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**Lecture title: CNS Drugs**

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**Stages of general anesthesia**

**Stage-I (stage of voluntary excitement, stage of analgesia):**

It is characterized by struggling and ataxia without CNS depression.

**Stage-II (stage of involuntary excitement, stage of delirium):**

It begins with unconsciousness and loss of voluntary control.

**Stage-III (stage of surgery, stage of anesthesia):**

Characterized by unconsciousness, loss of neuromuscular reflexes, loss of pain sensation and muscle relaxation. All surgical operations can be performed at this stage.

This stage can be subdivided into 4 planes:

- a. Sleep
- b. Sensory loss
- c. Muscle paralysis
- d. Intercostal paralysis

The first two planes are called light surgical anesthesia and the last two are called deep surgical anesthesia.

**Stage-IV (medullary paralysis):**

Characterized by paralysis of the vital regulatory centers in the medulla like respiratory center and death may occur in this stage.



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**Notes:**

- Stage I and II are called the induction period.
- Some anesthetics bypass stage II into stage III which is the stage of surgery (e.g. Halothane, Methoxyflurane and Barbiturates).
- Other anesthetic agents induce all the stages of general anesthesia (e.g. Ether and Chloroform) while some anesthetics produce only stage I and II (e.g. Ketamine, N<sub>2</sub>O and Enflurane).

**Characteristic features of balanced anesthesia:**

1. Analgesia.
2. Muscle relaxation.
3. Hypnosis.
4. Hyporeflexia.

**Preanesthetics (Premedications)**

**Preanesthetics used with general anesthetics to produce balanced anesthesia:**

1. **Analgesics** like xylazine and morphine.
2. **Sedatives and hypnotics** like diazepam.
3. **Tranquilizers** like chlorpromazine.
4. **Muscle relaxants** like D-tubocurarine.
5. **Adrenergic blocking agents** like propranolol.



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6. **Cholinergic antagonists** like atropine because of:

- a. to reduce salivation.
- b. to reduce bronchial secretion.
- c. to prevent bradycardia.

### **A. Inhalational Anesthetics**

**1. Gaseous like N<sub>2</sub>O and Cyclopropane.**

**2. Volatile like Halothane, Methoxyflurane, Enflurane and Ether.**

Inhalational anesthetics are gases or vapors that diffuses readily across the pulmonary alveoli and then to the brain to produce anesthesia.

The transfer of inhalational anesthetics depends on the partial pressure of anesthetics and its solubility in the blood.

Lipid solubility is important for induction of anesthesia and recovery from it. High lipid solubility means long induction and long recovery periods of anesthesia (e.g. Ether) while low lipid solubility means rapid induction and fast recovery (e.g. Halothane).

#### **General mechanisms of action of inhalational anesthetics:**

- 1. Interaction with lipid molecules of the cell membrane.
- 2. Interaction with proteins of the neuronal membrane.
- 3. Interaction with water molecules of the cell membranes.

All general anesthetics causes stabilization of the cell membrane.



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### **Minimal Alveolar Concentration (MAC):**

It is the minimal concentration of the anesthetics at the alveolar level which is required to produce anesthesia in 50 % of the animals.

### **Halothane**

It is nonirritant, nonflammable, non-explosive and potent. It depresses all the functions of the brain. It bypass stage II. It has rapid induction and fast recovery because it is low lipid soluble.

### **Side effects of Halothane:**

1. Respiratory depression.
2. Depresses cardiac function.
3. Sensitizes the heart to catecholamines.
4. Decreases calcium ion binding to cardiac muscle and causes bradycardia.

### **Contraindication:**

Uses of epinephrine and norepinephrine are contraindicated in case of halothane anesthesia.

### **Advantages:**

1. It is potent and has rapid induction and rapid recovery from anesthesia.
2. It produces good muscle relaxation.



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**Disadvantages:**

1. Cardio-pulmonary depression.
2. Expensive.
3. Contraindicated in cardiac diseases.

**Methoxyflurane**

It is more potent than halothane, it has long induction and long recovery periods. During recovery, there is some CNS excitation because of high lipid solubility so that, preanesthetics are needed.

**Side effects:**

1. Decreases heart rate and blood pressure.
2. Sensitizes the heart to catecholamines.

**Advantages:**

Potent with good muscle relaxation and analgesia.

**Disadvantages:**

1. High lipid soluble with long induction and long recovery periods.
2. It is contraindicated in liver and kidney diseases.



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### **Nitrous oxide (N<sub>2</sub>O)**

It is colorless, odorless, nonirritant and nonflammable. It is usually given as 80% N<sub>2</sub>O and 20% O<sub>2</sub>. It produces stage I and II anesthesia. It produces good analgesia, muscle relaxant is needed and O<sub>2</sub> is given to prevent hypoxia. It is characterized by low lipid solubility so that, the induction and recovery from anesthesia is fast. It is used with other anesthetic because it has low potency.

### **Enflurane**

It is potent anesthetics and structural analogue to Methoxyflurane. It is also sensitizes the heart to catecholamines. It produces good muscle relaxation and may cause CNS excitations.

### **Ether**

It is flammable, highly explosive and used in laboratory animals. It causes respiratory irritation and produces all stages of anesthesia.

### **Chloroform**

It is used in laboratory animals but causes liver toxicity so that, not used in other animal species.