

# General Anesthetics

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## Historical Events

1842 Ether administration for dental extraction

1844 Nitrous oxide for dental extraction

1846 First surgical operation under ether anesthesia in England

## Phases of the general anesthesia

### The general anesthetic process extends:

Before surgery (pre-anesthetic medication)

During Surgery

After surgery

### Before surgery (pre-anesthetic medication)

#### The aim is to produce one or more of the following:

- a. anxiolysis and amnesia
- b. analgesia
- c. drying of bronchial and salivary secretions
- d. prevention of pulmonary aspiration of gastric contents

#### **a. Anxiolysis and amnesia**

A lot of adrenaline is secreted making the patient more liable to cardiac arrhythmias. Benzodiazepines may be used for this purpose

#### **b. Analgesia is given if the patient is in pain or to prevent postoperative pain**

- Parenteral opioid such as morphine can be given for severe pain
- Paracetamol can be given to prevent postoperative pain
- NSAIDs can be used with caution (they may prolong bleeding time and may cause intra or post-operative bleeding)

**Benzodiazepines** can cause respiratory depression and apnea especially in elderly or in patients with respiratory insufficiency. Combination of an opioid and a benzodiazepine is particularly dangerous.

#### **c. Drying of bronchial and salivary secretions by antimuscarinic drugs (e.g. with bronchoscopy). They are rarely used at the present time.**

#### **d. Prevention of pulmonary aspiration of gastric content.**

Patients at risk are those with full stomach, in the third trimester, or with incompetent gastro-esophageal sphincter

**Aspiration or its effect can be prevented by a single dose of one or more of the following:**

- antacids
- H2-blockers
- proton pump inhibitors
- Metoclopramide (which hastens gastric emptying and increases the tone of the lower esophageal sphincter; it is also an antiemetic)

#### **2. During Surgery**

**The aim is to induce:**

- unconsciousness
- analgesia
- muscle relaxation

**A typical general anesthetic procedure consists of:**

- A. Induction of anesthesia
- B. Maintenance of anesthesia

##### **A. Induction of anesthesia**

- a - usually by intravenous anesthetics  
(propofol, thiopental, etomidate, ketamine)
- b - less commonly, induction is achieved by inhalational anesthetics  
(usually used in children, for example, with sevoflurane)

##### **B. Maintenance of anesthesia**

is achieved by using oxygen with nitrous oxide, or with a volatile agent (e.g. sevoflurane or isoflurane) plus additional doses of a neuromuscular blocker or an opioid as required.

#### **3. After surgery**

**Relief of pain:** using parenteral morphine, oral or rectal paracetamol or an NSAID. Paracetamol and some NSAIDs can also be given by injection.

### **Postoperative nausea and vomiting:**

Cyclizine, metoclopramide or ondansetron can be used.

Dexamethasone also reduces incidence of postoperative nausea and vomiting. Combination of these drugs can be more effective in severe cases.

### **General Anesthetics**

#### **Mode of action of general anesthetics**

General anesthetics act on the brain primarily on the midbrain reticular activating system (hypnosis and amnesia) and the spinal cord (inhibiting motor response to painful stimuli).

They interact with proteins to alter the activity of specific ion channels.

In general, the more lipid soluble the general anesthetic, the more anesthetic effect it has.

#### **Inhalational anesthetics**

The preferred inhalational anesthetics are: minimally irritant and non-flammable. Examples: nitrous oxide and fluorinated hydrocarbons such as isoflurane.

An inhalational anesthetics with high blood solubility has low brain entrance and provides slow induction.

Low blood solubility → High brain entrance → Rapid induction  
e.g. nitrous oxide and sevoflurane have low blood solubility and provide rapid induction.

After discontinuation of the inhalational anesthetics, the drug flows from the blood to the alveoli which significantly lowers the alveolar oxygen concentration. This is called diffusion hypoxia and it is prominent with gases of low solubility in blood, having rapid diffusion rate.

#### **Nitrous oxide (1844)**

Sweetish smell

Non-flammable

Non-explosive

Provide light anesthesia without depression of respiration or vasomotor centre if oxygen tension is normal.

### **Advantages of nitrous oxide**

Has a strong analgesic action (50% of N<sub>2</sub>O in 50% oxygen (Entonox) has similar analgesic effect as morphine).

Induction is rapid

Recovery time is also rapid (4 minutes)

### **Disadvantage**

- Expensive
- Not potent as a sole anesthetic; it must be used with more potent anesthetics to produce full surgical anesthesia

### **Uses of nitrous oxide**

- To maintain surgical anesthesia with other agents.
- Nitrous oxide, in subanesthetic dose, provides analgesia e.g. in obstetrics, in emergency treatment of injuries and in changing painful dressings.
- N<sub>2</sub>O must always be mixed with at least 30% oxygen to avoid hypoxia.

For analgesia, 50% N<sub>2</sub>O with 50% oxygen can be effective

### **Adverse effects**

- Nausea and vomiting
- Prolonged exposure can cause megaloblastic bone marrow changes due to interference with vitamin B12 action
- Prolonged and repeated exposure of staff and patients, is associated with bone marrow suppression and a teratogenic risk.
  
- Nitrous oxide has a dangerous effect if used in patients with air-containing closed space e.g. pneumothorax since nitrous oxide diffuses into such spaces resulting in increased pressure that compromises respiration.

### **Halogenated anesthetics**

Halothane was the first to be used

Now, superseded by isoflurane and sevoflurane

## Halothane

- Has the highest solubility with slow induction and recovery
- Pleasant to breathe, non-irritant
- Sensitizes the heart to arrhythmic effect of catecholamine (arrhythmias are common)
- Moderate muscle relaxation
- 20% metabolized
- Halothane can induce hepatic enzymes and cause hepatic damage. Severe hepatotoxicity can follow halothane anesthesia particularly after repeated exposure (avoid repeated exposure within at least 3 months)

## Isoflurane

- A volatile colorless liquid
- Not flammable
  
- Can cause bronchial irritation (cough, breath-holding, laryngospasm)
- Causes respiratory depression
- Causes peripheral vasodilation and lowers BP
- May precipitate myocardial ischemia in patients with coronary disease (steal phenomenon)
  
- No arrhythmias. Does not sensitize the heart to catecholamine, heart rhythm is stable.
- No hepatotoxicity (minimally metabolized (0.2%))
- Relaxes voluntary muscles

## Sevoflurane

- Less soluble than isoflurane in blood
- rapid acting, rapid recovery
- Very pleasant to breathe, non-irritant (good choice in children)
- No arrhythmias
- No hepatotoxicity (only 2.5% is metabolized)

## **Intravenous General Anesthetics**

### **Propofol**

- The most widely used i.v. anesthetic for induction and maintenance in adults and children
- Induction within 30 seconds, smooth and pleasant
- Recovery is rapid with less hangover effects than other i.v. anesthetics
- Causes pain on i.v. injection
- Nausea and vomiting are extremely low
- Causes a fall in blood pressure
- May cause significant involuntary muscle movements
- Causes a fall in blood pressure

### **Thiopental sodium (thiopentone sodium)**

- Very short acting barbiturate
- Rapid and smooth induction
- Rapid distribution: initial half life is 4 minutes, terminal  $t_{1/2}$  is 11 hours
- Significant accumulation in fat on repeated doses
- Nausea and vomiting slightly higher than propofol
- pH of thiopental solution is alkaline (pH=11) and extravasation causes considerable local damage
- Accidental intra-arterial damage causes arterial spasm
- Has no analgesic activity
- Sedative effect can persist for 24 h

### **Etomidate**

Rapid induction and recovery without hangover

Less hypotension than thiopental and propofol during induction, cardiovascular stable

Produces high incidence of involuntary muscle movement

Pain on injection

## **Ketamine**

Is a phencyclidine (a hallucinogen) derivative

Is an antagonist of the NMDA receptors producing a state known as dissociative anesthesia (is a state of profound analgesia and anterograde amnesia with minimal hypnosis during which the eyes remain open; the patient feels dissociated from his environment in a trance-like state. It is useful if modern equipments are lacking).

### **Advantages**

- Anesthesia persist for 15 minutes after a single i.v. injection, and characterized by profound analgesia.
- Also has good analgesic properties in sub-anesthetic doses
- In contrast to most other anesthetics, ketamine usually causes:**
- tachycardia, increased blood pressure and cardiac output (advantage in shocked patients)
- Pharyngeal and laryngeal reflexes are only slightly impaired
- It is a potent bronchodilator

### **Disadvantages**

- Hallucination with delirium and nightmares can occur during recovery , particularly in adults (the main disadvantage). This is reduced by giving a benzodiazepine
- No muscle relaxation; high incidence of involuntary muscle movements
- Causes increased intracranial pressure and intraocular pressure
- Has abuse potential and can cause dependence
- Relatively slow in onset (2-5 min)

### **Uses of ketamine**

It is particularly valuable for children requiring frequent anesthesia. Subanesthetic doses can be given to provide analgesia for painful procedure such as dressing of burns, radiotherapy, ...

### **Contraindications**

Moderate to severe hypertension, CHF and history of stroke

Cerebral trauma

Eye injury

Psychiatric disorders

In pregnancy before term; because it has oxytocic activity

Properties	Propofol	Thiopentone	Etomedate	Ketamine
Induction	Rapid onset	Rapid onset	Rapid onset	Slow onset (2-5 minutes)
Hangover effect	No	Yes (24-36 h)	No	No
Duration	Few minutes	5-10 minutes	3-5 minutes	30 minutes and more (2 h)
Skeletal muscles	Involuntary M. movement	No	Involuntary M. movement	Involuntary M. movement
Blood pressure	Fall	Fall	Fall	Rise +tachycardia
Nausea and vomiting	Extremely low	More than propofol	More than propofol	More than propofol
Analgesia	No	No	No	Profound analgesia
Others	Pain on injection. Used also for sedation & amnesia,	Pain, if extravasation occurs –local damage	Pain on injection, adrenal suppression	Bronchodilator, abuse potential