General Anesthesia

General anesthesia is essential to surgical practice, because it renders patients analgesic, amnesia and unconscious reflexes, while causing muscle relaxation and suppression of undesirable reflexes. No single drug capable of achieving these effects both safely and effectively (a single drug can induce anesthesia effectively but with side effects so we need to combine drugs together).

Anesthesia is coming in 4 stages:-
1. Stage I : analgesia.
2. Stage II : excitement, amnesia and analgesia.
3. Stage III : unconsciousness, amnesia and analgesia (I need to reach this stage).
4. Stage IV : complete suppression of CNS and respiratory suppression (I don’t want to reach here).

Note : Increasing the dose of anesthetic agents will drive my patient to Stage IV, Also we have inter-individual variation (1 in every 35,000) will reach stage IV leading to death so to reduce this problem we combine drugs.

My goal in general anesthesia is to stop all of these in the picture above (motor reflexes, pain and autonomic reflexes).

Inhalation anesthetics are not particularly effective analgesics and vary in their ability to produce muscle relaxation; hence if they are used alone to produce general anesthesia, high concentrations are necessary. If inhalation anesthetics are used in combination with specific analgesic or muscle-relaxant drugs the inspired concentration of inhalation agent can be reduced, with an associated decrease in adverse effects. The use of such drug combinations has been termed balanced anesthesia.
So we conclude than we should always give anesthetic, analgesic, muscle relaxant and atropine (autonomic stabilizer).

Treatment with anesthesia we build it on 4 issues :-
1. Pre-op : using morphine and benzodiazepine (opioids) to reduce anxiety + Pentazocine as analgesic + atropine.
Note: Halogenated anesthetics are cardiotoxic, that's why we give anxiolytics before anesthesia to reduce the stress and hence reduce levels of catecholamines in the blood and prevent the cardiotoxic effects of anesthetics.

2. Induction: to induce the unconsciousness fastly within 30 seconds through injection (IV) reaching stage II and stage III.
   Barbiturates (thiopental) was used, but now limited due to the hangover and respiratory depression so now replaced by propofol.
   Note: We do intubation for the patient to help O₂ reaching the patient under relaxant state (relaxed respiratory muscles) that was given for him Succinycholine.

3. Maintenance: either I give him another dose of propofol or which is more commonly used is inhaled anesthesia (Halothane, N₂O and Pancuronium).

4. Recover: By removal of Halothane or by giving neostigmine (ACh esterase inhibitor to reverse the muscle relaxant state).

I. Inhalation Anesthesia (maintenance Anesthesia)

Inhaled gases are the core of anesthesia and are used primarily for the maintenance of anesthesia after administration of an intravenous agent. No one anesthetic is superior to another under all circumstances. The potency of inhaled anesthesia is defined quantitatively as median alveolar concentration (MAC). MAC is the minimum alveolar concentration of anesthetic that produces immobility in 50% of patients exposed to a standard noxious stimulus. MAC is usually expressed as a percentage of gas mixture required to achieve the effect and is small for potent anesthetics.

4 types of inhaled anesthesia: halothane, isoflurane, sevoflurane and enflurane (not used anymore because it causes fluoride toxicity which leads to kidney failure).

We give the patient inhaled anesthesia with oxygen (70% conc.), N₂O (29% conc.) and inhaled anesthesia (1% conc.).

MAC for halothane is 0.8% and this is the conc. that produces anesthesia in 50% of the patients while the other 50% need a higher MAC to induce anesthesia (e.g. 1.5% or 2%, but never exceed 3x MAC as you may reach stage IV).

MAC is an indication that tells us where to start. For example, the MAC for halothane is 0.8%, that’s the dose that we start with, then we start increasing the dose to reach stage III. Different patients need different MAC.

Isoflurane has a MAC of 1.2%, so it's less potent than halothane. Sevoflurane has a MAC of 4%, so it's less potent than halothane and isoflurane.
By increasing the MAC conc. we decrease the conc. of N₂O (e.g. the MAC for sevoflurane is 4%, so we reduce the N₂O conc. to 26% and the oxygen conc. remains constant (70%).

Halothane is the oldest and the worst because it's hepatotoxic in adults but NOT in children and the cause is due to the fact that it's more metabolized in adults leading to accumulation of toxic metabolites in the liver also Halothane produces bronchodilation and that's why it's still used especially in asthma patients.

Isoflurane and sevoflurane cause pungency (bronchoconstriction) and isoflurane has a pungent odor (sharp acidic smell).

In low income countries, Halothane can be used to induce and maintain anesthesia in children because it's not hepatotoxic and has a pleasant odor, which makes it suitable for children; while in high income countries isoflurance/sevoflurane is used to induce and maintain anesthesia in children.

Note: IV induction such as Thiopental and propofol are not used to induce anesthesia in children.

Note: Halothane sensitizes the heart to the catecholamines. Isoflurane and sevoflurane have much less cardiac effects than halothane (they don't sensitize the heart to catecholamines).

Note: Halothane increases blood flow to the brain so it may increase intracranial pressure while Isoflurane and sevoflurane do not cause this effect.

Note: Isoflurane costs much less than sevoflurane.

NITROUS OXIDE

It has a sedative and analgesic effect (but is not used in anesthesia due to this effect). Can be used in dental surgery.

Is a potent analgesic, but a weak general anesthetic (at 80% cannot produce surgical anesthesia) but we use it because of its fast uptake from the alveolar gas, Nitrous oxide produce what is called “second gas effect” which results from the ability of Nitrous oxide to concentrate the halogenated anesthetics (Halothane, Enflurane, Isoflurane) in the alveoli when they are coadmininistrated.

II. IV anesthesia (Inductive anesthesia)

Are often used for rapid induction of anesthesia, which is then maintained with appropriate inhalation agent. Work fast and finish fast (so we can start maintenance phase). We start anesthesia by giving IV thiopental (old) or IV propofol (new).

1. Thiopental: is a potent but weak analgesics. It is an ultrashort-acting Barbiturate and has high lipid solubility. Quickly enters the CNS and depresses its function, often in less than one minute. It has a short duration of action because its concentration in the CNS decreases quickly below that necessary to produce anesthesia.
   Main adverse effects are coughing, chest wall spasm, and bronchospasm (asthmatic patient).
Although it is a short acting anesthetic, it causes Hangover after surgery because of its high volume of distribution due to its high lipid solubility.

2. **Propofol**: Is an intravenous sedative/hypnotic used in the induction and maintenance of anesthesia, supplementary analgesics are required. Propofol is widely used and has replaced thiopental and became the first choice for induction anesthesia and sedation. It produces euphoric feeling in the patient and does not cause postanesthetic nausea and vomiting. Mechanism of action is not known but may be through GABA-Beta subunit. Can lead to hypotension caused mainly by vasodilatation rather than cardiac affect, depression, it's non-analgesic, antiemetic and promotes bacterial growth (hence short shelf life of open solution).

3. **Ketamine (NMDA-antagonist)**: is a short acting, induced anesthetic. It actually induces dissociated state in which the patient is unconscious but appears to be awake and does not feel pain. It stimulates the central sympathetic outflow, which causes stimulation of the heart and increased blood pressure and cardiac output and this property is especially beneficial in patients with either hypovolemic or cardiogenic shock as well as in patients with asthma. Induces postoperative hallucination (potentiates dopamine). Ketamine is mainly used in children for short procedure (10 min).

### III. Local anesthesia

It’s used in dental, ophthalmic, abdominal, lower limb surgeries and labour (where patient is conscious).

Mechanism of action: works by blocking voltage gated Na+ channels in the peripheral nerves. Local anaesthetics block the initiation and spread of action potentials in nerve fibres by preventing the voltage-dependent increase in Na+ conductance. They do this in two ways:

1. By acting non-specifically to stabilise the membrane.
2. By specifically plugging Na+ channels. This mechanism is the most important for most local anaesthesia.

Most are used with adrenaline to prolong duration of action by constricting blood vessels to keep my anesthesia confined to that place by reducing the perfusion.

### IV. Topical anesthesia

Local anesthesia is applied directly to mucous membranes such as those of the conjunctiva, nose, throat or urethra. Agents of choice is Tetracaine.

Patients may complain of a burning sensation (Less with Proparacaine).

Onset of anaesthesia takes about 20 seconds and duration of action is about 8 minutes.
V. Injection agents

The most commonly used agents are: procaine, Lidocaine, Tetracaine and Bupivacaine (lidocaine being the most used). They vary in their duration of action and time to onset of anaesthesia.

a) Infiltration or Local Anaesthesia

Local anesthesia is injected subcutaneously around sensory nerve endings. Useful in minor surgery. Infiltration anesthesia can be produced with 0.5–1% aqueous solution of lidocaine or procaine (usually with coadministration of adrenaline).

b) Intravenous Regional Anaesthesia

Local anesthesia injected intravenously distal to a pressure cuff to arrest blood flow. Remains effective until the circulation is restored.

Used for limb surgery. Mainly Lidocaine (Lignocaine) and Prilocaine.

c) Spinal Anaesthesia

Local anaesthesia is injected intrathecally into the CSF of the subarachnoid space to act on spinal roots and spinal cord.

Used for surgery to abdomen, pelvis or leg when general anaesthesia is not appropriate. Mainly Lidocaine and Tetracaine.

d) Epidural anaesthesia

Is injection of the Local anesthesia to the spinal column but outside the dura mater, used in obstetrics.

A side effect of epidural anesthesia is headache which is severe.

Note: A common side effect for general and local anesthesia is HYPOTENSION.

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Accidental dural puncture with headache (common, about 1 in 100 insertions). The epidural space in the adult lumbar spine is only 3-5mm deep, which means it is comparatively easy to cross it and accidentally puncture the dura (and arachnoid) with the needle. This may cause cerebrospinal fluid (CSF) to leak out into the epidural space, which may in turn cause a post dural puncture headache (PDPH). This can be severe and last several days, and in some rare cases weeks or months. It is caused by a reduction in CSF pressure and is characterised by postural exacerbation when the subject raises his/her head above the lying position.
SUMMARY

Therapeutic Disadvantages of Anesthetic Agents

INHALATION ANESTHETICS

Incomplete anesthesia  
No muscle relaxation

Nitrous oxide

Rapid onset & offset  
Good analgesia

Reduced liver & kidney blood flow  
Reduced BP  
Sensitizes heart to arrhythmia

Halothane

Pleasant smell  
Good for asthmatics & kids

Respiratory depression  
Seizure activity

Enflurane

Good muscle relaxation  
Rapid recovery  
Cardiac output stable  
Does not sensitize heart to arrhythmia

Expensive, irritant

Isoflurane

Therapeutic Advantages of Anesthetic Agents

INTRAVENOUS ANESTHETICS

No analgesia  
Little muscle relaxation  
Hangover

Thiopental

Rapid onset of effect

Excellent cardiovascular stability  
Reduced irritation of airway

Sometimes awareness present  
Respiratory depression  
Nausea, trunk muscle rigidity

Opioids

Rapid onset & offset  
No hangover

Bad dreams  
Hallucinations

Propofol

Potent analgesia  
Does not depress circulation  
Good for short procedures

Ketamine