GENERAL ANAESTHESIA

Introduction

- General anaesthetics (GAs) are drugs which causes reversible loss of all sensation and consciousness.
- The cardinal features of GA
  - Loss of all sensation, especially pain
  - Sleep (consciousness) and amnesia
  - Immobility and muscle relaxation
  - Abolition of somatic and autonomic reflexes

Classification

- **Inhalation Gas**: Nitrous Oxide
- **Volatile Liquid:** Halothane, Enflurane, Isoflurane, Desflurane, Sevoflurane
- **Intravenous**
  - **Inducing Agent:** thiopentone Sod., methohexitone, Sod Propfol, Etomidate
  - **Slower acting drugs:** Benzodiazepam, Diazepam, Lorazepam, Midazolam

Routes of Administration

- ENTERAL
  - Oral
  - Rectal.
- PARENTERAL
  - Sublingual.
  - Intra nasal.
  - Intra muscular.
  - Intra venous.

Overview

- It is a complex procedure involving :
  - Pre-anaesthetic assessment
  - Administration of general anaesthetic drugs
  - Cardio-respiratory monitoring
  - Analgesia
  - Airway management
  - Fluid management
  - Postoperative pain relief

Stages and signs

- Traditional Description of signs and stages of GA - Also called Guedel`s sign
- Typically seen in case of Ether
- Slow action as very much lipid soluble
- Descending depression of CNS
- Higher to lower areas of brain are involve
- Vital centers located in medulla are paralyzed last

Stages of GA

Stage I: Stage of Analgesia

- Starts from beginning of anaesthetic inhalation and lasts upto the loss of consciousness
- Pain is progressively abolished during this stage
- Patient remains conscious, can hear and see, and feels a dream like state
- Reflexes and respiration remain normal
- It is difficult to maintain - use is limited to short procedures only

Stage II: Stage of Delirium and Excitement

- From **loss of consciousness** to beginning of **automatic breathing**
- **Eyelash** reflex diasaapear
- Excitement - patient may shout, struggle and hold his breath
- Muscle tone increases, jaws are tightly closed.
- Breathing is jerky; vomiting, involuntary micturition or defecation may occur.
- No stimulus or operative procedure carried out during this stage.
- Potentially dangerous responses can occur during this stage including vomiting, laryngospasm and uncontrolled movement.
- **This stage is not found with modern anaesthesia – preanaesthetic medication, rapid induction etc**

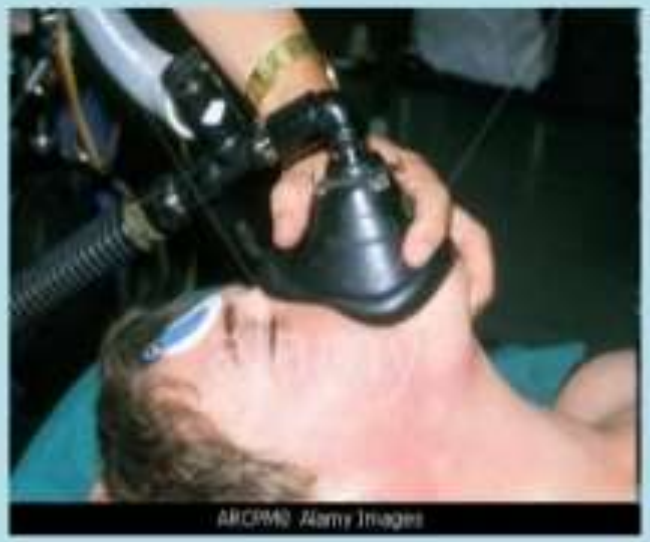
Stage III: Stage of Surgical anaesthe

- Extends from onset of **spontaneus respiration** to respiratory paralysis.
- This has been divided into 4 planes:
  - Plane 1: Roving eye balls. This plane ends when eyes become fixed.
  - Plane 2: Loss of corneal and laryngeal reflexes.
  - Plane 3: Pupil starts dilating and light reflex is lost.
    - This was the desired phase of surgery when muscle relaxant were not used
  - Plane 4: Intercostal paralysis, shallow abdominal respiration, dilated pupil.

Stage IV: Medullary / respiratory paralysis

- Cessation of breathing - failure of circulation - death
- Pupils: widely dilated
- Muscles are totally flabby
- Pulse is imperceptible
- BP is very low.

Individual **Inhalation** anaesthetic agents



Ideal Anaesthetic

Ideal For Patient

- Pleasant, nonirritating, no nausea or vomiting.
- Induction and recovery should be fast with no after effects

Ideal for Surgeon

- Adequate analgesia, immobility and muscle relaxation.
- Noninflammable and nonexplosive

1. Diethyl ether ($C_2H_5 – O – C_2H_5$)

- Colourless, highly volatile liquid with a pungent odour. Boiling point – 35ºC
- Produces irritating vapours and are inflammable and explosive
- Pharmacokinetics:
  - 85 to 90 percent is eliminated through lung and remainder through skin, urine, milk and sweat
  - Can cross the placental barrier

Ether – contd.

- Advantages
  - Can be used without complicated apparatus
  - Potent anaesthetic and good analgesic
  - Muscle relaxation
  - Wide safety of margin
  - Respiratory stimulation and bronchodilatation
  - Does not sensitize the heart to adrenaline
  - No cardiac arrythmias
  - Can be used in delivery
  - Less likely hepato or nephrotoxicity

- Disadvantages
  - Inflammable and explosive
  - Slow induction and unpleasant - atropine
  - Slow recovery – nausea & vomiting
  - Cardiac arrest
  - Convulsion in children
  - Cross tolerance – ethyl alcohol

2. Nitrous oxide/laughing gas (N_2O)

- NH_4NO_3 (s) → 2 H_2O (g) + N_2O (g)
- Colourless, odourless inorganic gas with sweet taste
- Noninflammable and nonirritating, but of low potency
- Very potent analgesic
- Carrier and adjuvant to other anaesthetics – 70% + 25-30% + 0.2-2%
- As a single agent used wit O_2 in dental extraction and in obstetrics

Nitrous oxide – contd.

- Advantages:
  - Non-inflammable and nonirritant
  - Rapid induction and recovery
  - Very potent analgesic (low concentration)
  - No nausea and vomiting
  - Nontoxic to liver, kidney and brain

- Disadvantages:
  - Not potent alone (supplementation)
  - Hypoxia
  - Inhibits methionine synthetase (precursor to DNA synthesis)
  - Inhibits vitamin B-12 metabolism
  - Dentists, OR personnel, abusers at risk
  - Gas filled spaces - dangerous

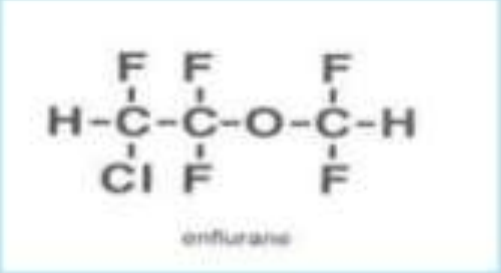
3. Halothane

- Fluorinated volatile liquid with sweet odour, non-irritant non-inflammable and supplied in amber coloured bottle
- Potent anaesthetic, 2-4% for induction and 0.5-1% for maintenance
- Boiling point - 50ºC
- Pharmacokinetics: 60 to 80% eliminated unchanged. 20% retained in body for 24 hours and metabolized

Halothane – contd.

- Advantages:
  - Non-inflammable and non-irritant
  - Pharyngeal and laryngeal reflexes – bronchodilatation
  - Potent and speedy induction & recovery
  - Controlled hypotension
  - Inhibits intestinal and uterine contractions
- Disadvantages:
  - Special apparatus
  - Poor analgesic and muscle relaxation
  - **Hypotension and – direct action (Ca++) and failure of sympathetic activity**
  - **Arrythmia**
    - **Direct vagal stimulation, direct depression of SA node and lack of baroreceptor action**
  - Respiratory depression
  - Decreased urine formation – due to decreased gfr
  - Hepatitis: 1 in 10,000
  - Malignant hyperthermia: Ryanodine receptor
  - Prolong labour

4. Enflurane:



- Non-inflammable, with mild sweet odour and boils at 57ºC
- Similar to halothane in action, except better muscular relaxation
- Depresses myocardial force of contraction and sensitize heart to adrenaline
- Induces seizure in deep anaesthesia and therefore not used now - Epileptiform EEG
- Metabolism one-tenth that of halothane-- does not release quantity of hepatotoxic metabolites
- Metabolism releases fluoride ion-- renal toxicity

5. Isoflurane:

- Isomer of enflurane and have simmilar properties but slightly more potent
- Induction dose is 1.5 – 3% and maintenance dose is 1 – 2%
- By special vapourizer

Isoflurane – contd.

- Advantages:
  - Rapid induction and recovery
  - Good muscle relaxation
  - Good coronary vasodilatation
  - Less Myocardial depression than no myocardial sensitization to adrenaline
  - No renal or hepatotoxicity
  - Low nausea and vomiting
  - No dilatation of pupil and no loss of light reflex in deep anaesthesia
  - No seizure and preferred in neurosurgery
  - Uterine muscle relaxation

- Disadvantages:
  - Pungent and respiratory irritant
  - Special apparatus required
  - Respiratory depression
  - Maintenance only, no induction
  - ß adrenergic receptor stimulation
  - Costly

Intravenous Anaesthetics:

- For induction only
- Rapid induction (one arm-brain circulation time
- For maintenance not used
- Alone – supplemented with analgesic and muscle relaxants

Intravenous:

- **Inducing agents:**

  Thiopentone, Methohexitone sodium, propofol and etomidate

  – Benzodiazepines (slower acting):

  Diazepam, Lorazepam, Midazolam

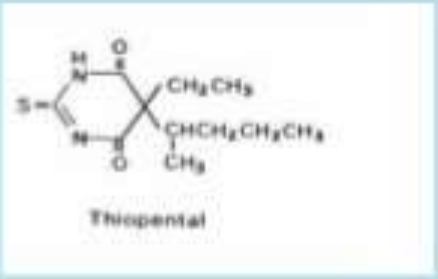
- **Dissociative anaesthesia:**

  Ketamine

- **Neurolept analgesia:**

  Fentanyl

Thiopentone sodium:



- Barbiturate: Ultra short acting
  - Water soluble
  - Alkaline
  - Dose-dependent suppression of CNS activity
  - Dose: 3-5mg/kg iv (2.5%) solution – 15 to 20 seconds
- Pharmacokinetics:
  - Redistribution
  - Hepatic metabolism (elimination half-life 7-12 hrs)
- CNS depression persists for long (>12 hr)

Side effects of Thiopentone:

- Pre-anaesthetic course - laryngospasm
- Noncompatibility - succinylcholine
- Tissue necrosis--gangrene
- Post-anaesthetic course - analgesic

Thiopentone – contd.

- Advantages:
  - Rapid induction
  - Does not sensitize myocardium to adrenaline
  - No nausea and vomiting
  - Non-explosive and non-irritant\
  - Short operations (alone)
  - Other uses: convulsion, psychiatric patients and narcoanalysis of criminals

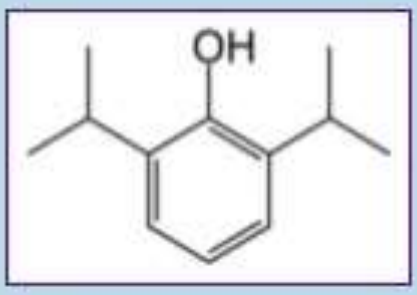
- Disadvantages:
  - Depth of anaesthesia difficult to judge
  - Pharyngeal and laryngeal reflexes persists - apnoea – controlled ventilation
  - Respiratory depression
  - Hypotension (rapid) – shock and hypovolemia
  - Poor analgesic and muscle relaxant
  - Gangrene and necrosis
  - Shivering and delirium

Thiopentone – contd.

- Advantages:
  - Rapid induction
  - Does not sensitize myocardium to adrenaline
  - No nausea and vomiting
  - Non-explosive and non-irritant
  - Short operations (alone)
- Other uses: convulsion, psychiatric patients and narcoanalysis of criminals

- Disadvantages:
  - Depth of anaesthesia difficult to judge
  - Pharyngeal and laryngeal reflexes persists - apnoea – controlled ventilation
  - Respiratory depression
  - Hypotension (rapid) – shock and hypovolemia
  - Poor analgesic and muscle relaxant
  - Gangrene and necrosis
  - Shivering and delirium

2. Propofol



- Replacing thiopentone now
- Oily liquid used as 1% emulsion
- Rapid induction (one arm-brain circulation time): 15 – 45 seconds and lasts for 5–10 minutes
- Rapid distribution – distribution half-life (2-4 min)
- Short elimination half-life (100 min)
- Dose: Induction - 2mg/kg bolus i.v.
  Maintenance - 9 mg/kg/hr i.v.
- Propofol is extensively metabolized
  - 88% of an administered dose appears in the urine
- Metabolized by hepatic conjugation of the inactive glucuronide metabolites

Propofol – contd.

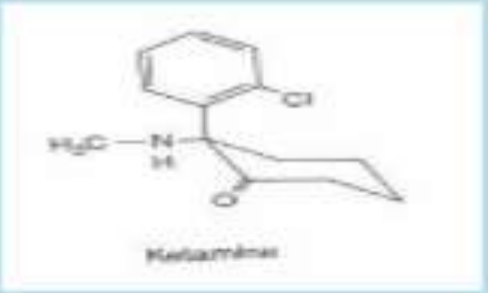
Advantages:

- Rapid induction
- Does not sensitize myocardium to adrenaline
- No nausea and vomiting
- Non-explosive and non-irritant
- Total i.v. anaesthesia
- Short operations (alone)

Disadvantages:

- Induction apnoea
- Hypotension
- Braddycardia
- Dose dependent respiratory depression
- Pain during injection: local anaesthetic combination

3. Ketamine:



- Phencyclidine derivative
- Dissociative anaesthesia: a state characterized by immobility, amnesia and analgesia with light sleep and feeling of dissociation from ones own body and mind and the surroundings.
- Site of action – cortex and subcortical areas – NMDA receptors
- Dose: 5-10mg/kg im or 1-2mg i.v.

Ketamine – contd.

- Disadvantages:
  - Limb movements and nystagmus
  - Emergence phenomenon – 50% patients
  - Hypertensives
  - Increase in IOT and ICP
  - Uterine stimulation
  - Psychosis and shizophrenia
  - Rare laryngospasm
  - Poor muscle relaxation

Ketamine – contd.

Uses:

1. Characteristics of sympathetic nervous system stimulation (increase HR, BP & CO) – hypovolumic shock
2. In head and neck surgery
3. In asthmatics
4. Short surgical procedures – burn dressing, forceps delivery, breech extraction manual removal of placenta and dentistry
5. Combination with diazepam - angiography, cardiac catheterization
6. OPD surgical procedures

4. Fentanyl

- Neurolept analgesia: droperidol
- 4-acylanilino derivative
- Opioid analgesic
- Duration of action: 30-50 min.
- Uses:

- in combination with diazepam used in diagnostic, endoscopic and angiographic procedures
- Adjunct to spinal and nerve block anaesthesia

Fentanyl – contd.

Advantages:

- Smooth onset and rapid recovery
- Suppression of vomiting and coughing
- Commanded operation
- Less fall in BP and no sensitization to adrenaline

Disadvantages:

- Respiratory depression
- Increase tone of chest muscle
- Nausea, vomiting and itching during recovery

Complications of anaesthesia:

During anaesthesia:

- Respiratory depression
- Salivation, respiratory secretions
- Cardiac arrhythmias
- Fall in BP
- Aspiration
- Laryngospasm and asphyxia
- Awareness
- Delirium and convulsion
- Fire and explosion

After anaesthesia:

- Nausea and vomiting
- Persisting sedation
- Pneumonia
- Organ damage – liver, kidney
- Nerve palsies
- Emergence delirium
- Cognitive defects

Preanesthetic medication:

- Definition:

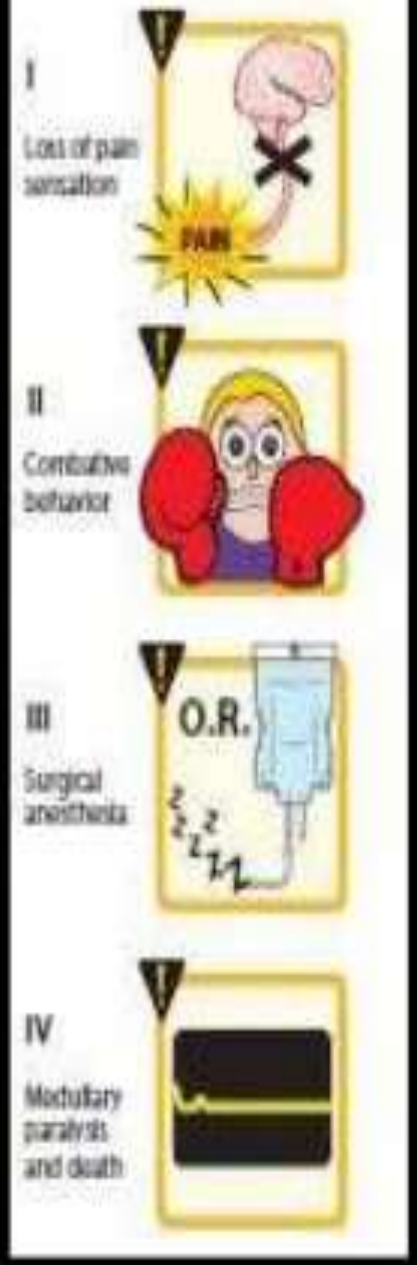
It is the term applied to the use of drugs prior to the administration of an anaesthetic agent to make anaesthesia safer and more agreeable to the patient.

- Aim:

- Relief of anxiety
- Amnesia for pre and post operative events
- Analgesia
- Decrease secretions
- Antiemetic effects
- Decrease acidity and volume of gastric juice

Preanaesthetic medication – contd.

- Drugs used: 6 A's
  - **Anxiolytics** –SEDATIVES – diazepam or lorazepam, midazolam, promethazine etc.
  - **Amnesia**: lorazepam
  - **Anticholinergics** – Atropine
  - **Antacids:** H_2 blockers – ranitidine, famotidine etc.
  - **Antiemetics** – Metoclopramide, domperidone etc.
  - **Analgesia** - Opioids – Morphine and its congeners



	Respiration	Eyeball Activity	PUPILS: No Pre-Anaesthetic Medication	PUPILS: Morphine with Scopolamine or Atropine	PUPILS: Morphine Alone	Eyelid Reflex	Area of Swallowing	Area of Vomiting
Stage 1								
Stage 2		++++						
Stage 3	1	++++ +++ ++ +						
	2							
	3							
	4							

Selection of preanaesthetic drug

- Patient's mental makeup
- Anaesthetic agent to be used
- Type of surgery
- Presence of preoperative problems

Antimuscarinics Drugs:

Atropine, Glycopyrollate, Hyoscine

- Decrease salivary and bronchial secretions
- Prevents laryngospasm, bronchospasm, Nausea and Vomiting
- Prevent Vasovagal attack, Prevent Bradycardia, Hypotension, Cardiac arrhythmia and arrest
- Hyoscine – Sedation, amnesia, Antiemetic
- They ↑ body temperature
- Produce Pupillary dilation – alter pupil sign

Benzodiazepines:

Diazepam, Lorazepam, Midazolam

- Anxiolytic
- Perioperative amnesia
- Sedative
- Smooth induction

Neuroleptics:

Chlorpromazine, Haloperidol

- √ Sedation,
- √ Antianxiety
- √ Antiemetic
- x Hypotension
- x Extrapyramidal Side effects

Antiemetics: Metoclopramide, Domperidone

- Prevent Gastric reflux and aspiration pneumonia
- Antiemetic action in perioperative period
- Metoclopramide – EP Side effects
- Promethazine- Antiemetic+ Sedative+ Anticholinergic
- Promethazine reverses EP Side effects

Antacids, H_2 Blockers, Proton Pump Inhibitors

- Antacids neutralize gastric acidity, H_2 Blockers and Proton Pump Inhibitors decrease acid secretion
- Useful for emergency surgeries, Prolonged surgeries, CS, Obese Patients
- Given night before and in the morning
- Prevent stress ulcers

Phases of Anaesthesia

- Induction: Beginning of administration of anaesthesia to the development of surgical anaesthesia
- Maintenance: Sustaining the state of anaesthesia.
- Recovery: At the end of surgical procedure administration of anaesthetic is stopped and consciousness regains

Induction and Maintenance

- Induction: Thiopentone/ other IV agent
- Maintenance: 1. $N_2O + O_2$+ Ether

  2. $N_20 + O_2$ + Halothane + SM Relaxant

  3. O_2 + Halothane + SM relaxant + Analgesic
- Prevent/ Treat undesired side effects:
  - Anticholinergics, Antiemetics, Analgesics

After Anaesthesia

- Oxygen: Prevent Diffusion Hypoxia
- Neostigmine: Reverse effect of SM relaxant
- Analgesic: Pain relief postoperatively
- Antiemetic: to Control vomiting

Complication of Anaesthesia

During Anaesthesia

- Bradycardia, Cardiac arrhythmia, Cardiac arrest
- Hypotension
- ↑ Salivary and bronchial secretion
- Respiratory depression, Hypercapnia
- Aspiration pneumonia
- Delirium, Convulsions
- Hypoxia
- Awareness and recall of events
- Fire and explosion

After Anaesthesia

- Nausea and Vomiting
- Delayed recovery, Persistent sedation
- Atelectasis and pneumonia
- Liver and Kidney damage
- Delirium
- Nerve palsy

Drug Interactions

- Patient on antihypertensive: fall in BP
- Neuroleptics, Opioids, Clonidine and MAO Inhibitors potentiate Anaesthetics
- Halothane sensitize heart to adrenaline
- Insulin need of diabetic increased

Classification-mechanism & duration of action

Depolarizing

Short-acting

- Succinylcholine

Nondepolarizing

Short-acting

- Gantacurium
- Mivacurium
- Rocuronium

Intermediate-acting

- Atracurium
- Cisatracurium
- Vecuronium
- Rocuronium

Long-acting

- Pancuronium
- Pipecuronium
- Doxacurium

TABLE 20-1 DEFINITION OF NEUROMUSCULAR BLOCKING DRUGS ACCORDING TO THE ONSET AND DURATION OF BLOCK AT THE ADDUCTOR POLLICIS

Onset to Maximum Block	
Ultra rapid (<1 min)	Succinylcholine
Rapid (1–2 min)	Rocuronium
Intermediate (2–4 min)	Atracurium
	Vecuronium
	Pancuronium
Long (>4 min)	Cisatracurium
	Doxacurium
Duration to 25% Recovery of T1	
Ultra short (<8 min)	Succinylcholine
Intermediate (20–50 min)	Atracurium
	Cisatracurium
	Rocuronium
	Vecuronium
Long (>50 min)	Doxacurium
	Pancuronium

REVERSAL AGENTS

Cholinesterase Inhibitors & Other Pharmacologic Antagonists to Neuromuscular Blocking Agents

Anticholinesterases

Inhibit the action of acetylcholinesterase at the neuromuscular junction,

- Thus prolonging the half-life of acetylcholine and potentiating its effect, especially in the presence of residual amounts of non-depolarizing muscle relaxant at the end of surgery.

The primary clinical use of cholinesterase inhibitors, also called anticholinesterases, is to reverse nondepolarizing muscle blockade.

Some of these agents are also used to diagnose and treat myasthenia gravis.

Newer agents, such as cyclodextrins and cysteine, with superior ability to reverse neuromuscular blockade from specific agents, are being investigated

NEOSTIGMINE

Physical Structure

- consists of a carbamate moiety.....provides covalent bonding to acetylcholines-terase.
- quaternary ammonium group.....renders the molecule lipid insoluble, so that it cannot pass through the blood–brain barrier.

Dosage & Packaging

- The usual dose of neostigmine .....0.04-0.08mg / kg in combination with either
- atropine 0.02 mg /kg OR 0.4 mg of atropine per 1 mg of neostigmine or
- glycopyrrolate 0.01 mg/kg OR 0.2 mg glycopyrrolate per 1 mg of neostigmine

Neostigmine takes at least **2 min** to have an initial effect, and recovery from neuromuscular block is maximally enhanced by **10 min**.

TABLE 12–3 The choice and dose of cholinesterase inhibitor determine the choice and dose of anticholinergic.

Cholinesterase Inhibitor	Usual Dose of Cholinesterase Inhibitor	Recommended Anticholinergic	Usual Dose of Anticholinergic per mg of Cholinesterase Inhibitor
Neostigmine	0.04–0.08 mg/kg	Glycopyrrolate	0.2 mg **OR 0.01 mg/kg**
Pyridostigmine	0.1–0..25 mg/kg	Glycopyrrolate	0.05 mg
Edrophonium	0.5–1 mg/kg	Atropine	0.014 mg
Physostigmine[1]	0.01–0.03 mg/kg	Usually not necessary	NA

[1]Not used to reverse muscle relaxants. 0.02 mg /kg OR 0.4 mg of atropine per 1 mg of neostigmine