GENERAL ANESTHESIA

A drug-induced, reversible state characterized by

- **Unconsciousness**
- **Amnesia**
- **Immobility**
- **Antinociception (Suppression or blocking of the body's response to painful stimuli)**

(Nociception: Process by which the nervous system detects and responds to painful stimuli)

The cardinal features of general anaesthesia are:

- **Loss of all sensation, especially pain**
- **Sleep (unconsciousness) and amnesia**
- **Immobility and muscle relaxation**
- **Abolition of somatic and autonomic reflexes.**

Milestones in Anesthesia History:

- **Pre-19th century: alcohol, opium, cannabis, concussion, asphyxia used for pain relief**
- **1844: Horace Wells uses nitrous oxide (N2O) for dental pain**
- **1846: Morton demonstrates ether anesthesia**
- **1847: Chloroform used by Simpson for obstetrics**
- **1935: Thiopentone (IV anesthetic) introduced**
- **1956: Halothane introduced**
- **1929: Cyclopropane introduced**

Early Anesthetics:

- **Nitrous oxide (N2O)**
- **Ether**
- **Chloroform**
- **Cyclopropane**
- **Halothane**
- **Thiopentone (IV)**

Mechanism of General Anesthesia:

- **Not precisely known**
- **Related to physicochemical properties of drugs**
- **Meyer-Overton Hypothesis: anesthetic potency correlates with lipid/water partition coefficient (1901)**

- **In other words, GAs likely work by interacting with lipid components of nerve cell membranes, affecting neuronal function.**

Minimal Alveolar Concentration (MAC)

- **Definition: Lowest alveolar concentration of an inhalational anaesthetic that prevents immobility to painful stimulus (surgical incision) in 50% of individuals.**
- **Significance: Standard measure of potency of inhalational general anaesthetics (GAs).**
- **Age effect: MAC decreases with age, especially after 50 years.**
- **Correlation: MAC correlates with oil/gas partition coefficient (lipid solubility), reflecting CNS penetration — but not mechanism of action.**

Theories of Mechanism

- **Unitary hypothesis (old): All GAs act via a single mechanism (membrane fluidization).**
- **Agent-specific theory (current): Different anaesthetics act via different molecular mechanisms.**
- **Evidence supports direct interaction with hydrophobic domains of membrane proteins.**

Site of Action in CNS

Different components of anaesthesia involve different sites:

- **Unconsciousness: Thalamus / reticular activating system**
- **Amnesia: Cerebral cortex & hippocampus**
- **Immobility: Spinal cord**

Molecular Targets

1. **Ligand-Gated Ion Channels (Major Targets)**

- **GABAA receptor (Cl^- channel): most important target**
- **Potentiated by: inhalational anesthetics, barbiturates, benzodiazepines, propofol**
- **Each anesthetic has its own binding site on GABAA receptor complex**
- **Glycine receptors (Cl^- channels): in the spinal cord and medulla is augmented by barbiturates, propofol and many inhalational anaesthetics contributing to immobility**
- **Nicotinic cholinergic receptors: inhibited by some fluorinated anesthetics and barbiturates, contributing to analgesia and amnesia**

2. **NMDA type of glutamate receptor**

- **N2O and Ketamine don't affect GABA or glycine gated Cl^- channels**
- **Selectively inhibit NMDA type glutamate receptors (excitatory)**
- **Block Ca2+ influx, reducing neuronal excitation**
- **Volatile anesthetics have minimal effect on NMDA receptors**

3. **Two-Pore Domain K^+ Channels**

- **Activation → neuronal hyperpolarization**
- **Decreases presynaptic transmitter release**
- **Contributes to CNS depression**

STAGES OF ANAESTHESIA

- **GAs cause an irregularly descending depression of the CNS, i.e. the higher functions are lost first and progressively lower areas of the brain are involved, but in the spinal cord lower segments are affected somewhat earlier than the higher segments.**
- **The vital centres located in the medulla are paralysed the last as the depth of anaesthesia increases.**

Guedel described four stages with ether anaesthesia, dividing the III stage into 4 planes.

Guedel's Stages of Anaesthesia (Ether)

I. Stage of Analgesia

- **(Beginning of inhalation → Loss of consciousness)**
- **Pain progressively abolished**
- **Patient conscious; hears, sees; dream-like state**
- **Amnesia develops toward end**
- **Reflexes and respiration normal**
- **Minor short procedures possible but difficult to maintain**

II. Stage of Delirium (Excitement)

- **(Loss of consciousness → Onset of regular respiration)**
- **Apparent excitement: shouting, struggling**
- **Increased muscle tone; tightly closed jaws**
- **Irregular/jerky breathing; breath-holding**
- **Vomiting, micturition, defecation may occur**
- **↑ HR, ↑ BP, dilated pupils (sympathetic stimulation)**
- **⚠ No surgery should be performed in this stage**

III. Stage of Surgical Anaesthesia (4 Planes)

- **Plane 1: roving eyeballs → fixed eyes**
- **Plane 2: intercostal muscle paresis & loss of corneal and laryngeal reflexes**
- **Plane 3: intercostal muscle paralysis & pupil dilation, loss of light reflex**
  Plane 4: diaphragmatic paralysis, shallow abdominal breathing, dilated pupil
  As anaesthesia passes to deeper planes, progressively—muscle tone decreases, BP falls, HR increases with weak pulse, respiration decreases in depth and later in frequency also.

IV. Stage of Medullary paralysis:

- **Cessation of breathing to failure of circulation and death.**
- **Pupil is widely dilated, muscles are totally flabby, pulse is thready or imperceptible and BP is very low.**

<u>INDICATION OF GENERAL ANESTHESIA</u>

- **All above umbilicus surgeries**
- **Heart surgeries**
- **Brain surgeries**
- **Lung surgeries**

<u>Properties of Ideal Anesthetic</u>

For Patient:

- **Pleasant, non-irritating**
- **No nausea/vomiting**
- **Fast induction/recovery, no after-effects**

For Surgeon:

- **Analgesia, immobility, muscle relaxation**
- **Noninflammable, nonexplosive (cautery safe)**

For Anesthetist:

- **Easy administration, controllable, versatile**
- **Wide safety margin (no BP fall)**
- **No organ toxicity (heart, liver, etc.)**
- **Potent (low concentration, good oxygenation)**
- **Rapid depth adjustments possible**
- **Cheap, stable, easy storage, compatible with equipment**

CLASSIFICATION

Inhalational

Gas	*Volatile liquids*
Nitrous oxide	Ether
	Halothane
	Isoflurane
	Desflurane
	Sevoflurane

Intravenous

Fast acting drugs	*Slower acting drugs*
Thiopentone sod.	*Benzodiazepines*
Methohexitone sod.	Diazepam
Propofol	Lorazepam
Etomidate	Midazolam
	Dissociative anaesthesia
	Ketamine
	Opioid analgesia
	Fentanyl

Cyclopropane, trichloroethylene, methoxyflurane and enflurane are no longer used.

Table 14.3 General Anesthesia: Detailed Planning

	Premedication	Airway Management	Induction of Anesthesia	Maintenance of Anesthesia[a]	Postoperative Analgesia
Management options	- Anxiolysis - Disease-specific (e.g., nonparticulate antacid for active GERD symptoms, bronchodilator for symptomatic asthma)	- Facemask - SGA - Endotracheal intubation[a] 1. Awake 2. Postinduction	- Intravenous - Inhaled	- One-drug - Two-drug - Multimodal	- Nonopioid medications: acetaminophen, gabapentin, NSAIDs, ketamine, lidocaine infusion - Local anesthetic infiltration - Regional anesthesia - Opioids—IV a nd/ or oral

[a]See text for details.
GERD; Gastroesophageal reflux disease; *NSAIDs*, nonsteroidal antiinflammatory drugs; *SGA*, supraglottic airway.

Preanesthetic Medications:

1. **Benzodiazepines (diazepam, lorazepam, midazolam): anxiolysis, amnesia, sedation**
2. **Opioids (morphine, pethidine, fentanyl): analgesia, sedation (use restricted to patients with pain)**
3. **Anticholinergics (atropine, glycopyrrolate): reduce secretions, prevent bradycardia**
4. **H2 blockers/PPI (ranitidine, omeprazole): reduce gastric acidity and volume**
5. **Antiemetics (metoclopramide, ondansetron): prevent postoperative nausea and vomiting**

PREOXYGENATION (DENITROGENATION)

- **Replaces nitrogen in functional residual capacity (FRC) with 100% oxygen.**
- **Done by: Eight vital capacity breaths of 100% oxygen over 60 seconds, or tidal volume breathing of 100% oxygen for 3 minutes**
- **Replaces ~80% of FRC with oxygen.**
- **Purpose: Prevents/delays hypoxemia during apnea between induction and ventilation.**

INDUCTION

Inhalational Induction

- **Common in children (IV access difficult). Useful in anticipated difficult airway**
- **Limitation: Loss of airway reflexes and pharyngeal tone.**
- **Sevoflurane is the most commonly used anesthetic for inhaled induction of anesthesia because of its low pungency, high potency, and rapidity of onset.**

Intravenous induction

- **The most common technique in the adult patient.**
- **Pharmacologic options include propofol, thiopental, etomidate, ketamine, and a benzodiazepine–opioid combination**

Rapid-Sequence Induction (RSI)

- **In patients with increased aspiration risk:**
  - GERD - Delayed gastric emptying - Unknown fasting state - Full stomach

RSI Sequence:

1. **Preoxygenation (100% oxygen)**
2. **Give Hypnotic (e.g., propofol)**
3. **Rapid-onset neuromuscular blocker (e.g., succinylcholine, rocuronium)**
4. **Application of cricoid pressure (using a force of 30 N, ~7 pounds)**
5. **Avoid ventilation via mask**
6. **Tracheal intubation**
7. **Release cricoid pressure after tube placement confirmation**

Airway Management

- **After putting the patient to sleep, doctors secure the airway using: A breathing tube (intubation) Or a supraglottic airway device**
- **If a difficult airway is expected, the breathing tube may be placed while the patient is still awake (awake intubation) for safety.**

MAINTENANCE

- **Combination of anesthetic drugs, titrated for effect**
- **The goal is to maintain the patient in an unconscious state using inhalational agents, ensure muscle relaxation with long-acting muscle relaxants, and support ventilation mechanically.**
- **Single agent (e.g., propofol, inhaled agent) often requires high dose to block stress responses (rise in heart rate and BP).**

RECOVERY AND REVERSAL

- Reversal Agents:

- **Neostigmine**
- **Sugammadex**
- **Pyridostigmine**
- **Edrophonium**
- **L-cysteine**

- Goals:

- **Make patient conscious (stop inhalational agent)**
- **Restore muscle function (stop muscle relaxant, give reversal agent)**
- **Extubate patient**

Balanced Anesthesia

- **Named by John Lundy**
- **The use of two drugs to maintain anesthesia represents an approach called balanced anesthesia**
- **Benefits: improved control of ANS responses, reduced side effects**
- **e.g., opioid + propofol/inhaled agent**
- **Opioid risks: respiratory depression, addiction concerns**

Multimodal General Anesthesia

- **Address multiple targets in nociceptive system**
- **Uses multiple types of pain-control drugs targeting different pain pathways.**
- **Goal: effective pain control, reduced opioid use**
- **Part of multimodal pain management strategy**

Complications of General Anesthesia

During Anesthesia:

1. **Respiratory depression, hypercarbia**
2. **Salivation, secretions**
3. **Cardiac arrhythmias, asystole**
4. **Hypotension**
5. **Aspiration, acid pneumonitis**
6. **Laryngospasm, asphyxia**
7. **Excitatory effects (delirium, convulsions)**

After Anesthesia:

- **Nausea, vomiting**
- **Persisting sedation, impaired psychomotor function**
- **Pneumonia, atelectasis (partial or complete collapse of lung tissue (alveoli), causing reduced oxygen exchange)**
- **Organ toxicities (liver, kidney)**
- **Nerve palsies**
- **Cognitive defects (especially in elderly)**

Anesthetic Drug Interactions (If a patient on)

1. **Antihypertensives + GA: risk of severe hypotension**
2. **Neuroleptics, opioids, clonidine, MAOIs: potentiate anesthetics**
3. **Corticosteroids: give with hydrocortisone (100 mg) during surgery to prevent adrenal insufficiency**
4. **Insulin need of a diabetic is increased during GA: switch over to plain insulin even if the patient is on oral hypoglycaemics**