

GENERAL ANAESTHETICS

General Anesthetics

- General anaesthetics are CNS depressants which cause partial or complete loss of consciousness, sense or pain. The effect is reversible and generally used to produce unconsciousness during painful surgeries.
- General anaesthetics bring about descending depression of the central nervous system (CNS), starting with the cerebral cortex, the basal ganglia, the cerebellum, and finally the spinal cord.

Stages of General Anesthesia



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graph TD; A[Stages of General Anesthesia] --> B[Stage I (Stage of analgesia)]; A --> C[Stage II (Stage of delirium)]; A --> D[Stage III (Stage of surgical anesthesia)]; A --> E[Stage IV (Stage of medullary depression)];
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Stage I
(Stage of analgesia)

Stage II
(Stage of delirium)

Stage III
(Stage of surgical anesthesia)

Stage IV
(Stage of medullary depression)

Stage I (Stage of analgesia):

- ❖ This is the period from the beginning of anesthetic administration to the loss of consciousness. The patient progressively loses pain. This stage is also called stage of analgesia.

Stage II (Stage of delirium):

- ❖ This period extends from the loss of consciousness through a stage of irregular and specific breathing to the reestablishment of regular breathing. Respiration is normal and regular. The patient may laugh, vomit or struggle and for this reason it is called the stage of excitement.

Stage III (Stage of surgical anesthesia):

- ❖ In this stage excitement is lost and skeletal muscle relaxation is produced. Most types of surgeries are done in this stage.

Stage IV (Stage of medullary depression):

- ❖ Overdose of the anesthetic may bring the patient to this stage. Respiratory and circulatory failure occur in this stage.

An ideal characteristic of anesthetics-

1. It should be inert potent and non-inflammable.
2. It should be economical.
3. It should be compatible with adjuvant drugs used in anesthesia and should not show any interaction or adverse effect.
4. It should not produce nausea ,vomiting and severe hypotension.
5. It should be stable to heat, light and alkalies.
6. It should be non-irritating to mucous membrane and able to produce rapid loss of consciousness along with prompt recovery.
7. It should produce analgesia and muscle relaxation in addition to anesthesia.

Classification of General Anesthetics

Inhalation Anaesthetics

1. Halothane
2. Methoxyflurane
3. Enflurane
4. Sevoflurane
5. Isoflurane
6. Desflurane

Ultra short acting Barbiturates

1. Methohexital sodium
2. Thiomytal sodium
3. Thiopental sodium

Dissociative Anaesthetics

1. Ketamine hydrochloride

1. Inhalation Anaesthetics-

Volatile Inhalation general anesthetics: They are administered by inhalation and are further sub divided as

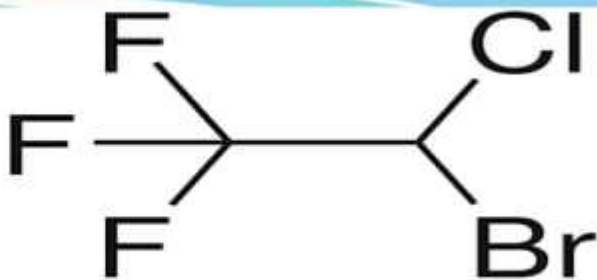
1. Gases: Cyclopropane: Ethyl chloride, Nitrous oxide
2. Liquids: Diethyl ether, Halothane, Chloroform Trichloroethylene

Non-Volatile or Intravenous anesthetics:

They are non-volatile at room temperature and are administered by I.V route.

1. Barbiturates: Thiopental sodium, Methohexital sodium.
2. Non-barbiturates: Propanidid, Propofol.

1. Halothane

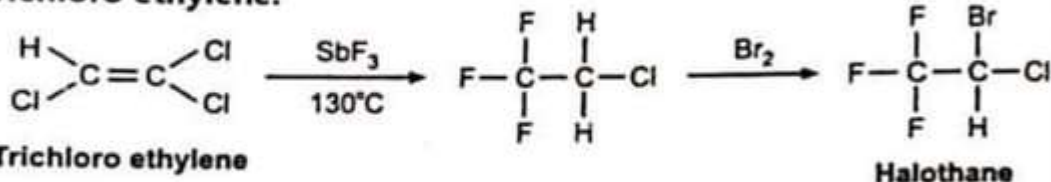


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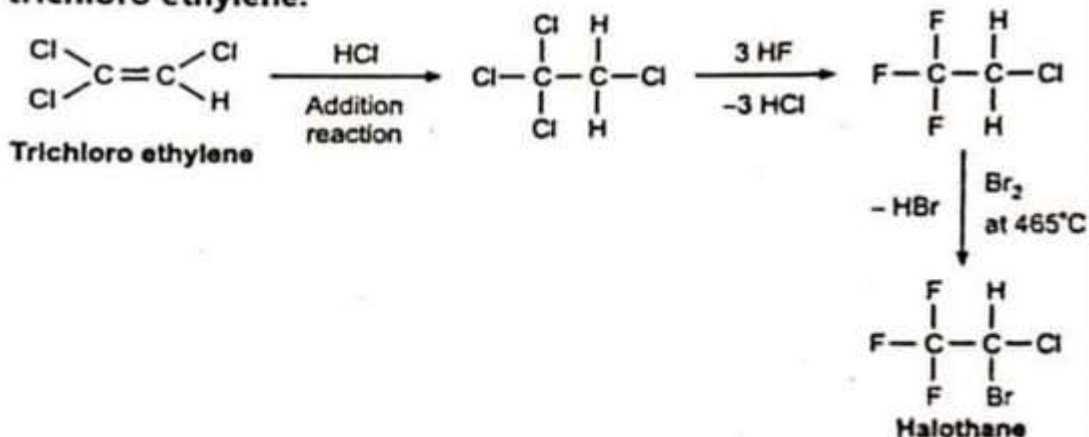
- ❖ Chemically it is 2-bromo,2-chloro,1,1,1-trifluoroethane.
- ❖ It is a clear, colorless, heavy, non-flammable liquid, slightly soluble in water, miscible with ethanol, and with trichloroethylene.
- ❖ Halothane lacks flammability thus safe to use and store.

Synthesis:

(a) From trichloro ethylene:



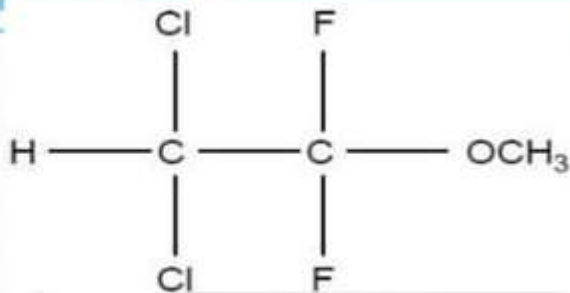
(b) From trichloro ethylene:



Uses :

- It may produce any depth of anaesthesia without causing hypoxia.
- Being a non-irritant, its inherent hypotensive effect retards capillary bleeding and renders a comparatively bloodless field.
- It is a potent, relatively safe general inhalation anaesthetic used in conjunction with N₂O.
- For skeletal muscle relaxation, it is used with succinyl choline or tubocurarine.
- **Storage:**
- It should be stored in well-closed airtight containers, protected from light, at a temperature not exceeding 25°C in a nonreactive metal container.

2. Methoxyflurane-



- ❖ Chemically Methoxyflurane is 2,2-dichloro-1,1-difluoro-1-methoxyethane.

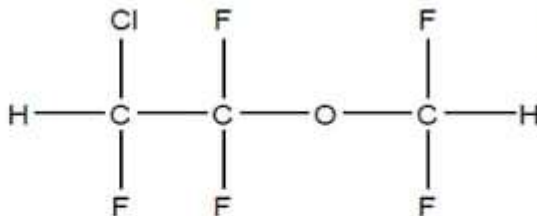
Properties:

- ❖ It is a clear, colorless liquid, non-inflammable and non-explosive in air or oxygen in anaesthetic concentrations.

Uses:

- ❖ It is employed to cause light anaesthesia with deep analgesic and muscle relaxation feature, which makes it convenient for surgical operations.

3. Enflurane-



Chemically, Enflurane is (2-chloro-1,1,2- tri-fluroethyl)(di-fluoromethyl) ether.

Properties:

- ❖ It is a clear, colourless, volatile liquid with pleasant hydrocarbon-like odour.
- ❖ Soluble in water, miscible with organic solvents, chemically it is extremely stable.

Uses:

- ❖ Enflurane used in the treatment of Sotus Aathmotics Ventricular premature complexes.

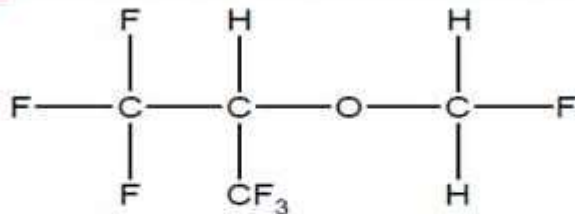
Uses:

- ❖ It is used for the induction and maintenance of general anaesthesia during surgery and cesarian section and during delivery.

Side Effects:

- ❖ Nausea, Vomiting, irritation of eyes, nose, throat, skin, Headache, Drowsiness, arrhythmias, respiratory depression and liver/kidney dysfunction.

4. Sevoflurane-



- ❖ Chemically sevoflurane is 1,1,1,3,3,3-hexafluoro-2-(fluoromethoxy)propane.

Properties:

- ❖ Low boiling liquid with a slight odour; miscible with most organic solvents including fats or oils; practically insoluble in water. It is a nonflammable, nonirritating agent.

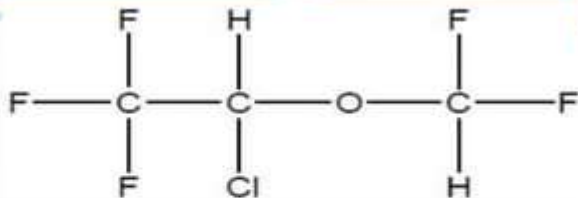
Uses:

- ❖ It is one of the most commonly used volatile anaesthetics.
- ❖ It is often used to put children on sleep for surgery by inhalation.

Side effects:

- ❖ Nausea, Vomiting, Hypotension, Agitation and cough.

5. Isoflurane-



- ❖ Chemically Isoflurane is (1-chloro-2,2,2-trifluoroethyl)(difluoro methyl) ether.

Properties:

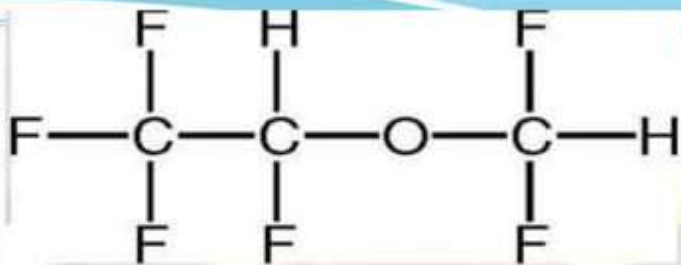
- ❖ It is a clear, colorless, heavy liquid, insoluble in water, miscible with ethanol, and trichloroethylene.
- ❖ It is not flammable in air or oxygen.

Uses:

- ❖ It is used for induction and maintenance of general anaesthesia.

Side-effects: Respiratory depression, lower B.P and irregular heart beat.

6. Desflurane-



- ❖ Chemically Desflurane is (1,2,2,2-tetrafluoroethyl difluoro methyl) ether.

Properties:

- ❖ It has a pungent odor, irritating and unpleasant to inhale .
- ❖ Low boiling liquid with a slight odour; miscible with most organic solvents including fats or oils; practically insoluble in water.
- ❖ It is a non-flammable, non-irritating agent.

Uses:

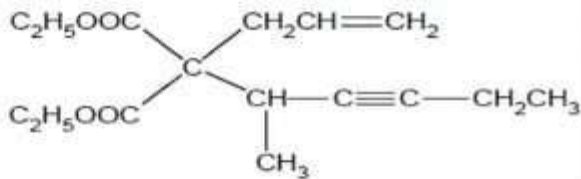
1. It is used to cause general anaesthesia by inhalation before or during the surgery in adults.
2. It has the most rapid onset and offset of all the volatile anaesthetic drugs used for general anaesthesia due to its solubility in blood.

Side Effects:

- Bluish lips or skin, Body ache, pain cough, running nose, blurred vision, dizziness, headache.

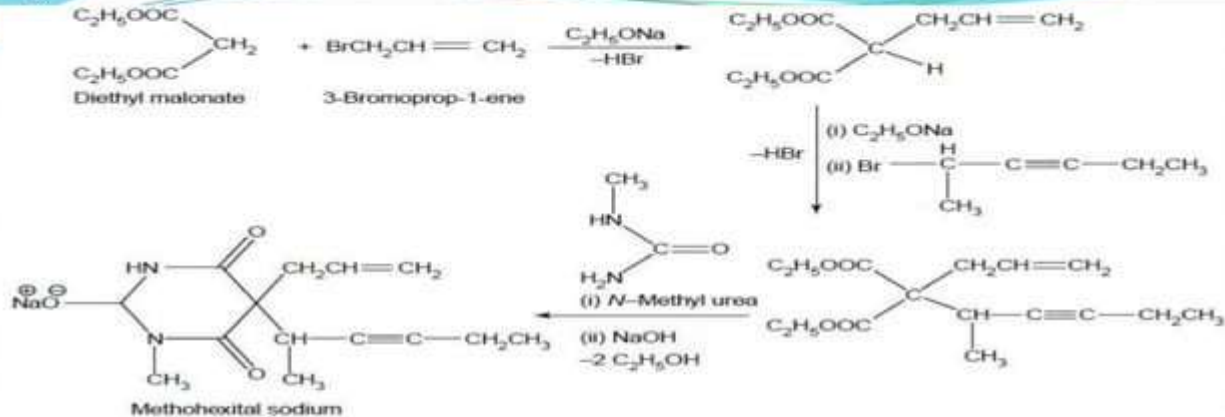
- ❖ **Ultra short acting Barbiturates** are non volatile at room temperature and are administered by intravenous route.
- ❖ These are used to produce rapid unconsciousness for surgical and basal anaesthesia
- ❖ These drugs induce anaesthesia during surgery which then maintained by inhalation anaesthetics.

1. Methohexital sodium*-



- ❖ Methohexital is also a derivative of barbituric acid.
- ❖ Chemically it is methohexital sodium -1-methyl-5-allyl-5-(1-methyl-2-pentynyl)

Synthesis-



- ❖ It is prepared by condensation of ethylcyanoacetate with 2-chloro-3-pentyne in presence of sodium ethylate yields ethyl-1-methyl-2-pentynyl cyanoacetate which on further condensation with allylbromide yields ethyl(1-methyl-2-pentynyl)allylcyanoacetate. Reaction with N-methyl urea yields the iminobarbituric acid which on acid catalyzed hydrolysis forms methohexital.

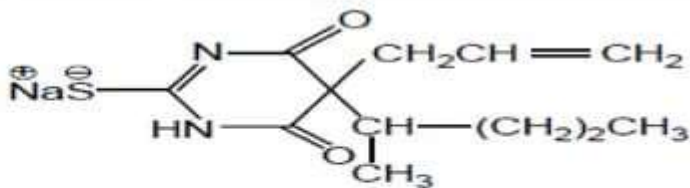
Properties-

- ❖ It is white to off-white hygroscopic powder, essentially odourless, and the solution is alkaline to litmus, soluble in water.

Uses-

- ❖ It is used as a general anaesthetics and hypnotic drug for oral surgery, in gynaecological procedures, genitourinary investigations and electro convulsive therapy.
- ❖ It is more potent than thiopentone sodium.

2. Thiamylal sodium-



- ❖ It chemically it is salt of 5-allyl -5 (1-methyl butyl)-2-thiobarbiturates.

Properties:

- ❖ Thiomytal is a highly hydrophobic thiobarbiturate having its structural features very much related to thiopental.
- ❖ Its biological activities are almost identical to thiopental.

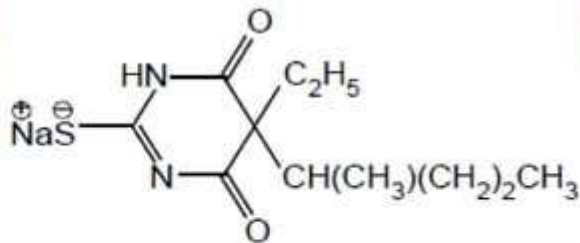
Uses:

- ❖ It is used as intravenous anaesthetic drug used to induce drowsiness or sleep or psychological excitement(anxiety).

Side Effects:

- ❖ Coughing, sneezing, slow breathing, slow heart rate, shivering, cardiac arrhythmia.

3. Thiopental sodium-



- ❖ Chemically it is Thiopental sodium is a [5-Ethyl-4,6-dioxo-5-(pentan-2-yl)-1,4,5,6-tetrahydropyrimidin-2-yl] sulfanide sodium.
- ❖ **Properties:** A yellowish-white powder, hygroscopic, freely soluble in water, and partly soluble in ethanol.
- ❖ These are usually administered intravenously for the production of complete anaesthesia of a short duration.
- ❖ It belongs to the category of ultra short-acting barbiturates.

- ❖ By rectal route it is administered as a solution, suspension, or suppositories as basal anaesthetic.

Uses:

- ❖ It is used in caesarean delivery and also used in maintaining anaesthesia during surgery.
- ❖ It is also used as a sedative, hypnotic and anticonvulsant.

Storage:

- ❖ It should be stored in well-closed airtight containers and protected from light.

Dosage forms: Thiopental injection B.P.

Side Effect:

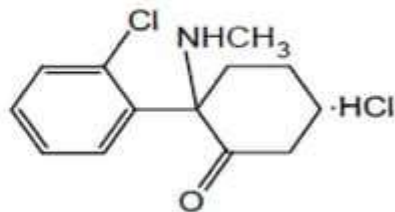
- ❖ Reduce cardiac output, Cause hypotension.

DISSOCIATIVE ANESTHETICS-

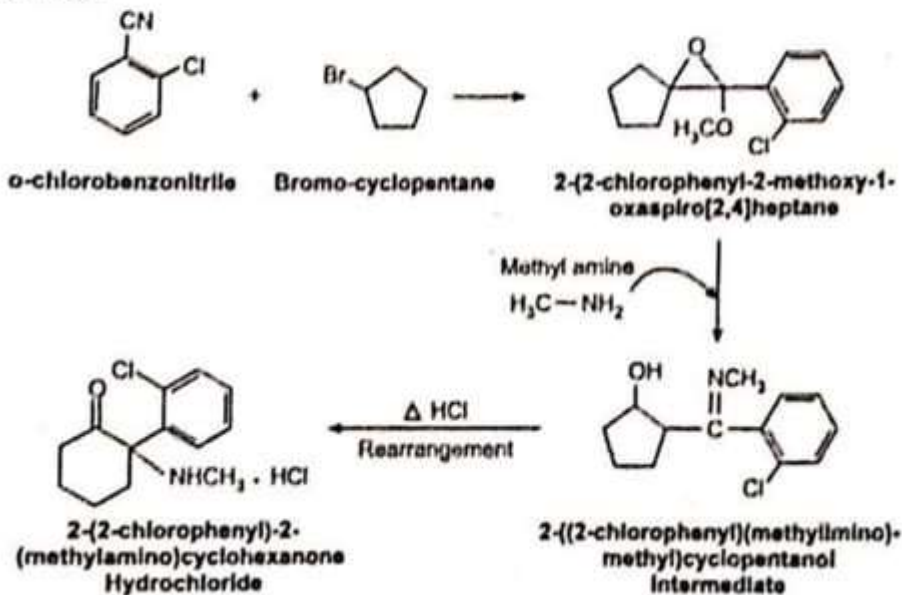
- ❖ Dissociative anesthesia is a state in which a patient feels dissociative completely from the surroundings dissociative anaesthesia is a class of hallucinogen, which distort perception of sight and sound and produce feelings of detachments- dissociation from the environment self.

Ketamine hydrochloride –

- ❖ Ketamine is a cyclohexanol derivative .Chemically ketamine is (+) 2 (o-chlorophenyl)-2-methylaminocyclohexanone.



Synthesis: Ketamine is prepared by Grignard reaction. In the presence of strong alkali, *o*-chlorobenzonitrile reacts with bromocyclopentane to give an epoxy compound which converts to an imine in the presence of methylamine. It then rearranges to give ketamine on heating with HCl.





Uses:

- ❖ It can be used as a general anaesthetic and analgesic. It causes the relaxation of skeletal muscles.

Side Effect:

- ❖ Include agitation, confusion or hallucinations, low blood pressure and muscle tremors, Spasms of the larynx may occur sometimes.