General Anesthetics

Drugs used to induce loss of consciousness, loss of pain sensation, skeletal muscle relaxation, analgesia, amnesia and inhibitions of undesirable reflexes.

Features of ideal anesthetic

1. Rapid and smooth induction and recovery.
2. Wide safety margin.
3. Minimal side effects.
4. Characters of pre-anesthetic medication

Balanced anesthesia

Use of more than one agent to obtain ideal anesthesia

Adjuncts to general anesthetics

I. Skeletal Muscle relaxants

II. Pre-anesthetic medication.

Skeletal Muscle relaxants

- Facilitate intubation
- Suppress muscle tone
- Atracurium, Vecuronium, Succinylcholine

Pre-anesthetic medications

Anticholinergics: prevent secretion of fluids into the respiratory tract .

Benzodiazepines: relieve anxiety.

Antiemetics : post surgical N&V.

Antihistaminics: allergic reactions.

H2-receptor blockers: reduce gastric acidity

Opiates: induce analgesia.

Classification of general anesthetics

Inhalation Anesthetics

Intravenous Anesthetics

Mechanism of action

1. Interaction with membrane ion channels.

2. Enhance the action of inhibitory neurotransmitters as **GABA and glycine** so decrease neuronal excitability

3. Inhibit the actions of excitatory neurotransmitters

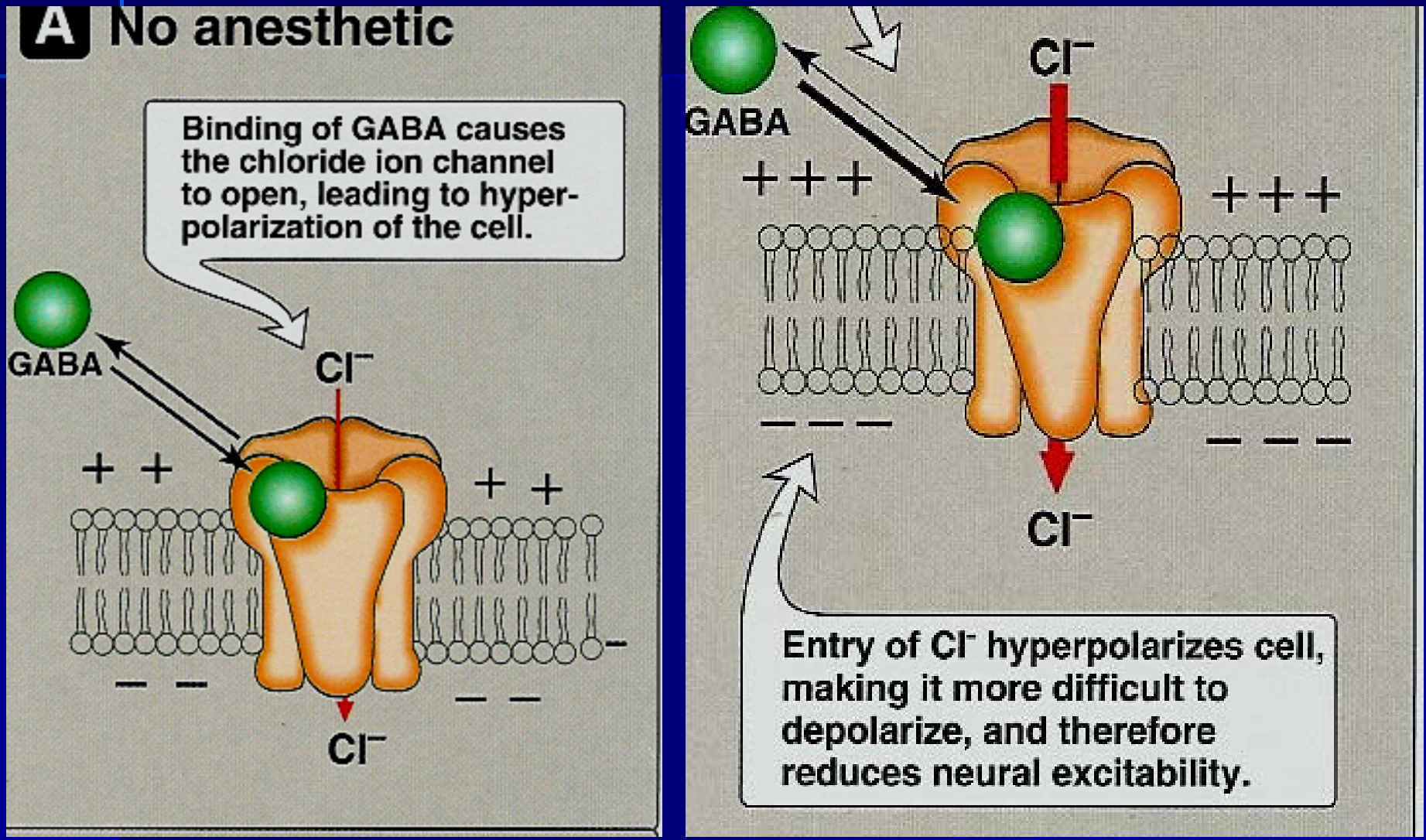
Inhalation Anesthetics

- Gases (nitrous oxide)
- Volatile liquids (halogenated hydrocarbons)
  - Methoxyflurane
  - Halothane
  - Enflurane
  - Isoflurane
  - Desflurane
  - Sevoflurane

Mechanism of action of Inhaled anesthetics

Interaction with membrane ion channels.

Modulation of ligand-gated membrane channel modulated by inhaled anesthetics



Stages of anesthesia
(Depth of anesthesia)

Stage I

- Analgesia
- Loss of pain sensation.
- The patient is conscious and conversational

Stage II

- Excitement.
- Increased, irregular blood pressure
- Increased respiratory rate.
- Patient may experience delirium & violent behavior.
- Eye dilated & reactive.

Stage III

- Surgical anesthesia
- Regular respiration
- Eye reflexes decrease untill the pupil is fixed

Stage IV

- Medullary paralysis
- Severe depression of vasomotor and respiratory centers
- Death may occur

Induction, Maintenance and Recovery

Induction

Time elapsed between onset of administration of anesthetic and development of effective surgical anesthesia (Brain).

Maintenance

Time during which the patient is surgically anesthetized

Recovery

The time from discontinuation of anesthetic drug until consciousness is regained.

Pharmacokinetics

- Rate of induction
- Depth of anesthesia and recovery

Factors controlling induction & recovery

1. The anesthetic concentration in the inspired air (**Direct**).
2. Rate and depth of ventilation (**Direct**).
3. Blood: gas partition coefficient (blood solubility) (**Inverse relation**)

DRUG	Solubility	Induction & Recovery
Methoxyflurane	12	Slow
Halothane	2.3	Slow
Enflurane	1.8	Medium
Isoflurane	1.4	Medium
Sevoflurane	0.69	Rapid
Desflurane	0.42	poor
Nitrous oxide	0.47	Rapid

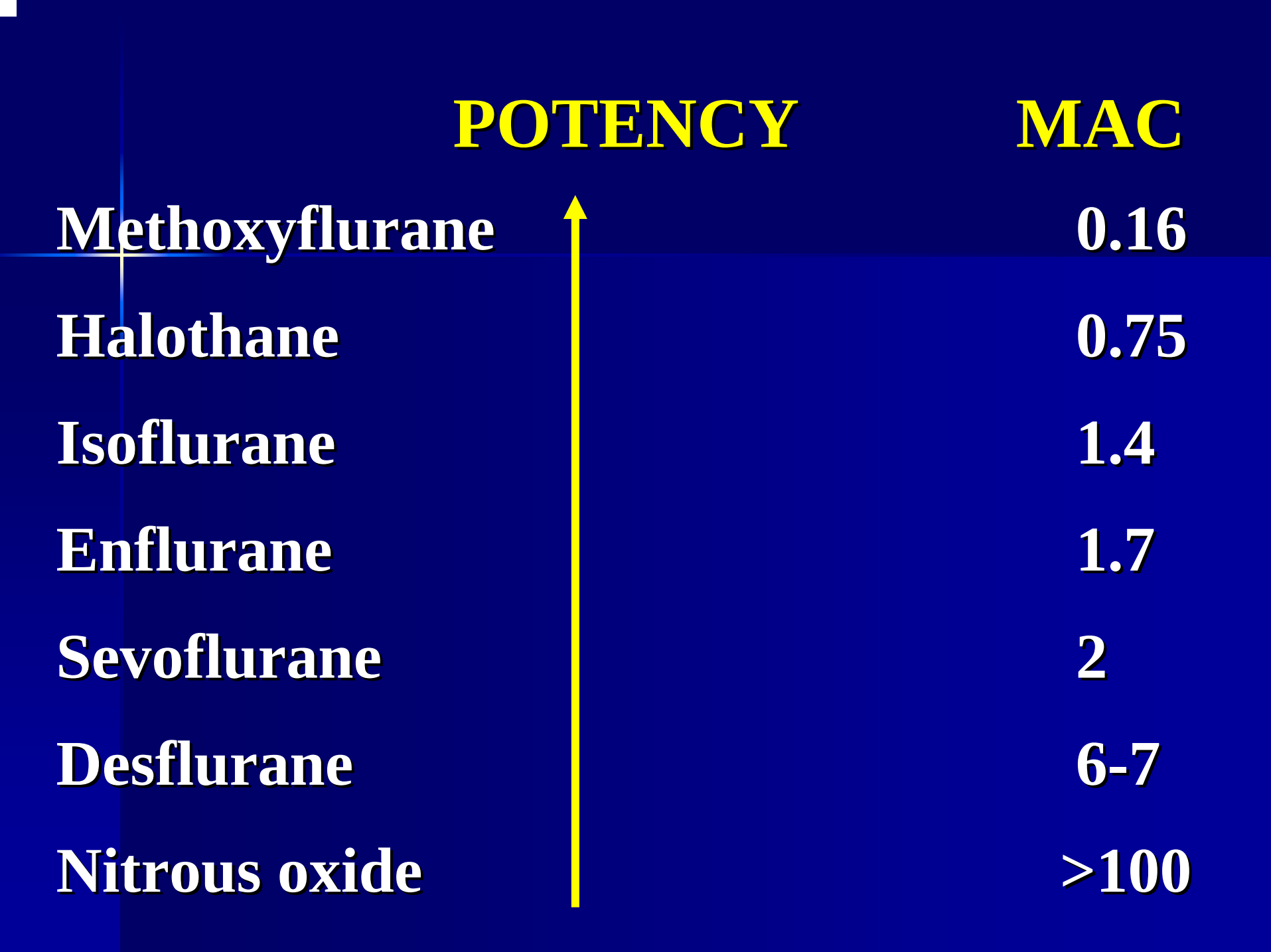
Minimum Alveolar Concentration (MAC)

- is the concentration of inhalation anesthetic that produce immobility in 50% patients in response to surgical incision.
- depends upon potency of anesthetic agents

- **The lower the MAC value the more potent the drug.**

MAC value is

- **Decreased by CNS depressants, old people.**
- **Increased by CNS stimulants.**


POTENCY
MAC
Methoxyflurane
0.16
Halothane
0.75
Isoflurane
1.4
Enflurane
1.7
Sevoflurane
2
Desflurane
6-7
Nitrous oxide
>100

Pharmacological Actions

CNS

- ↓ metabolic rate
- ↑ ICP (due to cerebral vasodilatation) # in head injuries
- Dose dependent EEG changes (Enflurane)

Cardiovascular system

- Hypotension
- Bradycardia
- Tachycardia **Isoflurane& Desflurane**
- Myocardial depression with **Halothane & Enflurane**
- Sensitize heart to catecholamines (**Halothane**)

Respiratory

- All are respiratory depressants
- All are bronchodilators (halothane – sevoflurane)
- ↓ mucociliary movement
- Some produce airway irritation (Desflurane - enflurane - isoflurane)).

Liver

Decrease hepatic flow

Hepatotoxicity (**Only halothane**)

Uterus & Skeletal Muscles

- All are skeletal muscle relaxants enhance the effects of neuromuscular blocking drugs **except nitrous oxide**
- Are uterine relaxants **except nitrous oxide** that has minimal relaxant effect (labor)

Methoxyflurane

- The most potent (high lipid solubility).
- 50 % is metabolized to fluoride (nephrotoxic).
- Slow induction (20 minutes).
- For veterinary use only.

Halothane (Fluothane)

- has pleasant odor - non irritant
- Potent anesthetic
- Slow induction and recovery (due to blood solubility).
- Weak analgesic
- Weak skeletal muscle relaxant.

- CVS depression
  - Hypotension
  - Bradycardia (vagomimetic action)
  - ↓ Myocardial contractility.
  - ↓ Cardiac output

- Halothane is hepatotoxic due to the metabolite (trifluroethanol)

- Respiratory depression.
- The agent of choice in children (Pleasant).

Adverse effects of halothane

1. Hepatotoxicity (repeated use).
2. Malignant hyperthermia.
3. Cardiac arrhythmias.
4. Sensitizes heart to action of catechalamines → arrhythmias.

Enflurane (Ethrane)

- More rapid induction and recovery than halothane.
- Less potent than halothane.
- Better muscle relaxation.
- Better analgesic propertics.
- is metabolized to fluoride (8%).
- Excreted in the kidney

Enflurane

- CVS depression

  - Hypotension

  - ↓ Cardiac output

  - No sensitization of the heart to catecholamines

Disadvantages

- Epilepsy-like seizure and abnormal EEG
- Pungent odor

(Less induction- not suitable for pediatrics)

Contraindication

patients with seizure disorders

Isoflurane (Forane)

- Potent anesthetic
- Rapid induction & recovery
- has analgesic action.
- No sensitization of the heart.
- No cardiac arrhythmias.
- Stable compound (2%).
- Low biotransformation (Less fluoride).
- No nephrotoxicity - no hepatotoxicity.

- **CVS depression**
  - **Hypotension**
  - **Potent coronary vasodilator**
  - **slight ↑ H R**

Desflurane (Suprane)

- Pungent odor (irritation - Cough)
- Rapid induction & fast recovery (Low solubility).
- Less potent than halothane
- Less metabolized (0.05 %)
- Low boiling point (special equipment).
- CVS depression
  - Hypotension
  - ↑ H R

Sevoflurane

- Better smell
- Less potent than halothane
- Rapid onset and recovery (Low solubility)
- Less metabolized (3- 5% fluoride)
- No airway irritation (children)
- Little effect on HR
- CVS depression
  - Hypotension
  - ↓ cardiac output

- sevoflurane is the most effective clinical **bronchodilator** of the inhalational anesthetics

Nitrous Oxide (N2O)

- Potent analgesic
- Weak anesthetic (Low potency, combined).
- Rapid induction & Recovery (Low solubility).
- No muscle relaxation.
- No respiratory depression.
- Not hepatotoxic.
- Minimal CVS adverse effects.

Adverse Effects of nitrous oxide

1. Diffusion Hypoxia
2. Nausea and vomiting
3. Inactivation of B 12 $\longrightarrow$ megaloblastic anemia.
4. Bone marrow depression - leukopenia (**chronic use**).
5. Abortion - congenital anomalies

Therapeutic Uses

1. Outpatient anesthesia (Dental procedures)
2. Delivery
3. Balanced anesthesia
4. As component of neuroleptanesthesia

Contraindications

1. Chronic exposure during pregnancy
2. Pernicious anemia
3. Immunosuppression

Intravenous Anesthetics

1. Ultra short acting barbiturates.
2. Benzodiazepines.
3. Opioids.
4. Ketamine.
5. Propofol
6. Etomidate

Benzodiazepines

Midazolam (Versed) - Diazepam (Valium

Lorazepam (Ativan)

- **The best one is midazolam (i.v - i.m.)**
- **Amnesic action.**
- **Reduce anxiety.**
- **No analgesic activity**
- **Slow induction & recovery.**

Uses

1. Induction of general anesthesia.
2. Alone in minor procedure (endoscopy).
3. Balanced anesthesia (Midazolam).

Side Effects

1. Slow induction & recovery.
2. Respiratory depression.

Ultra Short acting barbiturates

Thiopental (Pentothal)

Methohexital (Brevital)

Thiamylal (Surital)

Thiopentone

Pharmacokinetics

1. Rapid onset of action, 1 min (high lipid solubility)
2. Ultra short duration of action 15 - 20 min
2. Metabolized slowly by the liver

Pharmacodynamics

- Potent anesthetic
- No analgesic activity
- has anticonvulsant activity
- CNS: ↓ ICP (Used in head injuries).
- CVS: Hypotension & Dysrhythmia.
- Respiratory system
  - Laryngospasm
  - bronchospasm.

Uses

1. As anesthetic alone in minor surgery.
2. Induction of anesthesia in major surgery.

Adverse Effects

1. Respiratory depression (dose - dependent).
2. CVS collapse
2. Extravasations
3. Precipitation of porphyria attack.
4. Hypersensitivity reaction.

Contraindication

1. Chronic obstructive lung disease
2. Porphyria
3. Hypersensitive patients
4. Severe hypotension (hypovolemic & shock patient)

Propofol

- Hypnotic (Non Barbiturate)
- Fast onset – rapid recovery
- Short duration of action
- Rapidly metabolized in liver

(10 times - Elimination ½ = 30 – 60 min)

- No analgesic activity
- Hypotension.

- Decreases ↓ ICP
- Respiratory depression
- Antiemetic action

Uses

1. Induction of anesthesia
2. Maintenance of anesthesia (Balanced anesthesia).

Side Effects

1. Excitation (involuntary movements).
2. Pain at site of injection.
3. Expensive.
4. Clinical infections due to bacterial contamination.

Etomidate (Amidate)

- Ultrashort acting hypnotic (Non barbiturates)
- Rapid onset of action
- Short duration of action
- No analgesic activity
- rapidly metabolized in liver
- Produce CVS stability
- Minimal respiratory depressant effects
- Decreases ↓ ICP

Uses

- used for induction of anesthesia in patients prone to hemodynamic instability (Hypotension, coronary artery disease, cardiomyopathy, cerebral vascular disease, or hypovolemia)

Side Effects

- Involuntary movements during induction (diazepam)
- Postoperative nausea and vomiting
- Adrenocortical suppression
- Pain at sit of injection

Ketamine

- Non barbiturate
- Dissociative anesthesia
  - Analgesia
  - Amnesia
  - Immobility
  - Complete separation from the surrounding environment

ketamine acts by inhibiting excitatory neurotransmission at glutamatergic synapses.

Pharmacokinetics

rapid onset of action (Slower than thiopental)

Short duration of action.

Metabolized in the liver to active metabolite (Norketamine)

Pharmacodynamics

1.↑ BP, HR and cardiac output (↑central sympathetic activity)

2. ↑ Increases plasma catecholamine levels.

3. ↑ ICP

4. Potent bronchodilator (asthmatics).

Advantages

- Can be given IV, IM, oral, rectal (Children).
- Suitable for patients at high risk for hypovolemia, shock, bronchospasm

Side Effects

1. Post operative hallucination
2. vivid dreams & disorientation &illusions (Diazepam).
3. Risk of hypertension & cerebral hemorrhage.
4. ↑ ICP

Contraindications

1. CVS diseases (hypertension-stroke).
2. Head injuries

Uses

1. Minor operations (children, elderly, shock patients).
2. Short duration diagnostic procedures

Opiate Drugs

Fentanyl (Sublimaze)

Sufentanil (Sufenta) **Alfentanil (Alfenta)**

- fast onset of action
- Short duration of action.
- Potent analgesia.
- No skeletal muscle relaxation

Uses

1. Cardiac surgery
2. Neuroleptanalgesia (Fentanyl + droperidol)
3. Neuroleptanesthesia (Fentanyl+Droperidol+ nitrous oxide)

Neuroleptanalgesia

- A state of analgesia, sedation and muscle relaxation BUT No loss of consciousness
- Innovar (Fentanyl + Droperidol)
- Contraindicated in parkinsonism
- Diagnostic procedures that require cooperation of the patient.

Neuroleptanesthesia combination of (Fentanyl + Droperidol + nitrous oxide)

Side Effects of opiate drugs

1. Respiratory depression, bronchospasm (wooden rigidity)
2. Hypotension
3. Nausea & vomiting
4. Increase in ICP
5. Prolongation of labour & fetal distress
6. Urinary retention.

Contraindication

1. Head injuries
2. Pregnancy
3. Bronchial asthma
4. Chronic obstructive lung diseases
5. Hypovolemic shock (Large dose only)

Intravenous Anesthetics

- Rapid induction & recovery **EXCEPT BZs**
- Injected slowly (rapid induction).
- Recovery is due to redistribution from CNS.
- Analgesic activity (Opioids & ketamine).
- Amnesic action (BZs & ketamine).
- Can be used alone in short operation.
- Out patients anesthesia.
- NO need for special equipments.

Summary of Parenteral Anesthetics

Thiopental and propofol are the two most commonly used parenteral agents.

Etomidate usually is reserved for patients at risk for hypotension and/or myocardial ischemia.

Ketamine is best suited for patients with asthma or for children undergoing short, painful procedures.

Thank you