HYDROCHLORIDE[ED] [CD]

(see section . 7.5.1)

There are many similarities between structure of pethidine and morphine and share many of desirable and undesirable propertied of morphine. All types of pain are relieved by the drug but is more effective in pain of visceral origin, probably because of atropine like action. The drug is of value in the relief of intractable pruritus which may be aggravated by giving morphine.
Indications: same as that of morphine; also for labour analgesia

Contraindication: same as that of morphine
Side-effects: same as that of morphine. Pethidine is metabolized to norpethidine, which may accumulate, particularly in renal impairment; norpethidine stimulates the central nervous system and may cause convulsions, especially in children
Dose: may be given by mouth, IM, IV.
For analgesia: Oral/IM- 50-100mg every 3-4h as necessary.For premedication:IM 50-100mg ig given before operation.
As blanced anaesthesia;10-15 mg IV, Supplementary necessaey every 20-30min
In tachypnoea IV Upto 25mg.
For obstetric use: 100-150 mg IM when labour pain become regular then repeated every 2-3 h as required.

Proprietary Preparation
see also section 7.5.1

REMIFENTANIL

Remifentanil is unique among opioids in having the predictable and very short duration of action

Indications: supplementation of general anaesthesia during induction and analgesia during the maintenance of anaesthesia

Cautions, Contraindications & Side-effects: It has all the features of opioids, *see notes above.*

Dosages and administration: Induction, *by intravenous infusion*, 0.5-1microgram/kg/minute, with or with-out an initial bolus *by intravenous injection* (of a solution containing 20-250 micrograms/ml) over not less than 30 seconds, 1microgram/kg.

Note: If patient is to be intubated more than 8 minutes after start of intravenous infusion, initial intravenous injection dose is unnecessary

Maintenance in ventilated patients, *by intravenous infusion,* 0.05-2 microgram/ kg/minute according to anaesthetic technique and adjusted according to response; supplemental doses in light anaesthesia, *by intravenous injection* every 2-5 minutes
Maintenance of anaesthesia with spontaneous respiration, *by intravenous infusion,* initially 40 nanograms/kg/ minute adjusted according to response, usual range 25-100 nanograms/kg/ minute. CHILD: 2-12 years, not recommended

Generic Preparation
Injection, 1mg/vial; 2mg/vial

TRAMADOL

Tramadol is a narcotic-like pain reliever. The extended-release form of tramadol is for around-the-clock treatment of pain. This form of tramadol is not for use on an as-needed basis for pain. It is thought to have fewer opioid side effects but it is not as effective as other opioid analgesics in severe pain and would seem to be ideal for administration just before recovering from anaesthesia.

Indications: moderate to severe pain.

Contraindications: severe asthma, intestinal obstruction, patients taking narcotic medicines or sedatives
Side-effects: headache, dizziness, drowsiness, constipation, diarrhoea,

nausea, vomiting, stomach pain; feeling nervous or anxious; itching, sweating, flushing, seizure, shallow breathing

Dose: Usual ADULT Dose for Pain: For acute pain 3mg/kg IV, increment of 50-100mg, until adequate relief is obtained, upto 400mg per day.For mild to moderate severe chronic pain not requiring rapid onset of analgesic effect:
Initial dose: 25 mg every morning
Titration: increase in 25 mg increments as separate doses every 3 days to reach 100 mg per day taken as 25 mg 4 times per day. Then the total daily dose may be increased by 50 mg as tolerated every 3 days to reach 200 mg per day taken as 50 mg 4 times per day.
Maintenance: After titration, tramadol 50 mg to 100 mg can be administered as needed for pain relief every 4 to 6 hours not to exceed 400 mg per day.
Tramadol Extended-Release (ER)
16 years and older: Initial: 100 mg once daily. Titrate by 100 mg increments every 2 to 3 days if needed for pain control Maximum: 300 mg/day

Proprietary Preparations
see section 7.5.1

8.1.3.2 NON-OPIOIDS

(see also section 9.1.1)

Because non-steroidal anti-inflammatory drugs (NSAIDs) do not depress respiration, do not impair gastro-intestinal motility and do not cause dependence, they are considered as useful alternatives (or adjuncts) to the opioids for the relief of postoperative pain. NSAIDs may, however, be inadequate for the relief of severe pain.

Paracetamol, diclofenac,ibuprofen, ketoprofen, and **ketorolac** are indicated for postoperative use *(see sec. 9.1.1)*. These drugs can be given by injection as well as by mouth. Intramuscular injections of diclofenac and ketoprofen are given deep into the gluteal muscle to minimize pain and tissue damage; diclofenac can also be given by intravenous infusion for the treatment of postoperative pain. Suppositories of diclofenac and ketoprofen may be effective alternatives to the parenteral use of these drugs. Ketorolac is less irritant on intramuscular injection; it can also be given by intravenous injection.

Note. It should be noted that NSAIDs have the potential to produce thrombocytopenia, thromboasthenia, gastrointestinal bleed-ing, wound bleeding, and to decrease prostaglandin dependent renal blood flow causing decreased renal output.
For the **preparations** of NSAIDS, *see section 9.1.1.*

DICLOFENAC

(*see section 9.1.1)*

Indications: moderate pain of musculoskeletal origin including tendinitis and bursitis conditions, rheumatoid and osteorarthritis.

Side effects: gastro-intestinal effects; long-term diclofenac treatment can raise plasma aminotransrferase levels, allergic reactions, fluid retention and CNS effects

Cautions: should be taken with food or other gastro-intestinal protective agents to reduce stomach upset

Dose:100-200 mg 2 to 4 times daily. Depending on the diclofenac formulation used and the condition being treated.
Diclofenac is available as
Powder for Solution, Capsule, Liquid, Tablet Enteric Coated, immediate-release, dispersible, gastro-resistant, prolonged-release or, extended release forms, suppositorries and IV and IM preparations.

Proprietary Preparations
see section 9.1.1

IBUPROFEN[ED]

NSAIDs of modest potency is used for the treatment of mild to moderate pain, inflammation and fever

Indications: dysmenorrhea, osteoarthritis, rheumatoid arthritis and juvenile idiopathic arthritis

Contraindication and side effects: similar to other NSAIDs

Dose: 10 mg/kg can be administered by

mouth every 6–8 hours. Individuals should not use ibuprofen for more than 10 days for the treatment of pain or more than 3 days for the treatment of a fever unless directed by a physician. Ibuprofen should be taken with meals to prevent stomach upset. Children 6 months to 12 years of age usually are given 5-10 mg/kg of ibuprofen every 6-8 hours for the treatment of fever and pain. The maximum dose is 40 mg/kg daily.

Proprietary Preparations
see section 9.1.1

KETOROLAC

(see also section 9.1.1)

Indications: moderately severe pain, usually after surgery
Caution: It should be taken at around the same times every day
Contraindication: CHILD under two years
Side-effects: headache, somnolence, dyspepsia, pruritus, oedema, Increased blood urea nitrogen, constipation, purpura, drowsiness, hypertension, abnormal thinking, anaphylaxis, blurred vision, bronchospasm, cholestatic jaundice, depression, insomnia, laryngeal/lingual edema
Dose:ADULT Moderately Severe Acute Pain
Short-term (≤5 days) management of moderately severe acute pain that requires analgesia at opioid level; not indicated for minor or chronic painful conditions
IV: 30 mg as single dose or 30 mg q6hr; not to exceed 120 mg/day
IM: 60 mg as single dose or 30 mg q6hr; not to exceed 120 mg/day
PO: 20 mg once after IV or IM therapy, THEN 10 mg q4-6hr; not to exceed 40 mg/day
Dosing Considerations
Always begin with parenteral therapy; oral administration indicated only as continuation of IV/IM dosing, if necessary. Duration of therapy should not exceed 5 days.
Dosage beyond maximum or labeled doses will not provide better efficacy but will increase risk of serious adverse events
Decrease daily dose in patients >65 years, <50 kg, or with moderately elevated serum creatinine
Following intravenous therapy, the recommended dose is one or two tablets initially followed by 1 tablet every 4-6 hours.

PAEDIARTIC
Moderately Severe Acute Pain
2-16 years
Single dose: 0.5 mg/kg IV/IM once; not to exceed 15 mg
Multiple doses: 0.5 mg/kg IV/IM q6hr; not to exceed 5 days
GERIATRIC
Moderately Severe Acute Pain
Short-term (≤5 days) management of moderately severe acute pain that requires analgesia at opioid level; not indicated for minor or chronic painful conditions
IV: 15 mg as single dose or 15 mg q6hr; not to exceed 60 mg/day
IM: 30 mg as single dose or 15 mg q6hr; not to exceed 60 mg/day
PO: 10 mg once after IV or IM therapy, THEN 10 mg q4-6hr; not to exceed 40 mg/day

Proprietary Preparations
see section 9.1.1.

PARACETAMOL[ED]

Indication: for minor pain.
Side effects: Nausea, vomiting, anorexia and abdominal pain. Dose dependent hepatic necrosis
Dose:Paracetamol 10–15 mg/kg every 4–6 hours administered by mouth or rectally is a safe and effective method for controlling postoperative pain.

Proprietary Preparations
see section 7.5.2.

8.1.4 MUSCLE RELAXANTS

Muscle relaxants used in anaesthesia are also known as **neuromuscular blocking drugs**. By specific blockade of

the neuromuscular junction they enable adequate relaxation of the muscles of the abdomen and diaphragm. They also relax the vocal cords and allow the passage of a tracheal tube.

NON-DEPOLARISING MUSCLE RELAXANTS

Non-depolarizing muscle relaxants (also known as competitive muscle relaxants) compete with acetylcholine for receptor sites at the neuromuscular junction and their action may be reversed with anticholinesterases (e.g. neostigmine, *see section 8.1.6)*. Non-depolarising muscle relaxants may be divided into the aminosteroid group, which includes **pancuronium, pipecuronium rocuronium** and **vecuronium**, and the benzylisoquinolinium group, which includes **atracurium, cisatracurium** and **gallamine.**

Non-depolarising muscle relaxants have a slower onset of action than **suxamethonium.** These drugs can also be classified by their duration of action as short acting (10-20 minutes), intermediate-acting (40-60 minutes) and long-acting (60-120) minutes), although duration of action is dose-dependent. Drugs with a shorter or intermediate duration of action, such as **atracurium** and **vecuronium**, are more widely employed than those with a longer duration of action such as **pancuronium** or **pipecuronium.**

Non-depolarizing muscle relaxants have no sedative or analgesic effects and are not considered to be a triggering factor for malignant hyperthermia.

CAUTIONS: Allergic cross-reactivity between neuromuscular blocking agents has been reported; caution is advised in cases of hypersensitivity to these drugs. Their activity is prolonged in patients with myasthenia gravis and in hypothermia where lower doses are required. Resistance may develop in patients with burns who may require increased doses.

SIDE-EFFECTS: Benzylisoquinolinium non-depolarizing muscle relaxants (except cisatracurium) are associated with histamine release, which can cause skin flushing, hypotension, tachycardia, bronchospasm and rarely, anaphylactoid reactions.

INTERACTIONS: Intensification or prolong-ation of action of inhalational or intra-venous anaesthesia; reduction of action of corticosteroids

ATRACURIUM BESYLATE

Atracurium having short duration of action. It undergoes non-enzymatic metabolism, which is independent of liver and kidney function, thus allowing its use in patients with hepatic or renal impairment. Cardiovascular effects are associated with significant histamine release

Indications: used in surgery of moderate duration in the presence of real or hepatic impairment.

Cautions and Side-effects: *see notes above*

Dose: *by intravenous injection*, ADULT and CHILD over 1 month initially 0.3-0.6 mg/kg, then 0.1-0.2 mg/kg as required

by intravenous infusion, 5-10 micro-grams/kg/ minute (300-600 micrograms/ kg/hour)

Proprietary Preparations
Relaxton *(Techno),* Inj., 25 mg/2.5 ml, Tk.80.00/2.5 ml
Tracrium [I] *(GSK.),* Inj., 25 mg/2.5 ml, Tk.645.49/2.5 ml

CISATRACURIUM

Cisatracurium is a single isomer of atracurium. It is more potent and has a slightly longer duration of action than atracurium and provides greater cardio-vascular stability because cisatracurium lacks histamine-releasing effects

Indications: same as that of atracurium
Cautions and Side-effects: *see notes above*

Dose: *by intravenous injection*, intubation, 150 micrograms/kg; maintenance, 30micrograms/kg approx.

every 20 minutes

CHILD over 2 years, initially, 100 micrograms/kg; maintenance, 20 micrograms/kg approx. every 9 minutes

by intravenous infusion, ADULT and CHILD over 2 years, initially, 3 micrograms/kg/minute, then 1-2 mg/kg/minute; dose reduced by up to 40% if used with inhalation anesthetist
CHILD under 2 years not recommended.

Generic Preparations
Injection 2 mg/ml 2.5 ml amp; 5 mg/ml 30 ml vial.

PANCURONIUM BROMIDE

Pancuronium having long duration of action, is often used in patients receiving long-term mechanical ventilation in intensive care units. It lacks histamine releasing effect; vagolytic and sympathomimetic effect can cause tachycardia and hypertension.

Indications: neuromuscular relaxation of fairly long duration (more than 30 min.) in poor risk and emergency cases

Cautions: hepatic and renal impairment and myasthenia gravis

Side-effects: *see notes above*

Dose: *by intravenous injection*, initially for intubation, 50-100 micrograms/kg then 10-20 micrograms/kg as required. CHILD initially 60-100 micrograms/kg, then 10-20 micrograms/kg; NEONATE 30-40 micrograms/kg initially then 10-20 micrograms/kg
Intensive care, *by intravenous injection* 60 micrograms/kg every 60-90 minutes.

Generic Preparation
Injection 2 mg/ml

PIPECURONIUM BROMIDE

Pipecuronium, a long-acting muscle relaxant which has onset and duration of action similar to those of pancuronium but lacks the cardiovascular side effects.

Indications: operation requiring for long time muscle relaxation

Cautions: neuromuscular disorders, obese patients, hepatic or renal impairment

Contraindications: myasthenia gravis and pregnancy;*see also notes above*

Dose: 100µg/kg to allow intubation.

Proprietary Preparations
Arduan (I) *(Richter)*, Inj. 4 mg/2 ml
Tk.1 72.52/Amp
Pycuron*(Techno)* Inj. 4 mg/2 ml
Tk.475.00/Amp

ROCURONIUM BROMIDE

Rocuronium has the most rapid onset of any of the competitive muscle relaxants with an intermediate duration of action. It is reported to have minimal histamine-releasing and cardiovascular effects; high doses produce mild vagolytic activity.

Indications, Cautions and Side-effects: *similar to vecuronium.*

Dose: *by intravenous injection*, intubation, 600 micrograms/kg; maintenance, 150micrograms/kg

by intravenous infusion, 300-600 micrograms/kg/hour (after initial intravenous injection of 600 micrograms/kg).

CHILD similar to adults; NEONATE not recommended

Proprietary Preparations
Rocuron IV *(Incepta),* Inj, 1 gm/100 ml,
Tk.300.00/Vial
Esmeron (I) *(Organon),* Inj. 10mg/ml 5ml vial
Tk. 4400.00/Vial.

VECURONIUM BROMIDE[ED]

Vecuronium having an intermediate duration of action, is unstable in high concentrations and is presented as a freeze-dried, buffered powder, which can be kept at room temperature without deterioration. It does not generally produce histamine release and lack of cardiovascular effects

Indications: any operation requiring muscle relaxation of any duration.
Cautions: same as for other competitive muscle relaxants.

Anaphylactoid reactions have occasionally been reported. Reduce dose in renal impairment. The duration of action of vecuronium is prolonged in the presence of renal and hepatic failure

Side-effects: *see notes above*

Dose: because of its lack of cardiovascular side effects, vecuronium can be given in larger doses which shorten the time to onset and extend the duration of action. B*y intravenous injection*, intubation, 80-100 micrograms/kg; maintenance 20-30 micrograms/kg according to response; NEONATE and INFANT up to 4 months, initially 10-20 micrograms/kg then incremental doses to achieve response; CHILD over 5 months, as ADULT dose (up to 1 year onset more rapid and high intubation dose may not be required)

By intravenous infusion, 0.8-1.4 micrograms/kg/minute (after initial intravenous injection of 40-100 micrograms/kg).

Note. To be monitored continuously

Proprietary Preparations
Nor Q *(Incepta),* Inj., 10 mg/Vial, Tk. 185.00/Vial
Vencur*(Popular),* Tab., 10 mg/Vial, Tk. 200.00/Vial
Vencuron *(Techno),* Inj., 10 mg/Vial, Tk. 185.00/Vial; 4 mg/ml, Tk. 80.00/Vial

DEPOLARISING MUSCLE RELAXANTS

SUXAMETHONIUM CHLORIDE[ED]

Suxamethonium has the most rapid onset of action of any of the muscle relaxants and is ideal if requires fast onset and brief duration of action e.g. with tracheal intubation. Its duration of action is about 2 to 6 minutes following intravenous doses of about 1 mg/kg; Suxamethonium acts by mimicking acetylcholine at the neuromuscular junction but hydrolysis is much slower than for acetylcholine; hyperthermia is therefore prolonged resulting in neuromuscular blockade. Unlike the non-depolarising muscle relaxants, its action cannot be reversed and recovery is spontaneous; anticholinesterases such as neostigmine potentiate and prolong the neuromuscular block.
Suxamethonium should be given after induction of anaesthesia because paralysis is usually preceded by painful muscle fasciculations. Bradycardia and excessive salivation may occur with repeated doses. Premedication with atropine reduces bradycardia as well as the excessive salivation
Individuals with myasthenia gravis are resistant to suxamethonium but can develop dual block resulting in delayed recovery. Prolonged paralysis may also occur in those with low or atypical plasma cholinesterase. In such cases, assisted ventilation should be continued until muscle function is restored (usually within 40-120 minutes).
Indications: used whenever profound skeletal muscles relaxation is required for short periods. It is, therefore, particularly useful in endoscopies, manipulations and electroconvulsive therapy and as an aid to tracheal intubation

Cautions: patients with cardiac, respiratory or neuromuscular disease; raised intraocular pressure and hyper kalaemia

Contraindications: severe liver diseases, burned patients, degenerating muscle mass, paraplegia of recent onset and major limb trauma, family history of malignant hyperthermia, known low plasma cholinesterase activity and penetrating eye injury. etc.

Side-effects: postoperative muscle pain, myoglobinaemia, tachycardia, arrhythmia, bronchospasm, prolonged respiratory depression, hyperkalaemia, hyperthermia, s*ee also notes above*

Dose: *by intravenous injection*, ADULT 1 mg/kg (range 0.3-1.5 mg/kg); usual range 20-100 mg; max. 500 mg/hour; CHILD 1-12 years, 1-2 mg/kg; INFANT under 1 year, 2 mg/kg.*By intravenous infusion* of a solution containing 1-2 mg/ml (0.1-0.2%),2–5mg/minute; max. 500 mg/hour.
By intramuscular injection, CHILD up to 4 mg/kg; max. 150 mg; INFANT up to

4–5 mg/kg

Proprietary Preparations
G-Suxamethonium *(Gonoshasthaya),* Inj., 100mg/2ml, Tk. 7.50/amp.
Neosuxa*(Popular),* Inj., 100mg/2ml, Tk.8.40/amp.
Rapilax *(ACI),* Inj., 100mg/2ml, Tk. 8.43/amp.
Suxonium *(Techno),* Inj., 100mg/2ml, Tk.8.40/amp.

8.1.5 ANTICHOLINESTERASES USED IN ANAESTHESIA

(see also section 9.2.1)

Anticholinesterases reverse the effects of non-depolarizing (competitive) muscle relaxant drugs but they prolong the action of the depolarizing muscle relaxant. Commonly available preparation are **edrophonium**, **neostigmine, physostigmine, pyridostigmine.**

Neostigmine has a much longer duration of action and is the specific drug for reversal of non-depolarising blockade. It acts within one minute of intravenous injection and lasts for 20 to 30 minutes; a second dose may then be given if felt necessary. Atropine or glycopyrronium should be given before or with neostigmine in order to prevent bradycardia, excessive salivation.

NEOSTIGMINE METHYLSULPHATE[ED]

Indications: to antagonize the effects of competitive neuromuscular blocking drugs and in the treatment of atony of the intestinal tract, atony of the bladder, myasthenia gravis, glaucoma and sinus tachycardia. It has also been employed to potentiate the effect of analgesica and the relaxation of muscle spasm

Cautions: A parasympathetic antagonist should always be given when nicotinic effects only are required, should be used with particular care in the presence of asthma and heart disease, must not be used in an attempt to reverse the action of suxamethomium

Side-effects: Overdose of neostigmine may cause sudden death due to cardiac arrest; restlessness, weakness, muscular twitching, dysarthria, pin-point pupils, nystagmus, sweating, salivation, nausea and vomiting, hypotesion. Respiration is embarrassed by bronchospasm and excessive secretions and death due to respiratory paralysis and pulmonary oedema may follow

Dose: reversal of non-depolarising neuromuscular blockade, *by intravenous injection* over 1 min, 50–70 micrograms/kg (max. 5 mg) after or with atropine sulphate 0.6-1.2mg

Proprietary Preparations
G-Neostigmine *(Gonoshasthaya),* Inj., 0.5mg/ml, Tk. 6.00/Amp.
Neos-R *(Renata),* Inj., 0.5 mg/ml, Tk.7.00/Amp.
Neostig *(Popular),* Inj., 0.5 mg/ml, Tk.6.05/Amp.
Prostig *(Chemist),* Inj. 1 ml, Tk. 80/1ml amp.
Stigmin *(Techno),* Inj., 0.5 mg/ml, Tk.6.00/Amp.
Stignal *(ACI),* Inj., 0.5 mg/ml, Tk. 6.05/Amp.
Versia *(Square),* Inj., 0.5 mg/ml, Tk. 7.02/Amp.

8.1.6 ANTAGONISTS FOR RESPIRATORY DEPRESSION

Respiratory depression is a major concern with opioid analgesics. It may be reversed by **naloxone** (analgesia may also be reversed). Alternatively, the respiratory stimulant **doxapram** may be used which does not reverse the analgesic effect of the opioids.

NALOXONE HYDROCHLORIDE [ED]

Naloxone will immediately reverse opioid-induced respiratory depression but the dose may have to be repeated due to the short duration of action;however naloxone will also antagonize the analgesic effect of the opioid.
Indication: reversal of opioid-induced respiratory depression

Cautions: cardiovascular disease or those receiving cardiotoxic drugs; physical dependence on opioids (precipitates withdrawal); pain *(see also under Titration of Dose, below)*; has

short duration of action (repeated doses or infusion may be necessary to reverse effects of opioids with longer duration of action)

Side-effects: nausea, vomiting, tachycardia and fibrillation

Dose: *by intravenous injection*, 100-200 micrograms (1.5-3 micrograms/kg); if response inadequate, increments of 100 micrograms every 2 minutes; further doses *by intramuscular injection* after 1-2 hours if required

TITRATION OF DOSE: In postoperative use, the dose should be titrated for each patient in order to obtain sufficient respiratory response while maintaining adequate analgesia

CHILD: *by intravenous injection*, 10 micrograms/kg; subsequent dose of 100 micrograms/kg if no response; if intravenous route not possible, may be given in divided doses *by intramuscular or subcutaneous injection*

NEONATE: *by subcutaneous, intramuscular, or intravenous injection*, 10 micrograms/kg, repeated every 2 to 3 minute or 200 micrograms (60 micrograms/kg) *by intramuscular injection* as a single dose at birth (onset of action slower)

Proprietary Preparation
Naloxone Hydrochloride [I] *(Mayne Pharma),* Inj. 400 microgm/ml; Tk. 141.87/Vial

8.1.7 DRUGS FOR MALIGNANT HYPERTHERMIA

DANTROLENE SODIUM

Dantrolene is used in the treatment of malignant hyperthermia, which is a rare but potentially lethal complication of anaesthesia. It is characterized by a rapid rise in temperature, increasing muscle rigidity (especially trismus), tachycardia, acidosis and can be triggered off by volatile anaesthetics and suxamethonium. Dantrolene acts on skeletal muscle by interfering with calcium efflux in the muscle cell and stopping the contractile process.

Indication: malignant hyperthermia as a complication of anaesthesia

Cautions: avoid extravasation

Interactions: *see Appendix-2* (muscle relaxants)

Dose: *by rapid intravenous injection,* 1 mg/kg, repeated as required to a cumulative max. of 10 mg/kg

Generic Preparation
Injection 20 mg/vial.

FLUMAZENIL

Flumazenil is a benzodiazepine antagonist. Flumazenil has a shorter half-life than that of diazepam and midazolam; therefore, it may have to be administered repeatedly. The drug is given initially in a bolus of 0.2 mg intravenously and then in 0.1 mg increments until the desired end-point is reached. A total dose of 0.5 mg is usually sufficient. By continuous intravenous rates up to 1mg/h may be necessary to maintain a patient in a 'safe' condition.

Proprietary Preparation
Anexate[I] *(Cenexi),* Inj., 0.5 mg/5 ml, Tk. 2,054.13/5 ml Vial

8.2 LOCAL ANAESTHESIA

Local anaesthetics act by producing a reversible block to the transmission of peripheral nerve impulses. The drugs used vary widely in their potency, toxicity, duration of action, rate of absorption, stability, solubility in water, and ability to penetrate mucous membranes. These variations determine their suitability for use by various routes, e.g. topical (surface), infiltration, plexus, epidural or spinal block.

Used very widely in dental practice, for brief and superficial interventions and obstetric procedures. Local anaesthetics commonly used are **lignocaine, ethyl chloride** and **bupivacaine**. Other local anaesthetics include **prilocaine, amethocaine, ropivacaine, mapivacaine, benzocaine and cocaine**

but their uses are very limited.

ADMINISTRATION: in estimating safe dosage of these drugs, it is important to take account of the rate at which they are absorbed and excreted as well as their potency. The patient's age, weight, physique, and clinical condition, the degree of vascularity of the area to which the drug is to be applied, and the duration of administration are other factors which must be taken into account.

Local anaesthetics do not rely on blood circulation to transport them to their sites of action, but uptake into the general circulation is important in terminating their action. Following most regional anaesthetic procedures, maximum arterial plasma concentrations of anaesthetic develop within about 10 to 25 minutes; so careful surveillance for toxic effects is necessary during the first 30 minutes after injection. Great care must be taken to avoid accidental intravascular injection.

Epidural anaesthesia is commonly used during surgery, often combined with general anaesthesia, because of its protective effect against the stress response of surgery. It is often used when good postoperative pain relief is essential (e.g. aortic aneurysm surgery or major gut surgery).

Toxic effects associated with the local anaesthetics are usually a result of excessively high plasma concentrations, and systemic effects whether associated with acute or cumulative overdose or with accidental intravascular injection, repeated dosage and the injection is too rapid.

Hypersensitivity reactions occur mainly with the ester-type local anaesthetics such as amethocaine, benzocaine, cocaine, and procaine; reactions are less frequent with the amide types such as lignocaine, bupivacaine, prilocaine, and ropivacaine.

Local anaesthetics should not be injected into inflamed or infected tissues nor should they be applied to the traumatised urethra. Under these conditions the drug may be so rapidly absorbed that a systemic rather than a local reaction is produced.

Use of vasoconstrictors: Most local anaesthetics, with the exception of cocaine, cause dilation of blood vessels. The addition of adrenaline vasoconstric, diminishes blood flow, slows the rate of absorption and prolongs its effects. Adrenaline must be used in a low concentration for this purpose and it should not be given with a local anaesthetic in digits and appendages.

When adrenaline is included the final concentration should be 1 in 2,00,000 (5 micrograms/ml.). In dental surgery up to 1 in 80,000 (12.5 micrograms/ml) of adrenaline is used with local anaesthetics. There is no justification for using higher concentrations. The total dose of adrenaline should ***not*** exceed 500 micrograms.

LIGNOCAINE HYDROCHLORIDE[ED]

(Lidocaine Hydrochloride)

It is an effective local anaesthetic with rapid onset of action which is intense and lasts some 60-90 minutes. Lignocaine *(see also section 3.6)* is effectively absorbed from mucous membranes and is a useful surface anaesthetic in concentrations of 2 to 4%. Except for surface anaesthesia, solution should not usually exceed 1% in strength.

Indications: Lidocaine is used for the production of local anaesthesia by infiltration, nerve, spinal, epidural and caudal block and topical application. It is employed for the control of myocardial irritability and ventricular arrhythmias, particularly in the acute treatment following myocardial infarction

Cautions: rapid and extensive absorption may result in systemic side-effects. Do not use for wound, mucous membranes or atopic dermatitis; avoid use near eyes or middle ear; caution in anemia, or congenital or acquired methaemoglobinaemia.epilepsy, hepatic or respiratory impairment, impaired cardiac conduction, bradycardia;

porphyria; reduce dose in elderly or debilitated; resuscitative equipment should be available.

Contraindications: hypovolaemia and complete heart block

Side-effects: numbness, paraesthesiae, pallor, tinnitus, excitement, restlessness, confusion, convulsions, respiratory depression; prolong conduction time, ventricular fibrillation, bradycardia and hypotension (may lead to cardiac arrest); hypersensitivity reported.

Dose: Epinephrine, unless otherwise contra-indicated, is normally used with lidocaine to delay absorption and prolong the action. *Infiltration anaesthesia*- a 0.5 per cent solution is commonly employed. According to patient's weight and nature of procedure max. 200 mg without or 500 mg with adrenaline. *Nerve block* -A 1 per cent solution is used with epinephrine, up to 10 ml for single nerves and 15-30 ml for brachial plexus block. *Epidural and caudal block*-A solution of 2 per cent lidocaine with 1:200 000 epinephrine is normally used. Spinal block-5 per cent hyperbaric solutions. (Not used at present).Intravenous *local anaesthesia* - 25-40 ml of 0.5 per cent lidocaine is used for the arm.

Surface anaesthesia, 2–4%.
May be in various forms, (a) *Cream* containing lignocaine 2.5 % with prilocaine 2.5 % ; (b) *Antiseptic gel* containing anhydrous lignocaine hydrochloride 2 % with chlorhexidine gluconate 0.25 % in a sterile lubricant basis; (c) *Anhydrous gel* containing anhydrous lignocaine hydrochloride 2% in a sterile lubricant water-miscible basis; (d) *Topical preparation* containing anhydrous lignocaine hydrochloride 40 mg/ml; (e) *Ointment*, containing lignocaine 5% in a water-miscible base (may include propylene glycol).
Indications: *EMLA* before vein puncture and split skin grafting, apply a thick layer of a surface anaesthetic *cream* under an occlusive dressing, 1hour before the procedure.

For application into urethra, sterile *anhydrous gel* (2%), men 10ml, followed by further 10ml (total up to 40ml for cystoscopy); women 5-10 ml. Endoscopy, *anhydrous gel*, 10–20 ml.

Endotracheal intubation, *anhydrous gel,* 5 ml applied to surface of tube (avoid putting gel into the tracheal lumen).

bronchoscopy, *topical preparation (4%),* 2-3 ml as a suitlable spray. *Biopsy in mouth, topical preparation (4%),* 3-4 ml as a suitable spray or swab, max. 7.5 ml. Sucking of a lozenge (250 mg) may also be effective.

Contraindications: infants under 1 year

Proprietary Preparations
G-Lignocaine *(Gonoshasthaya),*Inj.2%,
Jasocaine (*Jayson)*, Inj. 1%, Inj 2%
Jasocaine *(Jayson),* Gel 2%
Leecain *(Gaco),* Gel 2 %,
Lido *(Square),* Spray Tk. 300.00/30ml
Xylone *(ACI)*, Inj., 2%Tk. 3.56 /2 ml Amp;4% Tk. 3.73 /2 ml Amp

LIGNOCAINE INJECTION FOR DENTAL USE[ED]

***Note*:** A large variety of lignocaine injection, plain or with adrenaline or noradrenaline, is available in the form of dental cartridges.

BUPIVACAINE HYDROCHLORIDE[ED]

The great advantage of **bupivacaine** over other local anaesthetics is its longest duration of action of the existing drugs. It has a slower onset of action. The degree of motor block increases with increasing concentration, and at the highest available concentration (0.75 per cent) may outlast the sensory block.

Indications: particularly suitable for continuous epidural analgesia in labour and for single-dose epidural injections for surgery

Cautions: Avoid accidental intravascular injection; because of its relatively greater toxicity on the heart and more resistant to treatment; precaution about over dose and hepatic imapairement

Contraindication: intravenous regional anaesthesia

Interactions: *see Appendix-2*

Side-effects: *see under Lignocaine Hydrochloride.*

Dose: adjusted according to patient's weight and nature of procedure. Maximum safe dose for bupivacaine is 0.5 mg/kg given at one time or in any 4-hour period.

Local infiltration-0.25% solution is commonly employed.

Peripheral nerve block- 0.5% solution is commonly employed.

Epidural block: 0.25–0.5% (max.30 ml)

Spinal anaesthesia, 0.5 % anhydrous bupivacaine in 8 % dextrose solution, sterile injection, 2–4 ml

Note. 0.75% is contraindicated for epidural use in obstetrics.

Proprietary Preparations

Bupivacaine 5%,
Bupi *(Popular),* Inj., Tk. 60.23/30 ml
Nerkein *(Beximco),* Inj., Tk. 60.00/30 ml
Ultracaine *(Jayson),* InjTk. 60.23/30 ml
Bupicain Heavy *(Chemist),* Inj., 2.5 mg/1 ml, Tk. 28.00/4 ml

Bupivacaine0.5% + Dextrose8%,
Anespine *(Square),* Inj.,Tk. 30.11/4 ml Amp.
Bupi Heavy *(Popular),* Inj., Tk. 30.11/4 ml Amp.
Bupicain Heavy*(Chemist)* Inj., Tk. 28/4 ml
Pivacain-D *(ACI),* Inj.,Tk. 30.11/4 ml Amp.
Sivicaine Heavy *(Renata,),* Inj., Tk. 30.11/4 ml Amp.
Spino *(Incepta),* Inj., Tk. 30.00/4 ml Amp.
Ultracaine Heavy *(Jayson),* Inj., Tk. 30.11/4 ml Amp.
G-Bupivacaine Heavy*(Gonoshasthaya)* Inj., Tk. 28/4 ml

ETHYL CHLORIDE

Topical Anesthetic Skin Refrigerant (vapocoolant). This is a gas at room temperature but is usually stored under pressure in a glass containers. When sprayed on the skin it evaporates and can cause refrigeration topical anaesthesia.

It is intended to control the pain associated with injections, starting IV's and venipuncture, minor surgical procedures (such as lancing boils, incisions and drainage of small abscesses) and the temporary relief of minor sports injuries. It is also intended for the treatment of restricted motion associated with myofascial pain caused by trigger points.

Contraindications: Ethyl Chloride is contraindicated in individuals with a history of hypersensitivity.

Cautions: Inhalation of Ethyl Chloride should be avoided as it may produce narcotic and general anesthetic effects, deep anesthesia or fatal coma with respiratory or cardiac arrest. Ethyl Chloride is FLAMMABLE and should never be used in the presence of an open flame or electrical cautery equipment.

For external use only. Do not spray in eyes. Ethyl Chloride is known as a liver and kidney toxin; Do not use near fire or place on hot surfaces. Do not store on or near high frequency ultrasound equipment.

When used to produce local freezing of tissues, adjacent skin areas should be protected by an application of petrolatum. The thawing process may be painful and freezing may lower local resistance to infection and delay healing.

Generic Preparation

Spray 100ml