Chapter
4

Drugs Acting on Central Nervous System

- General anaesthetics
- Anticonvulsant drugs (antiepileptic drugs)
- Antidepressants/psychoanaleptics
- Nootropic agents
- Opioid analgesics
- Hypnotics and sedatives
- Antianxiety drugs/anxiolytics
- Antipsychotics
- Centrally acting muscle relaxants

A. GENERAL ANAESTHETICS

Q 1. What is anaesthesia? Explain various stages/mode of action/ mechanism of action of anaesthesia.

Anaesthesia

Anaesthesia is a state of controlled, temporary loss of sensation or awareness that is induced for medical purposes.

Stages of Anaesthesia (Mode/Mechanism of Anaesthesia)

a. Stage of Analgesia

This stage starts from beginning of inhalation of anaesthetic agent up to loss of consciousness. It involves sensation of falling, remoteness and feeling of warmth is observed in some patients. Analgesia is produced before consciousness is lost.

b. Stage of Delirium

This stage starts with loss of consciousness to beginning of surgical anaesthesia. This stage involves marked excitement, shouting, laughing, increased muscular activity, vomiting, pupils may dilate and patient shows development of marked hypertension and tachycardia.

c. Stage of Surgical Anaesthesia

As the more drug gets in, deep breathing starts and patient passes into the third stage. This gives gradual loss of reflexes, regular respiration and relaxation of skeletal muscle.

This stage is divided into four different planes:

Plane 1: The pupils are normal and eyeballs are roving. The pupils dilate and attain normal size. The respiration is full and regular. BP and pulse rate is normal.

Plane 2: Eyeballs are fixed and amplitude of respiration is diminished. Adequate muscular relaxation.

Plane 3: The BP begins to fall. Intercostal muscles are paralysed slowly. The pupillary light reflex is lost. Muscles relax completely.

Plane 4: Intercostal muscles completely paralysed. The pupils are further dilated. BP is low. All secretions are completely abolished.

d. Stage of Respiratory Paralysis

This stage is characterised by severe depression of vital medullary centres, initially the diaphragmic contractions are irregular. Respiratory arrest also leads to vasomotor collapse.

Four Planes of Surgical Anaesthesia

	Respiration	*Blood pressure*	*Reflex activity*	*Muscle relaxation*	*Pupils*
Plane 1	Full deep, thoracoabdominal decreased rate of respiration	Heart rate normal, blood pressure decreases	Loss of pharyngeal reflexes	Incomplete	Normal, roving eyeballs
Plane 2	Further decreased rate of respiration. Low amplitude of respiration	Heart rate normal, blood pressure further decreased	Laryngeal reflexes lost. Loss of skin incision reflex	Adequate	Fixed eyeballs. Eyelid reflex lost
Plane 3	Decreased rate of respiration. Respiration only abdominal	Hypotension	-do-	Complete	Dilated
Plane 4	Paralysis of respiration	Severe hypotension	-do-	Complete	More dilated

Q 2. Define and classify general anaesthetics giving examples.

General Anaesthetics

The drugs which produce a total or partial loss of the pain sensation along with loss of consciousness are called general anaesthetics.

Classification

1. Inhalation general anaesthetics
   a. **Volatile liquids:** For example, diethyl ether, chloroform, halothane, trichloroethylene, methoxy flurane, ethylchloride.
   b. **Gases:** For example, cyclopropane, nitrous oxide, ethylene.
2. Intravenous anaesthetics
   a. **Ultra short-acting barbiturates:** For example, thiopentone, methohexitone.
   b. **Nonbarbiturates:** For example, propandid, ketamine, althesin, etomidate.

Q 3. Write a note on 'volatile general anaesthetics'/inhalation anaesthetics.

Volatile General Anaesthetics

These are available in two forms.

a. **Liquids:** For example, diethyl ether, chloroform, halothane, methoxyflurane, ethylchloride, trichloroethylene.
b. **Gases:** Nitrous oxide, ethylene, cyclopropane.

1. Diethyl Ether (Anaesthetic Ether)

- Anaesthetic ether contains 96–98% diethyl ether.
- Ether is a colourless liquid of very volatile nature.
- Ether has characteristic odour, sweet burning taste.
- The concentration of 10–15% in inspired air is sufficient.

Pharmacological Action

- Only a minor portion of ether is oxidised in the body and is eliminated through the lungs.
- Ether irritates the respiratory tract and enhances the mucosal secretions.
- Ether is known to increase heart rate, blood pressure and blood sugar.
- Ether also causes peripheral vasodilation.
- Ether depresses myocardial contractility.

Adverse Effects

- Nausea, vomiting during recovery of anaesthesia.
- Very irritant and explosive anaesthetic.
- Children show a tendency to ether convulsions.

Contraindications

- Severe liver disease
- Impaired kidney function
- Diabetes mellitus

Therapeutic uses

- Safe general anaesthetic
- Used in pediatric anaesthesia
- Excellent analgesic
- Can be employed to reduce labour pains.

Dose: For induction of anaesthesia up to 15% in inspired air.

Advantages

1. It is a safe anaesthetic, can be used by unexperienced anaesthetist.
2. Preanaesthetic medication is not required.
3. It is an excellent analgesic.
4. Ether produces satisfactory muscular relaxation.

5. Ether does not modify blood pressure during anaesthetic stages.
6. Ether can be employed during delivery to reduce labour pains.
7. Ether can be administered without a complicated apparatus.
8. Ether anaesthesia is economical.

Disadvantages

1. Induction of anaesthesia is slow and is sometimes associated with marked excitement.
2. Irritant nature of the ether vapour may increase the salivary and bronchial secretions and induce cough and laryngeal spasms during induction of ether.
3. The heart rate is usually increases during ether anaesthesia.
4. Nausea and vomiting appear during recovery from ether anaesthesia.
5. The motility of GIT is reduced by ether and secretions are also depressed.

2. Chloroform

- It is a clear, volatile liquid of boiling point 61°C.
- It has a sweet, appreciable smell.
- In the presence of flame, it also decomposes to form phosgene.
- It is quickly absorbed and complete eliminated through lungs.

Pharmacological Actions

- It is a highly potent anaesthetic agent.
- It can produce all the stages of anaesthesia without causing hypoxia.
- Surgical anaesthesia can be achieved within 2 to 3 minutes.
- Chloroform produces arterial hypotension without much affecting the heart rate.
- Cardiac arrest may occur suddenly during chloroform administration.
- Chloroform gives a cooling sensation when dropped on the skin.
- Chloroform sometimes used as a rubefacient.

Adverse Effects

- Cirrhosis of liver
- Delayed chloroform poisoning
- Postanaesthetic toxemia
- Hypotension
- Cardiac arrest
- Arrhythmia
- Ventricular fibrillation and respiratory arrest
- Paralytic ileus.

Therapeutic uses

1. Chloroform is a powerful anaesthetic agent.
2. Chloroform is employed as counter-irritant and rubefacient.

3. Dilute solutions of chloroform administered internally as carminative, stomachic and flavouring agents.
4. Chloroform is used as a vehicle for extraction of organic drugs.

Advantages

1. It is a highly potent anaesthetic agent.
2. In very low concentration it acts as an analgesic.
3. Surgical anaesthesia can be achieved within 2–3 minutes.

Disadvantages

Chloroform is not a safe anaesthetic agent due to following toxic effects:

1. Chloroform depresses the respiratory centre.
2. It may produce arterial hypotension.
3. It may cause cardiotoxicity, hepatotoxicity and cirrhosis of liver.
4. It also precipitates "delayed chloroform poisoning" and "postanaesthetic toxemia".
5. It also produces cardiac arrest and arrhythmia.

3. Halothane (Fluothane)

- Halothane is a colourless, odourless, heavy fluid.
- It is a stable, volatile, non-inflammable and non-explosive liquid.
- 2–4% concentration is sufficient to induce anaesthesia.
- It is supplied in amber coloured bottles.

Pharmacological Actions

- A concentration of 3% is frequently used for quick induction of anaesthesia.
- All anaesthetic concentration depresses the respiration.
- Halothane inhibits salivation, laryngospasm and coughing as well.
- Halothane produces bronchodilation hence is an anaesthetic of choice in patients with the history of bronchial asthma.

Adverse Effects

- Several cardiac abnormalities.
- Hepatic damage (liver damage).

Therapeutic uses

It is used for induction and maintenance of anaesthesia.

Contraindication

- Family history of malignant hyperthermia and porphyria.

Dosage

- For adults : 2–4% concentration of halothane.
- For children : 1.5–2% concentration of halothane.

Brand name: Fluothane.

Advantages

- Induction of anaesthesia is very smooth as it has a sweet fruity odour.
- Recovery is also fast, smooth with low incidences of nausea and vomiting.
- It does not cause irritation of respiratory passage.
- It inhibits salivary secretions.
- It does not produce bronchospasm and laryngospasm hence useful in patients with bronchial asthma.

Disadvantages

- Muscular relaxation is inadequate.
- It causes respiratory, cardiovascular depression.
- Mental recovery is delayed.
- Shivering during recovery is very common.
- It is a poor analgesic.
- It is expensive, needs special apparatus for administration.

4. Nitrous Oxide (Laughing Gas)

- Nitrous oxide is a colourless gas with a slightly sweet odour.
- The gas is non-explosive and non-inflammable.
- Nitrous oxide is marketed in liquid form under 50 atmospheric pressure in royal blue steel cylinders.

Pharmacological Actions

- A mixture of nitrous oxide gas with oxygen containing 80% of it, causes unconsciousness and analgesia.
- For achieving full surgical anaesthesia with the gas, a higher concentration (up to 80%) is necessary which will cause anoxia with cerebral damage, if the inhalation continues for more than 2–3 minutes.

Adverse Effects

- Hypoxia
- Cardiac irregularities.

Therapeutic uses

1. As general anaesthetic
2. It is also employed for extraction of tooth, obstetrical analgesia and for certain painful procedures.

Dosage

For analgesia, 50% nitrous oxide mixed with 50% oxygen.

Advantages

- It is non-inflammable and non-irritant.
- It produces rapid induction and recovery.
- It has a good analgesic effect and hence can be used in dental practice.
- It is a safest anaesthetic agent.
- Incidences of nausea and vomiting are rare.

Disadvantages

- Preanaesthetic medication is required.
- Excitement may be violent.
- Special apparatus is required for administration.

5. Cyclopropane

- Cyclopropane is a very heavy colourless gas with a characteristic ether-like odour.
- Cyclopropane is marketed as a liquid, under pressure in orange coloured cylinders.
- Cyclopropane is an inflammable and explosive liquid.

Pharmacological Actions

- The quick induction of cyclopropane anaesthesia allows for a smooth and simple anaesthesia.
- Cyclopropane is a highly effective anaesthetic.
- The anaesthetic dose is sufficient to provide adequate muscular relaxation.
- The process of recovery from anaesthesia is quick.

Adverse Effects

- Cardiac abnormalities
- Cardiac arrhythmia
- Delirium
- Post-anaesthetic hypotension
- Headache.

Therapeutic uses

1. Cyclopropane is a highly effective anaesthetic.
2. It is a drug of choice for anaesthesia in cases of thoracic and abdominal operation.

Dosage

Cyclopropane IP : 30–35% concentration

Q 4. Write a note on 'intravenous anaesthetics'/'non-volatile anaesthetics'.

Intravenous/Non-volatile Anaesthetics

These are given by intravenous route for quick induction of anaesthesia for specific duration, e.g. thiopental sodium, methohexital, propandid, ketamine, althesin, etomidate.

Advantages

- Easy to administer.
- Indication is rapid and smooth.
- Post-anaesthetic complications are rare.
- Recovery is very fast.
- Respiratory and myocardial functions remain unaffected.
- No irritation of respiratory passage.

Disadvantages

- Usual stages of anaesthesia are not clear.
- Coughing, apnea is common during induction.
- Muscular relaxation is poor.
- Injection around nerve may produce palsy.

Thiopentone

- Thiopentone is a barbiturate with very high lipid solubility.
- Thiopentone sodium is a sodium salt of pentobarbitone which can be used as anaesthetic agent.

Pharmacological Actions

- Thiopentone sodium is given intravenously, usually to induce anaesthesia.
- Thiopentone is administered as 2.5–5% solution.
- When given intravenously, it is rapidly distributed and acts quickly on the brain and the effect of an initial dose of 25 mg lasts for about 15 minutes.
- Hence, it is an ultra short-acting. It is a poor analgesic.

Adverse Effects

- Respiratory depression
- Laryngospasm and bronchospasm.
- Coughing

Therapeutic uses

1. Intravenously used for induction of anaesthesia.
2. Used as a basal anaesthetic.
3. As anticonvulsant
4. As an anaesthetic in patients with history of malignant hyperthermia.

Contraindications

- Cardiovascular disease
- Dysponea
- Porphyria.

Dosage

Thiopental sodium 0.5–1 gm powder. It is used as a freshly prepared, 2.5% solution for intravenous anaesthesia, as basal anaesthesia.

Preparations and Doses of Intravenous Anaesthetics

1. Thiopentone sodium	2.5% solution	(Intraval)
2. Methohexitone	1% solution	(Brevital)
3. Propandid	4 mg/kg	
4. Ketamine	1.2 mg/kg	(Ketalar)

Q 5. Give the properties of an ideal anaesthetic agent. OR Give the requirements/ideal characteristics of an ideal general anaesthetic agent.

An ideal general anaesthetic agent should possess following properties:

a. For Patient

i. Anaesthetic agent should be pleasant to inhale without any irritation.
ii. The induction of anaesthesia should be pleasant and fast.
iii. The recovery of anaesthesia should be smooth and rapid.
iv. It should not produce any toxicity.
v. It should be non-irritant.

b. For Surgeon

i. The anaesthetic agent should produce good analgesia and adequate muscular relaxation.
ii. The capillary bleeding should be negligible.
iii. It should be nonexplosive and non-inflammable.

c. For Anaesthetist

i. It should be stable at room temperature.
ii. It should be easily controllable with a wide margin of safety.
iii. It should not cause respiratory or circulatory collapse or depression.
iv. It should be easily eliminated from the body.
v. It should not attack the materials used for anaesthesia such as rubber tubing or metal.

d. For Manufacturer

i. The cost of anaesthetic agent should be cheap.
ii. It should have no storage problem.

Q 6. What is preanaesthetic medication? Name the drugs commonly used for preanaesthetic medication.

The use of drugs before administration of anaesthetic agent to make anaesthesia safer and more aggreable to the patient is called preanaesthetic medication.

Reasons for Preanaesthetic Medication

1. To reduce anxiety, tension and nervousness.
2. To obtain synergistic effect.
3. To reduce preoperative and postoperative pains.
4. To suppress salivary and respiratory secretions.
5. To counteract adverse effects of anaesthetic agent.

Drugs Commonly used for Preanaesthetic Medication

1. **Narcotic analgesics:** These are given due to their sedative and analgesic properties, e.g. morphine 15 mg by IM.
2. **Barbiturates:** Drugs like pentobarbitone and secobarbitone are used to provide sedation and to relieve apprehension.
3. **Tranquillizers:** These agents produce calming effect and are safe muscle relaxants. They have less respiratory depression, e.g. diazepam 5–10 mg orally.
4. **Anticholinergics:** Anticholinergics such as atropine are used to reduce excessive salivary and respiratory secretions.
5. **Antiemetics:** These are used to prevent preoperative and postoperative vomiting, e.g. metoclopramide.

Q 7. What do you mean by 'basal anaesthesia'/'basal anaesthetics'? Mention the drugs used to produce based anaesthesia.

- **Basal anaesthesia:** A state of anaesthesia short of surgical anaesthesia is called basal anaesthesia.
- **Basal anaesthetics:** The drugs which are used to produce basal anaesthesia are called basal anaesthetics.
- **Uses of basal anaesthesia:** In case of extremely nervous patients and in case of hyperthyroid patients, it is always better to bring the patient in operation theatre in a state of 'basal anaesthesia'.
- The drugs used to produce basal anaesthesia are:
  1. **Thiopentone sodium:** The 2% salt is generally administered intravenously until the patient becomes unconscious.
  2. **Tribromoethanol:** It is administered as a retention enemia.
  3. **Paraldehyde:** It is also administered as a retention enemia.

Q 8. Differentiate between ether and chloroform.

Ether	*Chloroform*
1. It is a safe anaesthetic agent	1. It is not a safe anaesthetic agent
2. 10–15% concentration of ether is sufficient to produce anaesthesia.	2. 1% concentration is sufficient
3. Ether can be used during delivery to reduce labour pains	3. It is not used during labour pains due to its high toxicity
4. Ether is colourless volatile liquid, with pungent odour	4. Chloroform is a clear volatile liquid having sweet smell
5. Ether, when exposed to air, forms ether peroxides or presence of flame and forms acetic aldehydes	5. Chloroform decomposes in the phosgene gas which is toxic

Q 9. Differentiate between general anaesthetics and local anaesthetics.

General anaesthetics	*Local anaesthetics*
1. General anaesthetics are the agents which bring about loss of all modalities of sensation, particularly pain, along with a reversible loss of consciousness	1. It may be defined as any substance applied topically or by localized injection or infiltration to dull or block pain sensation
2. General anaesthesia is induced either by inhalation of valatile and gaseous anaesthetics like diethyl ether, halothane or parenteral administration of intravenous anaesthetics like thiopentone	2. Local anaesthesia is induced by topical application of drug to skin or mucous membrane or by injection into area subjected to surgical operation or injection into dural membrane of spinal cord
3. General anaesthesia is carried out before carrying out surgical operation or in obstetrics	3. Local anaesthesia is produced in short surgical operations and in dentistry
4. Care of vital organs is essential	4. Care of vital organs is not essential
5. In this case consciousness is lost	5. In this case effect is a limited area of the body
6. In this case site of action is on CNS	6. In this case site of action is on peripheral nerves
7. Examples: Ether, halothane, cyclopropane	7. Examples: Lignocaine, procaine, orthocaine

QUESTIONS: GIVE THE REASONS

Q 1. Why is chloroform not safe/good general anaesthetic agent? OR Why is chloroform not used as general anaesthetic in clinical practice?

Because:

i. Chloroform may produce toxic effects on heart, liver and kidney.
ii. It produces hepatotoxicity, cardiotoxicity, cirrhosis of liver.
iii. It also precipitates ‘delayed chloroform poisoning’ and ‘postanaesthetic toxemia’.
iv. It also produces hypotension, cardiac arrest and arrhythmia.

Hence, because of its less margin of safety, it is not used in clinical practice.

Q 2. Why is ether a safe anaesthetic agent?

Because:

i. Ether produces smooth effects during induction of anaesthesia.
ii. Ether has sweet, fruity odour.
iii. Recovery of anaesthesia is fast, smooth.
iv. Possibility of nausea, vomiting is less.
v. It does not produce bronchospasm and laryngospasm.
vi. It is also used to reduce labour pains.

Hence, ether is a safe anaesthetic.

Q 3. Why are halothane and cyclopropane costly anaesthetics?

Because:

i. Halothane and cyclopropane are poor analgesics and poor muscle relaxants. Hence, require preanaesthetic medication which adds to the cost of therapy.
ii. Administration of halothane and cyclopropane needs special apparatus.

Hence, halothane and cyclopropane are costly anaesthetics, i.e. expensive.

Q 4. Why is ether stored in amber coloured bottles?

Because:

i. Ether is a colourless volatile liquid with pungent odour.
ii. Ether when exposed to air or moisture or light, may form ether peroxides which are very irritant.
iii. To avoid this ether is marketed in amber coloured bottles covered with black paper.

Q 5. Why is atropine (anticholinergic) used in preanaesthetic medication?

Because:

i. Some volatile anaesthetics may cause nasal irritation and increase nasal and salivary secretions which interfere with anaesthesia.
ii. Atropine is antisecretory agent thus it blocks all secretions which interefere with anaesthesia.

Q 6. Why is atropine used with ether when ether is used as a general anaesthetic?/Combination of atropine and ether is used for general anaesthesia. Why?

Because:

i. Ether vapours are irritant, which irritate respiratory, lacrimal, salivary secretions.

ii. These secretions interefere with normal respiration as well as with anaesthetic process.
iii. Atropine is an antisecretory agent, it blocks all secretions and increases anaesthetic process.

Q 7. Why is nitrous oxide called 'laughing gas'?

Because nitrous oxide when administered along with air, produces a stage of excitement, delirium and also produces amnesia. It shows laughing expressions. Hence, called laughing gas.

Q 8. Why prolonged surgery cannot be undertaken with nitrous oxide alone?

The two main disadvantages which limit the use of nitrous oxide as anaesthetic agent are:

i. Low anaesthetic potency
ii. It produces hypoxia

At the maximum safe concentration of 85%, it cannot achieve surgical stage of anaesthesia. But since it possess many good properties such as non-explosive, non-irritant, pleasant smell, marked analgesia and rapid induction, which make it a valuable basal anaesthetic to be supplemented by other more potent agents.

Objective Questions with Answers in Bold Letters

1. **Crawford Long (1842) and Morton (1846)** achieved the first satisfactory result for a general anaesthetic.
2. Cyclopropane is a **gaseous** anaesthetic.
3. Postanaesthetic toxemia is an adverse effect of **chloroform**.
4. **Nitrous oxide** is known as laughing gas.
5. Cyclopropane is stored in **orange coloured cylinders** under pressure.
6. Thiopentone sodium is used to produce **basal anaesthesia**.
7. Etomidate, althesin, ketamine, propofol are **intravenous anaesthetics**.
8. **Thiopentone** is a barbiturate with very high lipid solubility.
9. The drugs used prior to anaesthetic agent are called **preanaesthetic medications**.
10. General anaesthetics are administered by **inhalation or intravenous routes**.
11. Halothane, nitrous oxide, enflurane, ether are **inhalation anaesthetics**.
12. A state of anaesthesia short of surgical anaesthesia is called **basal anaesthesia**.
13. Paraldehyde is administered as **retention enemia**.
14. Hepatotoxicity and cardiotoxicity are the major adverse effects of **chloroform**.
15. Ether is stored in **amber coloured** bottles.
16. **Anticholinergic (atropine)** is used in preanaesthetic medication.
17. **Atropine** is antisecretory agent.

B. HYPNOTICS AND SEDATIVES

Q 1. Define and classify hypnotics and sedatives giving suitable examples.

- **Hypnotics:** The drugs which induce a sleep resembling a natural sleep are called hypnotics.
- **Sedatives:** The drugs which produce calming effects without inducing sleep or the drugs which reduce excitement are called sedatives.
- **Insomnia:** Insomnia means lack of sleep or inability to sleep.

Classification of Hypnotics and Sedatives

1. Barbiturates

These are classified as follows:

a. **Long-acting barbiturates:** Duration of action is eight hours or more, e.g. barbitone, phenobarbitone.
b. **Intermediate-acting barbiturates:** Duration of action is four hours, e.g. amylbarbitone, cyclobarbitone.
c. **Short-acting barbiturates:** Duration of action is less than four hours, e.g. hexobarbitone, secobarbitone.
d. **Ultra short-acting barbiturates:** Duration of action is less than one hour, e.g. thiopentone, methohexitone.

2. Non-barbiturates

These include:

a. **Benzodiazepines**, e.g. diazepam, nitrazepam, oxazepam.
b. **Alcohol**, e.g. chloral hydrate, ethanol.
c. **Aldehyde**, e.g. paraldehyde.
d. **Acetylated carbinols**, e.g. ethionamate.
e. **Inorganic ions**, e.g. bromides.
f. **Miscellaneous**, e.g. meprobamate, antihistaminics with sedative action, hyoscine.

Q 2. Write a note on 'barbiturates'. OR Give pharmacological actions, adverse effects, therapeutic uses, brand names of barbiturates/ phenobarbitone.

Barbiturates

Barbiturates are the derivatives of barbituric acid. The hypnotic activity of barbituric acid is due to replacement of hydrogen atoms attached to carbon atom at position 5 by alkyl or aryl radical.

Barbiturates are classified according to duration of action:

a. Long-acting barbiturates (action is for 8 hours or more), e.g. phenobarbitone.

b. Intermediate-acting barbiturates (action is for 4–8 hours), e.g. amylbarbitone, butobarbitone, pentobarbitone.
c. Short-acting barbiturates (action is less than 4 hours), e.g. secobarbitone, hexobarbitone.
d. Ultra short-acting barbiturates (IV), e.g. thiopentone sodium, methohexitone, kemithal.

Mechanism of Action

- Barbiturates also facilitate the actions of GABA at multiple sites in the CNS.
- Barbiturates increase the duration of the GABA-grated chloride channel openings.
- At high concentrations, the barbiturates may also be GABA mimetic, directly activating chloride channels.

Pharmacological Actions

I. Effect on CNS

Barbiturates produce depression of CNS.

i. **Sedation and hypnosis:** The long-acting and intermediate-acting barbiturates are used for sedation and hypnosis.
ii. **Anaesthetic effect:** Ultra short-acting barbiturates, when administered intravenously, produce basal or general anaesthesia. For example, thiopentone.
iii. **Anticonvulsant effect:** Phenobarbitone is a selective anticonvulsant drug and is used for prevention of grand mal epilepsy.
iv. **Analgesic effect:** Barbiturates increase the analgesic effect of salicylates and p-aminophenol derivatives.
v. **Respiration:** Higher doses of barbiturates depress the respiratory centre in medulla oblongata and may lead to respiratory collapse.

II. Effect on CVS

Therapeutic doses of barbiturates may cause a slight fall in BP and decrease the heart rate.

Toxic doses of barbiturates produce sustained hypotension.

III. Effect on GIT

Larger doses of barbiturates retard the peristalsis.

IV. Effect on Kidney

Barbiturates cause decrease in glomerular filtration and hence urine output decreases.

Adverse Effects

1. Intolerance—includes excitement, vomiting, headache, diarrhoea.

2. Megaloblastic anaemia
3. If administered to pregnant women, may depress the foetal respiration.
4. Tolerance
5. Drug dependence
6. Hangover
7. Habituation.

Indications/Therapeutic uses

1. Used as hypnotics to relieve insomnia
2. Used as an anticonvulsant
3. Used as a preanaesthetic medication
4. Used as a general anaesthetics, e.g. thiopentone
5. The psychiatric uses, e.g. pentobarbitone, thiopentone
6. Cause sedation in case of anxiety.

Preparations and Doses

Phenobarbitone tablet IP

Sedative dose: 15–30 mg daily
Hypnotic dose: 100–200 mg daily

Trade Names

Gardenal, Luminal, Garoin.

Contraindications

- Liver disease
- Dyspnoea
- Impaired renal function
- Respiratory distress.

Q 3. Give the signs and symptoms and treatments of 'acute barbiturate poisoning'. OR Write a note on 'acute barbiturate poisoning'.

Acute Barbiturate Poisoning

Acute barbiturate poisoning is caused due to ingestion of an overdose either accidently or with suicidal intention.

Signs and Symptoms

The patient of barbiturate poisoning shows:

i. Weak and rapid pulse
ii. Cold clammy skin
iii. Slow or rapid shallow breathing
iv. Constriction of pupils
v. Paralytic dilation develops initially
vi. Respiratory depression
vii. Peripheral vascular collapse
viii. Urinary retention.

Treatments

1. Gastric lavage
2. Endotracheal intubation
3. Alkalinization of urine
4. IV administration of fluids
5. Use of prophylactic antibiotics
6. Dialysis
7. Forced diuresis

1. Gastric Lavage

If the patient is conscious then gastric lavage is carried out by using syrup of ipecac or salt solution.

If the patient is unconscious then gastric aspiration is carried out by inserting tube into the stomach.

2. Endotracheal Intubation

It is performed when respiration is inadequate and also to remove secretions from respiratory tract.

Adequate ventilation is of great importance in barbiturate poisoning.

3. Forced Diuresis

In this step, diuretics such as frusemide and mannitol are used in barbiturate poisoning to increase the flow and excretion of urine. This may lead to increase in excretion of barbiturates. Forced diuresis is most useful in poisoning due to phenobarbitone, barbitone, etc.

4. Alkalinization of Urine

Alkalinization of urine prevents tubular reabsorption of barbiturates by ionization of filtered barbiturates. This increases the excretion of barbiturates.

Sodium bicarbonate is used for alkalinization of urine.

5. Intravenous Administration of Fluid

Intravenous fluids are given in sufficient quantity to prevent dehydration. They are also useful for the maintenance of blood volume.

6. Use of Prophylactic Antibiotics

The antibiotics are used only when there is a possibility of infection due to catheterization of urinary bladder, etc.

7. Dialysis

Elimination of barbiturate from the body can be increased by peritoneal dialysis and haemodialysis.

Q 4. Write a note on 'benzodiazepines as a hypnotic and sedative'.

Benzodiazepines

- It is a group of structurally related drugs which acts on the CNS.
- The main site of action is limbic system, the region and brain concerned with emotions and anxiety.

- The drugs belong to benzodiazepine are effective for treatment of anxiety, anticonvulsant and central muscle relaxants.
- Benzodiazepines are inactivated by liver and excreted in the liver.
- Based on their duration of action, benzodiazepines are divided as:
  i. Short acting, e.g. triazolam, flurazepam.
  ii. Medium acting, e.g. alprazepam, lorazepam.
  iii. Long acting, e.g. diazepam, chlordizepoxide, clonazepam, nitrazepam.

Mechanism of Action

- GABA (gamma-aminobutyric acid) is the major inhibitory neurotransmitter in CNS.
- Benzodiazepines increase the efficiency of GABA ergic synaptic inhibition.
- The effect of benzodiazepines is to enhance the response to GABA, by facilitating the opening of GABA activated chloride channel.

Pharmacological Actions

1. Reduction of anxiety and aggression.
2. Depression of cognitive and psychomotor function.
3. **Sedation and induction of sleep:** At higher dose, benzodiazepines change sleep pattern.
   - Induction of normal sleep (latency of sleep is reduced).
   - The duration of stage 2 NREM sleep is increased.
   - The duration of slow-wave sleep is decreased.
4. **Skeletal muscle relaxant effect**, e.g. diazepam relaxes muscle spasticity by presynaptic inhibition in the spinal cord.
5. **Anticonvulsant effect:** Especially diazepam, lorazepam, clonazepam, nitrazepam.
6. **Respiratory system and CVS:** Minimal depressant effects in therapeutic doses.

Therapeutic uses/Clinical uses/Indications

1. As hypnotics and sedatives
2. As anticonvulsants
3. As preanaesthetic medication
4. As antianxiety agents
5. As good muscle relaxants
6. As tranquillizers
7. To treat insomnia
8. In acute alcohol withdrawl
9. In chronic muscle spasm and spasticity.

Adverse Effects

i. **Tolerance:** Physical and psychological dependance.

ii. **Withdrawal symptoms:** Anxiety, rebound insomnia, anorexia, tremors and convulsion.
iii. Hangover, drowsiness, sleep tendency, confusion especially in long acting drugs.
iv. Light headedness, ataxia, vertigo, blurred vision.

Contraindications

- Respiratory depression
- Acute pulmonary insufficiency, sleep apnoea.
- Severe hepatic impairment
- Myasthenia gravis.

Dosage

1. Diazepam : 5–40 mg daily (valium, calmpose)
2. Nitrazepam : 5–10 mg daily (hypnotex)
3. Lorazepam : 5–10 mg daily (ativan)
4. Chlordiazepoxide : 5–10 mg daily (librium)

QUESTION: GIVE THE REASONS

Q 1. Why is sodium bicarbonate given in barbiturate poisoning?

i. Sodium bicarbonate is an alkaline, and barbiturates are the derivatives of barbituric acid.
ii. In barbiturate poisoning, unionized barbiturate is reabsorbed into the body and increases toxicity.
iii. Sodium bicarbonate increases alkalinisation of urine and there is an ionisation of barbiturates.
iv. Ionised barbiturates are not reabsorbed by tubules and increases its excretion.
v. Sodium bicarbonate increases the excretion of barbiturates and hence, it is used in barbiturate poisoning.

Objective Questions with Answers in Bold Letters

1. The condition of lack of sleep is called **insomnia**.
2. **Hypnotics** are the agents that induces sleep resembling natural sleep.
3. **Sedatives** are the drugs which reduces excitement.
4. Thiopentone and methohexione are **ultra short-acting barbiturates**.
5. **Sodium bicarbonate** is used as antidote in acute barbiturate poisoning.
6. **GABA** is the major inhibitory neurotransmitter in CNS.
7. **Barbiturates** are the derivatives of barbituric acid.

8. Calmpose is a brand name of **diazepam**.
9. REM sleep means **rapid eye movement sleep**.
10. NREM sleep means **non-rapid eye movement sleep**.
11. Automatism is a stage which occurs in case of **barbiturates**.
12. Daily dose of diazepam is **5–40 mg**.

C. ANTICONVULSANT DRUGS (ANTIEPILEPTIC DRUGS)

Q 1. What is epilepsy? Explain various types of epilepsy.

Epilepsy/Seizures

It is a chronic convulsive disorder characterised by sudden disturbance of consciousness usually but not always with characteristic body movements and sometimes with autonomic hyperactivity.

- The term epilepsy is derived from the Greek word *epilabanein* which means to seize (i.e. to take sudden possession).
- Epilepsy is the most common neurological disorders characterized by paroxysmal cerebral dysrhythmia.
- Seizures are symptoms of disturbed electrical activity in the brain characterized by episodes of abnormal, excessive and synchronus discharge of a group of neurons within the brain that causes involuntary movement, sensation or thought.

Types of Epilepsy

1. **Grand mal epilepsy:** It involves a sudden loss of consciousness and major convulsions consisting of spasms of the whole body followed by jerky movements. Convulsions are followed by generalised CNS depression.
2. **Temporal lobe epilepsy:** It consists of sudden attacks of altered behaviour and emotions. Convulsions are absent. The entire attack consists of abnormalities of behaviour.
3. **Focal cortical epilepsy:** It consists of convulsions of single limb or a group of muscles.
4. **Minor epilepsy:** It consists of loss of consciousness without convulsions.
5. **Petit mal epilepsy:** It consists of impairment of consciousness associated with eyelid blinking (insensitivity of light).
6. **Myoclonic epilepsy:** It consists of isolated clonic jerks.
7. **Infantile epilepsy:** It occurs in infants and consists of mental deterioration.
8. **Motor epilepsy:** It involves involuntary movements of thumb, angles of mouth, movements of half side of the body may be affected like paralysis.
9. **Hypsarrhythmia:** It occurs in infants and consists of falling spell, head dropping and myoclonic jerks.

Q 2. Define and classify anticonvulsants/antiepileptic drugs.

Anticonvulsants

The drugs which are used in the treatment of convulsions/epilepsy are called anticonvulsants/antiepileptics.

Classification

1. **Drugs used in grand mal epilepsy**, e.g. phenytoin, methoin, phenobarbitone, primidone, carbamazepine.
2. **Drugs used in petit mal epilepsy**, e.g. tridione, paradione, phensuximide, ethosuximide.
3. **Drugs effective in psychomotor epilepsy**, e.g. phenytoin, primidone, tridione.
4. **Focal coritcal or jacksonian epilepsy**, e.g. phenytoin, methoin, phenobarbitone, primidone.
5. **Status epilepticus**, e.g. diazepam, paraldehyde, thiopentone.

Q 3. Describe 'phenytoin' as an anticonvulsant drug.

Phenytoin (Diphenyl Hydantoin)

It is a primary drug in the treatment of epilepsy.

Mechanism of Action (Antiepileptic Activity)

- Phenytoin exerts a selective antiepileptic action. This drug generally inhibits the spread of convulsions in the brain and shortens the duration after its discharge.
- The phenytoin decreases the neuronal sodium concentration which leads to reduction in the post-tetanic potentiation (PTP) and increase in the neuronal potassium concentration.
- The reduction in PTP by phenytoin stops the spread of convulsive discharge in the brain.

Adverse Reactions

1. Intolerance, skin rash, jaundice
2. Headache, confusion, hallucination
3. GIT irritation, nausea, vomiting
4. Megaloblastic anaemia
5. Cardiovascular collapse
6. Severe CNS depression
7. Ataxia, vertigo, liver damage.

Therapeutic uses

1. In treatment of grand mal epilepsy
2. In treatment of temporal lobe epilepsy
3. In focal cortical epilepsy
4. In cardiac arrhythmia
5. In trigeminal neuralgia.

Contraindications

- Porphyria
- Sinoatrial block
- Stokes-Adams syndrome

Preparation

Phenytoin tablet IP

Dose: 50–100 mg twice daily

Trade Names

Eptoin, Epileptin.

Q 4. Write the properties of an ideal antiepileptic agent.

1. It should be effective in all varieties of epilepsy.
2. It should have quick action and long duration of action.
3. It should have minimum side effects and non-addicting.
4. It should be orally effective.
5. It must be cheap and easily available.

Q 5. What is status epilepticus? Give its treatments.

Status epilepticus is a condition in which the epileptic attacks follow each other continuously.

The term *status epilepticus* is used to indicate repeated grand mal epileptic attacks without recovery of consciousness between the attacks.

The status epilepticus is a medical emergency and such patient must be hospitalized for proper treatment.

Treatments

1. Glucose saline is given intravenously.
2. Respiration is supported.
3. Diazepam is given intravenously for controlling convulsions.
4. Hypotension and respiratory depression may be watched carefully.
5. Paraldehyde is also given as an alternative in the dose of 5–10 ml by IM.

Q 6. Give the major use, brand name, dose of the following anticonvulsants.

Drug	*Brand name*	*Uses*	*Dose*	*Route*
1. Phenytoin	Dilantin	Grand mal epilepsy, status epilepticus	300–400 mg daily in divided doses	Oral
2. Primidone	Mysoline	Grand mal epilepsy, psychomotor epilepsy	125 mg daily for 3 days, 250 mg q.i.d.	Oral
3. Trimethadione	Tridione, Troxidone	Petit mal epilepsy	300 mg t.i.d. maintenance 2–3 gm/day	Oral
4. Paramethadione	Paradione	Petit mal epilepsy	300–600 mg t.i.d.	Oral
5. Ethosuximide	Zarontin	Petit mal epilepsy	500 mg/day initially, increased up to 1500 mg/day	Oral

Contd...

Contd...

Drug	*Brand name*	*Uses*	*Dose*	*Route*
6. Methosuximide	Celontin	Petit mal, psychomotor epilepsy	Initially 300 mg/day for a week, increased to 1000 mg/day	Oral
7. Carbamozepine	Tegretol, Mazetol	Trigeminal neuralgia, psychomotor epilepsy	100–200 mg twice daily, maintenance 400–800 mg/day	Oral
8. Sodium valproate	Epilim	Grand mal, petit mal epilepsy	1200–1500 mg/day in divided doses	Oral
9. Phenobarbitone	Gardenal, Luminal, Dilantin-P	Grand mal epilepsy	30–20 mg/day in divided doses	Oral

QUESTIONS: GIVE THE REASONS

Q 1. While treating the patient of epilepsy, the dose of drug should be reduced slowly? OR During the treatment of epilepsy, drug should be discontinued or withdrawn gradually, why? OR Why antiepileptics should not be withdrawn abruptly?

Because:

i. If antiepileptic drugs are discontinued suddenly, individual may suffer from rebound epileptic attack, which may be severe than previous one.
ii. The antiepileptic drugs show withdrawal symptoms such as delusions and hallucinations.
iii. All antiepileptic drugs are quite sedative in nature.

Hence, to reduce above side effects, the dose of drug is reduced slowly.

Q 2. Why is phenobarbitone used in epilepsy?

Because phenobarbitone inhibits the spread of convulsive discharge in the brain and exerts an antiepileptic effect. Due to this property it is used in epilepsy.

Q 3. Generally combination of phenytoin and phenobarbitone is used in the treatment of grand mal epilepsy.

i. Phenytoin prevents the spread of grand mal and other epileptic seizures.
ii. Phenytoin prevents the spread of abnormal electrical activity but does not seem to abolish the focus.
iii. Phenobarbitone reduces both the formation of focus and its spread.
iv. Phenytoin causes effux of sodium from cerebral neurones and thus stabilise their cell membranes for a particular electrical charge and prevents PTP.

v. Phenobarbitone increases the post-synaptic responses to the inhibitory transmitter GABA.
vi. The combination also considerable reduces the systemic toxicity due to decrease in the proportion of individual drug. This combination has synergistic action. Hence generally, combination of phenytoin and phenobarbitone is used in the treatment of grand mal epilepsy.

Objective Questions with Answers in Bold Letters

1. Carbamazepine belongs to **iminostilbene group**.
2. Epilepsy is a **neurological** disorder.
3. **Epilepsy** is also known as seizure/convulsion.
4. **Grand mal epilepsy** is also known as major epilepsy.
5. Phenytoin is a drug of choice in **grand mal epilepsy**.
6. **Diazepam** is a drug of choice in status epilepticus.
7. Primidone is an anticonvulsant which is structurally related to **phenobarbitone**.
8. Petit mal seizures are also known as **absence seizures**.

D. ANTIANXIETY DRUGS/ANXIOLYTICS

Q 1. What do you mean by anxiety? Define and classify antianxiety drugs.

Anxiety

It is an emotional state characterized by intense, excessive persistent worry and fear about defined or undefined future threat.

Anxiety is also associated with physical changes such as insomnia, hypersomnia, anorexia and weight loss.

Symptoms

- Feeling nervous, restless
- Increased heart rate
- Sweating
- Feeling tired
- Inability to concentrate on any other thing than the present worry.

Causes

- Difficult experience in childhood, adolescence or adulthood.
- Stress
- Trauma
- Physical/emotional abuse

Antianxiety Drugs

The drugs which are used in the treatment of anxiety are called antianxiety drugs.

Classification

1. **Minor tranquillizers:** Benzodiazepines: Diazepam, chlordiazepoxide, lorazepam, oxazepam and alprazolam.
2. **Antidepressants:** Further classified into the following classes:
   a. *Monoamine oxidase (MAO) inhibitors:* Isocarboxazid, nialamide
   b. *Tricyclic compounds:* Impiramine, desipramine, amitriptyline
   c. *Selective serotonin reuptake inhibitors:* Fluoxetin, citalopram
   d. *Lithium carbonate*.

Q 2. Describe any two antianxiety agents (minor tranquillizers).

Antianxiety Drugs

1. Benzodiazepines

Pharmacological actions:

- Chlordiazepoxide is a tranquillizer which has to a great replaced with meprobamate.
- Animal studies have shown that chlordiazepoxide has sedative, anti-convulsant and skeletal muscle relaxant properties.
- Chlordiazepoxide is rapidly absorbed from the GIT and peak blood levels are reached within 2–4 hours.
- The drug is excreted slowly and its plasma half life is 20–40 hours.

Therapeutic uses

1. Symptomatic relief anxiety
2. To reduce anxiety of psychosis
3. In prophylaxis of migraine
4. To treat acute symptoms of alcohol withdrawal
5. Effective in treatment of musculoskeletal diseases.

Adverse Reactions

- Drowsiness • Ataxia • Lethargy • Syncope

Dosage

1. Chlordiazepoxide tab 20–100 mg daily (librium)
2. Other benzodiazepines used an anxiety includes:
   Oxazepam (30–60 mg) : 2–3 divided doses
   Diazepam (5–30 mg)
   Lorazepam (1–6 mg)
   Alprazolam (0.25–1 mg)

2. Meprobamate

- Meprobamate is highly effective antianxiety agent and mild skeletal muscle relaxants.

- It produce mild sedation and relaxation.
- It is indicated for the relief of anxiety and tension.
- Meprobamate is an anxiolytic drug.
- Meprobamate is minor tranquillizer but has largely been replaced by benzodiazepine.
- Meprobamate is of little value in the treatment of psychoses.
- Tolerance may develop rapidly and a physical dependance may develop for the drug if it is taken for prolonged periods.
- Withdrawal symptoms appear in 95% of the patients when the drug is discontinued.
- Convulsions, delirium and grand mal seizures may be precipitated on withdrawal of a drug.

Adverse Effects

- Drowsiness
- Slurred speech
- Tolerance
- Ataxia
- Blood dyscrasias
- Depression
- Allergic reactions
- Euphoria
- Psychological dependance.

Indications/Therapeutic uses

1. Used in anxiety and neurosis.
2. As a hypnotic and sedative.
3. Used during withdrawal of alcohol.

Dosage

Meprobamate tablet :1200–1600 mg daily in divided doses

Brand Name: Miltown.

E. ANTIDEPRESSANTS/PSYCHOANALEPTICS

Q 1. What do you mean by 'depression'? Define and classify antidepressant drugs.

Depression

- Depression is a mental illness characterized by pathological changes in mood.
- Depression is a sadness, though possibly intense, it is usually of short duration.

Causes

Decrease the level of excitatory neurotransmitters (adrenaline, noradrenaline and serotonin).

Symptoms

1. Loss of pleasure in usual activities (anhedonia).
2. Sleep disturbances

3. Persistently sad, anxious, or empty moods
4. Feelings of helplessness, guilt, or worthlessness
5. Fatigue or decreased energy
6. Loss of memory, concentration, or decision-making capability
7. Restlessness, irritability
8. Change in appetite or weight

Antidepressant drugs: These are the agents that used to treat the depression.

Classification of Antidepressants/Psychoanaleptics/Mood Elevators/ Thymoleptics

1. **Tricyclic antidepressants**, e.g. imipramine, desipramine, amitriptyline, nortriptyline, doxepin.
2. **Monoamine oxidase inhibitors (MAOIs)**, e.g. isocarboxazid, nialamide, phenelzine, pargyline, tranylcypromine.
3. **Mood stabilizers**, e.g. lithium carbonate, mainserin.

Q 2. Write a note on •'MAO inhibitors'.

MAO inhibitors mean monoamine oxidase inhibitors. The drugs which inhibit the actions of monoamine oxidase enzyme are known as monoamine oxidase inhibitors. For example, phenelzine, pargyline, isocarboxazid, tranylcypromine.

- MAO inhibitors are a heterogenous group of drugs which block oxidation of naturally occurring amines.
- MAO inhibitors have a limited role in the management of depression.

Mechanism of Action

The enzyme monoamine oxidase is present intracellularly in most of the tissues. The highest concentration is found in liver, within the brain and its important function is to oxidise active biogenic amines, 5-HT, noradrenaline and dopamine.

These amines are normally stored in granules in neurons and are liberated by nerve stimuli.

MAO inhibitors inhibit the action of MAO enzymes which may lead to accumulation of these monoamines in the brain. MAO inhibitors prevent oxidation of catecholamine and histamine and increase functional availability of these monoamines in the brain. MAO inhibitors are effective in the treatment of mental depression of man because these drugs produce their pharmacological action by increasing the level of active amines like 5-HT.

Adverse Effects

1. Headache, excitement
2. Disturbed sleep
3. Hyperthermia
4. Convulsions
5. Sudden increase in BP
6. Constipation
7. Severe jaundice.

Therapeutic uses

1. As antidepressants
2. As antihypertensive agents
3. They potentiate the action of barbiturates, morphine and anaesthetics.

Preparation and Doses

1. Phenelzine sulphate tablet
   Dose: 50–60 mg daily orally **Trade name:** Nardil
2. Isocarboxazid tablet
   Dose: 10–30 mg daily orally **Trade name:** Morphan
3. Tranylcypromine tablet
   Dose: 10–30 mg daily **Trade name:** Parnate.

Q 3. Write a note on 'tricyclic antidepressants/imipramine.

Tricyclic Antidepressants

- These compounds inhibit the reuptake of norepinephrine and serotonin into adrenergic neurons.
- These compounds may be subdivided into:
  a. Tertiary amines: Amitriptyline, doxepin, imipramine, trimipramine.
  b. Secondary amines: Desipramine, amoxapine, protriptyline.
- All tricyclic compounds display anticholinergic activity.
- These compounds are more specifically effective in treating patients with endogenous depression.
- In combination therapy with phenothiazines or lithium carbonate may be beneficial in treating depression of schizophrenia or severe anxiety.

Impramine: Impramine is a dibenzazepine derivative and is commonly used as tricyclic antidepressant drug.

Pharmacological Actions

- **Behavioural effects:** It has antidepressant properties comparable to MAO inhibitors, but its mechanism of action is distinct. It also has some anxiolytic properties.
- **Central nervous system:** Drowsiness and lightheadedness are caused by a single dose. It also has sedative properties and improves sleep. It reduces the seizure threshold; thus, it should be used with caution in individuals who have seizures. Sedation and trouble concentrating and thinking are caused by repeated doses of the medication. The medication has no effect on breathing at therapeutic levels. Drug addiction is a rare occurrence.

- **Autonomic nervous system:** It has significant anticholinergic effects, such as dry mouth, constipation, palpitation and so on.
- **Cardiovascular system:** In anaesthetized animals, it reduces blood pressure. In humans, therapeutic doses cause moderate hypotension. Cardiac arrhythmia is caused by taking too much of the medicine.
- **Adverse effects:**
- **Anticholinergic disturbances:** Dry mouth, difficulty in adapting, tachycardia, difficulty in micturition, impotence, constipation and delayed ejaculation are all side effects of these medicines. Hyperpyrexia is a rare side effect.
- **CNS:** Tiredness, lethargy, headaches and drowsiness are common side effects. Tremors, muscle jerks, ataxia and hyperreflexia are also side effects of the drug.
- **Cardiovascular system:** Tachycardia, cardiac arrhythmia and hypotension are all possible side effects. In some cases, heart failure has been documented.
- It produces allergic reactions such as skin rashes, photosensitivity, cholestatic jaundice, edema and agranulocytosis.

Therapeutic uses/Indications

- It is indicated in phobic and obsessional states.
- It is used to treat anxiety disorders.
- It is used to treat pains due to its analgesic property.
- It is used to treat hyperactivity and disturbed attention.
- It is used to treat allergic conjunctivitis.
- To treat enuresis (bed wetting in children).

Preparations

- Imipramine tablet
- Imipramine injection
- Imipramine mixture
- Imipramine capsule.

Brand names: Antidep, Depranil, Depsonil, Imrotab.

Contraindications

- Recent myocardial infarction
- Arrhythmias
- Severe liver disease.

Dosage

Phobic and obsessional states: Initially 25 mg daily at bed time by mouth and may be increased over two weeks to 100–150 mg daily.

Q 4. Explain 'lithium carbonate' as antidepressant drug.

Lithium Carbonate

- Lithium carbonate is used for prophylactic treatment of recurrent maniac and depressive episodes.

- Lithium carbonate causes depletion of intraneural sodium and stabilises the neuronal membrane.
- It also prevents the release of norepinephrine.

Adverse Effects

- Nausea
- Diarrhoea
- Blurred vision
- Anorexia
- Hypothyroidism
- Convulsions
- Stomach irritation
- Thirst
- Coma.

Therapeutic uses

1. In treatment and prophylaxis of mania.
2. In prophylaxis of bipolar disorder and recurrent depression.
3. In treatment of prophylaxis of schizophrenia.

Contraindications

- Renal impairment
- Addison's disease.

Dosage

Lithium carbonate tablet : 250–2000 mg daily in divided doses
Brand names: Lithocarb, Licab.

QUESTION: GIVE THE REASONS

Q 1. Why eating of cheese is forbidden in patients with MAO inhibitor therapy?

- Cheese, butter, chocolates, bananas contain tyramine. Tyramine is metabolised in the liver by the enzyme monoamine oxidase.
- If individual is on MAO inhibitor therapy, then MAO inhibitors inhibit the detoxification or metabolism of tyramine.
- Thus, tyramine is not metabolised and it gets accumulated in the body.
- This tyramine causes release of noradrenaline from its binding sites.
- Increased level of noradrenaline causes hypertensive crisis.
- Therefore, eating of cheese is forbidden while on MAO inhibitor therapy.

F. ANTIPSYCHOTICS

Q 1. What are different psychic disorders/psychological disorders/ mental disorders?

Types of Psychic/Mental Disorders

Psychosis: It means a mental condition characterized by disturbances in mental functions.

- It is a psychic condition, which involves marked impairment of behaviour with a serious inability to think.
- Mental diseases have always been puzzling and frightening things.

- Psychosis can be defined as the psychotic illness with serious distortion of thought, behaviour and capacity to recognize reality and of perception and patient unable to meet the ordinary demand of life.

Psychoses may be of two categories:

a. **Organic psychosis:** It involves memory disturbances, clouding of consciousness, congestive disorders, like delirium and dementia with psychotic features.

   Prominent features are confusion, disorientation, defective memory, disorganized thoughts and behaviour. They may be due to endocrinal abnormalities or head injuries.

b. **Functional psychosis:**
   i. *Maniac:* Disturbance of mood, reduced sleep, hyperactivity, uncontrollable thoughts and speech, violent behaviour.
   ii. *Schizophrenia:* It is also known as split mind condition. It involves splitting of perception and interpretation from reality and inability to think. Disturbed emotions and motor behaviour.
   iii. *Hallucination:* A sensation of false perception without sensory stimulus.
   iv. *Anxiety:* It involves feeling of fear, apprehension.

c. **Neurosis:** It is a termed used to denote less severe form of psychosis.

d. **Depression:** It is a common psychiatric disorder characterized by a feeling of misery, apathy, hopelessness, ugliness, loss of appetite, insomnia, anorexia, alternation in moods, activities, etc.

Q 2. Define the terms with examples.

a. Antipsychotics/Psychotropics/Psychoactive Drugs

The drugs which are used in the treatment of psychic disorders are called antipsychotics or psychoactive drugs. For example, chlorpromazine, reserpine, haloperidol.

b. Antianxiety Agents/Anxiolytics/Minor Tranquillizers

The drugs which are used to reduce anxiety states and nervousness are called antianxiety agents. For example, diazepam, nitrazepam, oxazepam.

c. Antidepressants (Mood Elevators)

The drugs which improve the moods of depressed individuals are called antidepressants. For example, imipramine, desipramine, amitriptyline, nortriptyline.

d. Tranquillizers

The drugs which produce calming and quietening effect on the individuals are called tranquillizers. For example, chlorpromazine, haloperidol.

Q 3. Define and classify antipsychotics/psychoactive drugs/ psychotropic drugs/tranquillizers with suitable examples.

Psychotropic/Antipsychotic Drugs

The drugs which are used to treat psychiatric disorders are called psychotropic drugs.

Classification

A. **Typical antipsychotics:** These drugs act on the dopaminergic system, blocking the dopamine type 2(D_2) receptors.
   a. ***Phenothiazines***, e.g. chlorpromazine, trifluoperazine.
   b. ***Butyrophenone derivatives***, e.g. haloperidol, droperidol.
   c. ***Thiothixene derivatives***, e.g. thiothixene, chlorprothixene.
   d. ***Miscellaneous***, e.g. reserpine (Rauwolfia alkaloids).

B. **Atypical antipsychotics:** For example, clonazepine, risperidone.

Q 4. Write a note on 'major tranquillizers'/'phenothiazines'.

Major Tranquillizers/Phenothiazines

Chlorpromazine

- It is a phenothiazine derivative.
- It produces many pharmacological actions hence, it is called by the trade name 'Largactil'.

Pharmacological Actions

1. **Behavioural Effects:**
   - In patients, with major psychosis, it produces psychomotor slowing, emotional quietening, diminishing anxiety without affecting wakefullness.
   - The drug produces antipsychotic effect by blocking the receptors of dopamine and norepinephrine in the brain.
   - The antipsychotic action is due to competitive blockade of dopaminergic receptors in limbic system.
2. **Effect of ANS:** It has central depressant action on hypothalamic centre controlling sympathetic activity.
3. **Effect on CVS:** It produces hypotension because of depression of hypothalamus leading to decrease in sympathetic tone. It produces vasodilation.
4. **Antiemetic effect:** It depresses CTZ in the medulla and acts as a powerful antiemetic.
5. **Effect on temperature regulating centre:** It decreases temperature by adrenergic blocking effect which leads to vasodilation resulting in heat loss.

Adverse Effects

1. Skin rash, dermatitis
2. Parkinsonism
3. Excitement, restlessness
4. Tachycardia
5. Constipation
6. Hypotension
7. Aplastic anemia
8. Menstrual irregularities.

Therapeutic uses

1. In the treatment of schizophrenia.
2. In senile psychosis (aged).
3. In the treatment of maniac depressive psychosis.
4. For the treatment of behavioural disorders in children.
5. It acts as an antiemetic by acting on CTZ.

Preparation and Doses

Chlorpromazine tablet IP
Dose: 200–800 mg daily
Brand name: Largactil

Contraindications

- Bone marrow depression
- Pheochromocytoma.

Q 5. Explain the details of 'reserpine' as a tranquillizer.

Reserpine

It is a principal alkaloid of *Rauwolfia serpentina*.

Mechanism of Action (Tranquillizing Action)

Reserpine produces depletion of 5-HT and catecholamines (adrenaline and noradrenaline) from the brain and peripheral sites. This depletion of monoamines is necessary for its tranquillizing action.

Therapeutic uses

1. As antipsychotic (tranquillizer).
2. As an antihypertensive agent.
3. Used in the treatment of snake bite.

Preparation and Dose

Reserpine tablet IP
Dose: 0.25 mg daily
Trade name: Serpasil.

Q 6. Explain the terms and give the drugs of choice.

1. Schizophrenia

- It is a split mind condition characterized by disturbed thinking, emotional withdrawal from surrounding, delusions, and hallucination.

- The mental functions of schizophrenic patient are sufficiently impaired to interfere with his capacity to meet the ordinary demands of life.

Drug Treatment

Chlorpromazine, reserpine.

2. Motion Sickness

Motion sickness can develop during any form of travel but is mainly due to repetitive and rhythmic changes in speed or direction of travel.

It starts with a brief period of euphoria and then followed by uneasiness. The face becomes pale and a cold sweat breakout, nausea, salivation, and vomiting occurs with headache.

Drug Treatment

Scopolamine, promethazine, cyclizine, d-amphetamine.

Q 7. What is mania? Write in brief about antimanic drugs (mood stabilizers).

Mania

It is also known as bipolar disorder. It causes serious shift in mood energy thinking and behaviour—from the highs of mania on one extreme, to the lows of depression on the other.

Symptoms

1. Sleeping very little, but feeling extremely energetic.
2. Talking so rapidly that others cannot keep up.
3. Feeling unusually 'high' and optimistic or extremely irritable.
4. Highly distractible, unable to concentrate.

Antimanic drugs: These are the agents that are used to stabilize the mood of individuals is called antimanic drugs.

Lithium

Mechanism of action: Lithium decreases the body sodium content. It is equally distributed in and out of the cell and effects its ionic environment. It decreases NA and DA release in brain.

Pharmacological Actions

1. It inhibits the ADH (antidiuretic hormone) action on distal tubule and produce polyuria and thirst.
2. It has insulin-like action on glucose metabolism.

Therapeutic uses

1. Mainly used to treat manic episodes 2. Treatment of bipolar disorder.

Adverse Effects

Increased thirst and urination, polydipsia, nausea, weakness, drowsiness and fatigue.

QUESTIONS: GIVE THE REASONS

Q 1. Why is chlorpromazine 'called 'Largactil'?

Because chlorpromazine shows a large number of pharmacological actions as follows:

i. It causes sedation.
ii. In psychotic patients cause tranquillizing effect.
iii. It has an antiemetic effect.
iv. It causes hypothermia by acting on hypothalamus.
v. It promotes lactation in women and blocks ovulation.
vi. It has weak antihistaminic activity.
vii. In normal individuals, it causes emotional quietening.

Due to all these actions, chlorpromazine is called Largactil.

Q 2. Why is chlorpromazine not effective in the vomiting of motion sickness?

Because:

i. Motion sickness means vomiting induced during travelling, may be due to repetitive and rhythmic changes in the speed or direction of travel.
ii. Motion sickness is caused by stimulation of vestibular nucleus but not by CTZ.
iii. Chlorpromazine is antiemetic drug and it prevents the vomiting induced due to stimulation of CTZ only.

Thus, chlorpromazine is not effective in motion sickness.

Q 3. Why reserpine is not useful in immediate quietening of manic patients?

i. Reserpine is an antipsychotic drug.
ii. It causes depletion of serotonin and catecholamines from the brain and peripheral sites which results in tranquillizing action.
iii. Reserpine stimulates the CNS excessively leading to firing of all central neurons synchronously developing epilepsy.
iv. This is followed by severe mental depression resulting in suicidal tendencies.
v. Therefore, reserpine is not useful in immediate quietening of manic patients.

G. NOOTROPIC AGENTS

Q 1. What are nootropics? Explain various nootropic agents.

Nootropics

Nootropics are the drugs supplements and other substances that are claimed to improve cognitive function, particularly executive functions such as attention, memory, creativity or motivation, in healthy individuals.

Explanation

- Nootropics are 'smart drugs' that can boost brain performance.
- They are sometimes called cognition enhancers or memory enhancing substances.
- Nootropics are used to boost memory, improve concentration thereby focus creativity and postpone fatigue.
- The word nootropics is derived from the Greek words *nous* → means mind, *trepein* → means to bend or turn. Thus, nootropics means 'monitoring mind'.
- Nootropics can treat number of neurodegenerative and neuropsychiatric disorders.
- Nootropics are available in natural and synthetic forms:
  a. **Natural phytoconstituents:** These include caffeine, L-theanine, creatine, *Bacopa monnieri* (Brahmi), *Rhodiola rosea*, *Panax ginseng*, *Ginkgo biloba*, etc.
  b. **Synthetic agents:** These include piracetam, citicoline, levetiracetam, armodafinil, ampakines, cerebrolysin, phenibut, modafinil, selegiline, semax, inositol, etc.

A. **Natural phytoconstituents:** These include:

1. *Caffeine:* It is most widely consumed psychoactive substance in the world. It is found in coffee, tea cola nuts. It is added to many sodas, energy drinks and medications. It is taken as supplement either alone or in combination with others. Caffeine works by blocking adenosine receptors in the brain, making person feel less tired. Low to moderate caffeine intake 40–300 mg enhance alertness and attention. It reduces reaction time. It is especially useful for people with fatigue.
2. *L-Theanine:* It is a naturally occurring amino acid found in tea. Studies have shown that taking 200 mg of L-theanine has calming effect without causing drowsiness. Even 50 mg have been found to increase α-waves in the brain, linked to creativity. It is more effective when taken with caffeine (tea contains both caffeine and L-theanine).
3. *Creatine:* It is an amino acid required for protein synthesis. It is popular body building material that promotes growth. In brain, it combines with

phosphate and form a substance, useful as energy fuel for brain. It enhances short-term memory and reasoning skills especially in stressed people. Consumption of 5 g per day has been shown to be safe.

4. *Bacopa monnieri:* It is an ancient herb used in ayurvedic medicine. It improves brain, functions, speeds up information processing in the brain and reduce reaction time along with improvement in memory. The active compounds found in it are known as becosides which protect the brain from oxidative stress. 300–600 mg per day should be taken for several months to achieve maximum benefit.
5. *Rhodiola rosea:* Adaptogenic herbs that help to handle stress more effectively and improve mood, reduce feeling of burnouts in both anxious and highly stressed individuals. It relieves mental fatigue and enhance feeling of well-being in college students during stressful examination times.
6. *Panax ginseng:* Ancient medicinal plant that boosts brain function. Taking single dose of 200–400 mg of *Panax ginseng* has been shown to reduce brain fatigue.

B. **Synthetic compounds:** These include:

1. *Piracetam:* A nootropic agent which is derivative of γ-aminobutyric acid (GABA) used in Europe as enhancer of cognitive skills. Its exact mechanism is not clearly known but is supposed to act by enhancing acetylcholine and glutamate transmission. It improves memory and learning in humans.
2. *Citicoline:* A psychostimulant/nootropic agent that stimulates both motor and sensory systems. It has been observed that, the intake of citicoline has elicited changes in EEG and EMG, consistent with aurosal of consciousness. The effects are attributable to brain adrenergic, especially dopaminergic neurotransmitter systems.
3. *Levetiracetam:* A newer anticonvulsant that is claimed to improve cognition, i.e. showing nootropic effects.

Q 2. State important features of nootropics.

Important Features of Nootropics

- Nootropics are class of cognitive enhancing supplements that enhance concentration and boost memory.
- They are also referred to as 'smart drugs' as they are concerned with intelligence, motivation and mental strength.
- Long-term safety data about nootropics is not available, clinical research data suggest that only certain stimulants used in low doses can enhance cognition in general population.
- Nootropics act as direct or indirect agonists of dopamine, adrenoceptor or both in prefrontal cortex.

- Nootropics show signs of neuropreservation and neuroprotection.
- Some nootropics may show increased production of brain cells and showing down their destructions.
- These are drugs/supplements/nutraceuticals/functional foods that enhance one or more aspects of mental function.
- Use of prescription stimulants is prevalent among students facing examinations, e.g. dimethylamylamine, methylphenidate.
- Nootropics probably act by changing the levels of neurotransmitters, hormones or enzymes.
- They may also enhance the brain oxygen supply, energy supply or blood supply.
- There are nootropics available for providing sleep and rest and also for avoiding dizziness and to keep alert.

Q 3. What are the mechanisms of action of nootropic agents?

Principle mechanisms of action of nootropic agents:

1. Decreases malondialdehyde levels in brain and increases levels of antioxidant molecules such as glutathione and superoxide dismutase.
2. Interaction with dopamine D_2, serotonergic and GABA-B receptors.
3. Reduction of MAO-A and plasma corticosterone levels.
4. Reduces the concentration of noradrenaline and decreases turnover of central monoamines.
5. Inhibition of acetylcholinesterase activity in brain.
6. Increases content of lipids and phospholipids in brain.
7. Protects neurons against glutamate-induced toxicity.

H. CENTRALLY ACTING MUSCLE RELAXANTS

Q 1. Write a note on 'centrally acting muscle relaxants'.

Centrally Acting Muscle Relaxants

- Centrally acting muscle relaxants are used medically as adjuncts to rest, physical therapy and for the relief of discomfort associated with acute, painful musculoskeletal conditions.
- These agents are used in skeletal muscle spasms of local origin, multiple sclerosis, cerebral palsy, sprains, strains, fibrositis, rheumatoid spondylitis, arthritis.
- The muscle relaxant drugs can effectively reduce the rigidity of muscle without affecting the consciousness and normal voluntary movements of the muscles.
- Satisfactory muscle relaxation is valuable for operative procedure.
- These drugs are also useful for relieving convulsions of tetanus, strychnine poisoning drug-induced convulsions and various spastic disorders.

- These drugs act on muscle fibre or at neuromuscular junction or centrally in cerebrospinal axis.
- These drugs reduce muscle tone and cause paralysis.
- Centrally acting muscle relaxants act on selective areas in the CNS, thus effectively decreasing skeletal muscle tone and involuntary movements.
- Examples of centrally acting muscle relaxants:

1. Mephenesin
2. Methocarbamol
3. Chlorsoxazone
4. Metaxalone
5. Diazepam.

1. Mephenesin

- Mephenesin was the first drug found to cause muscle relaxation without producing unconsciousness.
- Mephenesin is an odourless, white crystalline powder, freely soluble in alcohol, chloroform and ether but insoluble in water.
- Mephenesin does not block the neuromuscular transmission.

Therapeutic uses/Indications

1. Mephenesin controls epileptic seizures within 30 seconds.
2. Mephenesin has a central sedative action and has been found to be useful in certain psychotic states.
3. Mephenesin antagonises strychnine convulsion.
4. Mephenesine provides muscular relaxation and relief from certain types of tremors as occurs in parkinsonism.
5. Mephenesin is used to obtain muscular relaxation in surgical anaesthesia.

Adverse Effects

- Damage to veins and haemolysis
- Weakness
- Nystagmus
- Double vision
- Drowsiness, nausea
- Respiratory depression.

Dosage

1. Mephenesin capsules : 250 and 500 mg capsules
2. Mephenesin injection : 10 mg per ml

Dose: 0.5–3 gm given slowly.

Brand name: Dolomed, Dolopar.

2. Methocarbamol

- It is a CNS depressant traditionally suggested for use in acute painful musculoskeletal conditions such as muscle tension and pains associated with anxiety states.
- The muscle relaxation property of this drug may be due to its sedative property.

Side Effects

- Drowsiness
- Dizziness
- Light headedness
- Blurred vision
- Black, blue or green discolouration of urine.

Therapeutic uses

1. To treat muscle spasm/pain.
2. Used in treatment of tetanus.
3. To treat muscle tension and pains associated with anxiety states.

Dosage

Mephenesin tablet : 1500 mg four times daily individed doses.
Brand names: Robaxin, ROBI-M, Robinax.

3. Chlorsoxazone

- Chlorsoxazone is a centrally acting muscle relaxant used to treat muscle spasm and the resulting pain or discomfort.
- It can also be administered for acute pain in general and for tension headache.
- It acts on the spinal cord by depressing reflexes.
- It also acts as muscle relaxant by virtue of its CNS depressant effect.
- The beneficial effect is due to sedative properties for the relief of muscle spasms.

Uses

1. As a centrally acting muscle relaxant.
2. To treat muscle spasm.
3. To reduce pain and discomfort.
4. To treat acute pain in general and tension headache.
5. For the relief of muscle spasms.

Adverse Effects

- Drowsiness
- Dizziness
- Nausea, vomiting
- Heartburn
- Constipation.

Dose: 750 mg 3–4 times daily orally.
Brand names: Lorzone, Remular-S.

I. OPIOID ANALGESICS

Q 1. Define and classify opioid analgesics/ narcotic analgesics with examples.

Opioid Analgesics

The drugs which produce narcosis along with analgesic effects are called opioid analgesics/narcotic analgesics/true analgesics.

Classification

a. Natural opium alkaloids, e.g. morphine, codeine.
b. Synthetic derivatives, e.g. heroin.
c. Synthetic morphine substitutes, e.g. pethidine, methadone.

Q 2. Write a note on morphine as opioid analgesic. OR Write a note on 'natural opium alkaloids' as opioid analgesics. OR Give the pharmacological actions, adverse effects, therapeutic uses, doses of the morphine.

Morphine

- Morphine is a principle alkaloid obtained from opium.
- Morphine belongs to phenanthrene class of alkaloids.
- Morphine was the first opioid analgesic discovered.
- Morphine has a biphasic effect on the CNS, i.e. it depresses the cerebrum while simultaneously depressing and stimulating the medulla.

Pharmacological Actions

a. **Antitussive:** Morphine acts as antitussive drug. It suppresses cough by depressing cough centres.
b. **Analgesic:** Morphine relieves severe pain, pain of trauma, with following mechanisms:
   i. It elevates the threshold and produces sleep.
   ii. It changes the emotional reaction to pain.
   iii. It elevates threshold of painful stimulus and relieves pain. Patient feels no pain.
c. **Action on eyes:** Morphine causes constriction of pupil (miosis). Morphine addicted persons have constricted eye pupils. Morphine produces a pinpoint constriction of the pupil.
d. **Action on respiratory system:** Morphine produces respiratory system depression. The depression of morphine on the respiration is central. Respiratory failure is the main cause of death. If patient dies of overdose of morphine.
e. **Action on urinary tract:** Morphine produces release of antidiuretic hormone (ADH) which results in decrease of urine output. The overall effect is of urinary retention.
f. **Action on central nervous system:** Morphine produces euphoria in presence of pain. In absence of pain, it produces dysphoria. Morphine when given in high doses produces sleep.
g. **Action on vomiting center:** Morphine stimulates the vomiting center, it produces vomiting due to stimulation of chemoreceptor trigger (CTZ). Tolerance develops to vomiting on prolonged used.
h. **Action on gastrointestinal tract:** Morphine decreases peristaltic movements. Secretions like hydrochloric acid, intestinal secretions are decreased. It

increases water absorption from intestinal tract so the faeces gets dried. These effects lead to constipation. Absorption of morphine from gastrointestinal tract is slow and incomplete. It is almost excreted in urine within 24 hours.

i. **Action on heart (cardiovascular system):** The morphine given in normal doses does not effect heart functioning or blood circulation. The higher doses of morphine cause hypotension.
j. **Action on biliary tract:** Morphine increases biliary pressure in man. Morphine evokes biliary spasm, due to its analgesic action.
k. **Action on smooth muscles:** It increases tone of uterus and decreases its peristalsis, produces constriction of bronchi.

Adverse Effects

1. Dryness of mouth
2. Constipation
3. Nausea, vomiting, headache
4. Mental clouding
5. Increased pressure in biliary tract
6. Skin rash, contact dermatitis
7. Hypotension
8. Tolerance
9. Dependence, addiction
10. It depresses foetal respiration if administered in pregnant women.

Therapeutic uses

1. It is used as a narcotic analgesic.
2. As a preanaesthetic medication.
3. For sedation and sleep.
4. To produce constipation or to treat diarrhoea.
5. It is a valuable drug in acute left ventricular failure.
6. It is most powerful analgesic agent for visceral pains.

Contraindications

Morphine is contraindicated in the following conditions:

- Acute respiratory depression
- Head injury
- Acute alcoholism
- Increased intracranial pressure.

Preparations and Doses

Preparation	*Dose*
1. Powdered opium IP	60–200 mg orally
2. Tincture opium IP	0.3–2 ml orally
3. Morphine hydrochloride tablet IP	8–20 mg orally
4. Morphine hydrochloride injection IP	8–20 mg subcutaneous or intramuscular injection

Q 3. Write a note on 'acute morphine poisoning'/acute opium poisoning.

Acute Morphine Poisoning/Acute Opium Poisoning

Acute morphine poisoning may occur due to clinical overdosage or accidental overingestion in an addict or from suicidal intention.

Signs and Symptoms

1. Dryness of mouth
2. Pinpoint pupil
3. Respiratory depression
4. Reduced body temperature
5. Reduced urinary output
6. Hypotension
7. Shock and coma
8. Constipation
9. Convulsions may occur in infants
10. Death is usually due to respiratory depression.

Treatments

A. Drug Treatment

The actions of morphine are antagonised by specific antagonists like naloxone and nalorphine.

These drugs significantly reverse morphine-induced respiratory depression.

a. **Naloxone:** It is usually preferred because of its specific antagonistic activity. It is given in the dose of 0.4–0.8 mg repeated every 10–15 minutes as required.

b. **Nalorphine:** It is antagonist of morphine and usually administered intravenously in the dose of 3–5 mg repeated within half an hour, if necessary.

B. Other Treatments

a. **Gastric lavage:** This is done by administration of emetic preparation to induce vomiting and withdrawal of gastric contents. For example, syrup of ipecac.

b. **Supportive treatments:** Such as maintenance of patient's airway, maintenance of BP, mechanical ventilation, nutrition by intravenous glucose saline and prevention of secondary infection.

c. **Anticonvulsants** like paraldehyde are used to reduce convulsions, if any.

Q 4. Write in brief about following opioid analgesics.

a. Codeine

- Methylmorphine is the chemical name for codeine.
- Codeine has a comparable pharmacological activity to morphine.
- In the body, it decomposes into methane and morphine.
- It is less potent and has a lower risk of addiction than morphine.
- It is less constipating than morphine.
- It depresses cough centre hence useful in the treatment of dry cough.
- It has synergistic effect with non-narcotic analgesic-like aspirin.

Adverse Effects

1. Respiratory depression
2. Drowsiness

Therapeutic uses

1. As an antitussive
2. To treat diarrhoea
3. As a opioid analgesic
4. As a sedative hypnotic
5. Also used in combination with aspirin.

Dose: 10–30 mg/day orally.

Brand names: Cosaka, Kefex, Glycodin.

b. Heroin

- Heroin is a diacetylmorphine.
- It is also known as dimorphine.
- Heroin is a semi-synthetic morphine derivative.
- It produces analgesic and respiratory depression.
- Analgesic effect of heroin is faster than morphine and it only lasts for 2–3 hours.

Adverse Effects

- Euphoria
- Drug addiction, drug dependance

c. Pethidine

- Pethidine is a synthetic narcotic analgesic.
- Pethidine has analgesic, sedative, spasmolytic and local anaesthetic action.
- Pethidine was discovered while looking for a spasmolytic with atropine-like effects.

Mechanism of Action

It depresses pain impulses by interacting with opioid receptors at the spinal cord level.

Adverse Effects

- Headache, sedation, drowsiness, dizziness.
- Euphoria
- Palpitation
- Blurred vision, miosis, diplopia, dryness of mouth.
- Nausea, vomiting, anorexia, constipation.
- Urinary retention, rash, urticaria.
- Respiratory depression.

Contraindications

- Hypersensitivity • Pregnancy and lactation • Respiratory depression.

Therapeutic uses

1. To relieve moderate to severe pains.
2. As a preanaesthetic medication.
3. As an analgesic during labour pains.
4. In treatment of morphine addiction as a substitute.
5. In the treatment of renal, biliary and intestinal colics.
6. In the treatment of pain in coronary thrombosis.

Q 5. What is euphoria? Name the drugs which produce this condition.

The condition of feeling of well-being is called euphoria. The drugs which produce euphoria are morphine, heroin, alcohol, etc.

Q 6. Give the difference between morphine and pethidine.

Morphine	*Pethidine*
• Absorption on oral administration is unpredictable. Administered by subcutaneous route	• Well absorbed on oral administration. Because of irritant nature, not administered by subcutaneous route
• Potent analgesic and narcotic	• Less potent analgesic
• Spasmogenic	• Spasmolytic
• Depress cough centre	• Does not depress cough centre
• Constrict pupil	• No effect
• Depress respiration in newborn hence, not useful to relieve labour pains	• Comparatively less depression of respiration, hence useful in labour pains

Q 7. Give the brand names, doses, route and major toxic effect of the following opioid analgesics.

Drug	*Brand name*	*Dose*	*Route*	*Major adverse effect*
1. Morphine	Morphitec	8–20 mg/day	Oral, SC, IM	Constipation, miosis
2. Codeine	Codicept, Glycodin	15–60 mg q.i.d.	Oral, SC, IM	Constipation, drowsiness
3. Pethidine	Meperidine, Demerol	300 mg/day	Oral, SC, IM	Sweating, dizziness, dryness of mouth

QUESTIONS: GIVE THE REASONS

Q 1. Why morphine causes constipation? OR Why tincture of opium is used in diarrhoea?

Morphine has spasmogenic action on smooth muscles of GIT.

i. It causes constriction of the sphincters and decreases in the peristaltic movements of GIT.
ii. This action of morphine results in stagnation of intestinal contents causing maximum absorption of water and drying of faecal matter.
iii. Morphine reduces sensitivity of intestinal walls to defaecation reflexes.
iv. The above actions of morphine cause constipation.
v. Tincture of opium contains morphine which possesses the constipating action. Hence, it is used in diarrhoea.

Q 2. In biliary colic, morphine is used along with atropine. Why?

Biliary colic means pains due to spasm of the biliary tract. To relieve the pains, analgesic drug morphine is used.

i. But morphine has spasmogenic action on the biliary tract which may aggravate the colicy pain.
ii. Hence, to relieve spasms, the antispasmodic drug-like atropine is used.
iii. These two drugs act synergistically in treatment of biliary colic.

Q 3. Morphine causes addiction. Why?

Morphine relieves severe type of pains associated with burns, fractures, parturition, terminal illness of cancer, myocardial infarction, etc.

i. When morphine is administered in absence of pain, it produces euphoria (false sense of well beingness).
ii. To experience the euphoria again and again individual develops habit.
iii. Tolerance to morphine is developed in the individual results in tendency to increase the dose to get the required euphoria.
iv. This eventually results in morphine addiction.

Q 4. Nalorphine (or naloxone) is used in morphine poisoning. Why?

Nalorphine is a rapidly acting drug, given parenterally to prevent the effects of morphine (opioids) poisoning.

i. It reverses the respiratory depressant, sedative hypotensive, analgesic and psychotomimetic effects of morphine.
ii. In the absence of morphine, it exhibits no pharmacological activity.
iii. Thus, nalorphine (or naloxone) acts as antagonist to morphine. Hence, nalorphine is used in morphine poisoning.

Q 5. A morphine addict is given methadone substitution therapy in hospital. Why?

Morphine is a narcotic analgesic having addiction liability.

i. Methadone is a synthetic compound having analgesic action equal to that of morphine.
ii. Methadone causes respiratory depression and constipation but it produces less euphoria and drowsiness than morphine.
iii. Methadone is slower in onset and longer in duration of action.
iv. Methadone suppresses the withdrawal syndrome in patients who are being withdrawn from morphine.
v. Methadone is effective orally and lacks hypnosis and addiction liability.
vi. Hence, a morphine addict is given methadone substitution therapy in hospital.

Q 6. Why morphine is not given in severe abdominal pain before diagnosis is made?

Morphine is narcotic analgesic which relieves pain without modifying the underlying pathological process.

i. It interferes with the diagnosis by masking pain and creates a false sense of security.
ii. It also induces vomiting.
iii. Its spasmogenic actions on the GIT and biliary tract are additional drawbacks.
iv. Therefore, morphine is not given in severe abdominal pain before diagnosis is made.

Q 7. Morphine is contraindicated in head injury. Why?

If morphine is administered in head injury, it further increases the intracranial pressure.

i. This masks the useful diagnostic and prognostic signs making management of the patient difficult.
ii. The effects of morphine such as respiratory depression, miosis and mental clouding also interfere with the diagnosis.
iii. Hence, morphine is contraindicated in head injury.

Q 8. Morphine is strictly contraindicated in children, old people and carrying women. Why?

Morphine if administered in children, may decrease the rate and depth of respiration because the systems in children are not properly developed to detoxify the drug.

i. In old people, morphine causes respiratory depression, bronchospasm and asthma.

ii. In carrying women, morphine may cross the placental barrier and depress the foetal respiration.
iii. Hence, it is strictly contraindicated in children, old people and carrying women.

Q 9. Pethidine is frequently employed as an obstetric analgesic. Why?

i. The advantage of pethidine as obstetric analgesic is its short duration which allows a better control on the level of drug.
ii. This reduces the risk of respiratory depression in the newborn.
iii. Pethidine causes relatively less respiratory depression in the newborn than does an equianalgesic dose of morphine.
iv. Pethidine lacks inhibitory action on uterine muscles. Pethidine does not suppress the cough reflex.
v. Hence, pethidine is frequently employed as an obstetric analgesic.

Objective Questions with Answers in Bold Letters

(Chapters: Antianxiety drugs, Antidepressants, Antipsychotics, Nootropics, Centrally acting muscle relaxants, Opioid analgesics).

1. Inability to sleep or lack of sleep means **insomnia**.
2. MAO inhibitors means **monoamine oxidase inhibitors**.
3. **Imipramine** is an example of tricyclic antidepressants.
4. Lithium carbonate is used as an **antianxiety drug**.
5. Librium is a popular brand name of **chlordiazepoxide**.
6. Meprobamate is an **anxiolytic drug**.
7. Depression is a **mental** illness, characterized by pathological changes in mood.
8. Nialamide and isocarboxazid are the examples of **MAO inhibitors**.
9. MAO inhibitors prevent oxidation of **catecholamine and histamine** in the brain.
10. **MAO inhibitors** potentiate the action of barbiturates, morphine and anaesthetics.
11. **Imipramine** is a dibenzazepine derivative used as a tricyclic antidepressants.
12. Imipramine is used to treat **enuresis**.
13. **Lithium carbonate** causes depletion of intraneural sodium and stabilises the neuronal membrane.
14. Lithium carbonate is contraindicated in **Addison's disease**.
15. Eating of **cheese** is forbidden in patients with MAO inhibitor therapy.
16. Schirophrenia means **'split mind' condition**.
17. Antidepressants are also known as mood **elevators/thymoleptics**.
18. Typical antipsychotic drugs act on dopaminergic system blocking the **dopamine type 2 (D_2) receptor**.
19. Chlorpromazine is a phenothiazine derivative used as **antipsychotic agent**.

20. Haloperidol is a **butyrophenone** derivative used as an antipsychotic agent.
21. Reserpine is a Rauwolfia alkaloid used as a **tranquillizer**.
22. **Chlorpromazine** is called 'Largactil'.
23. Antipsychotic action is due to competitive blockade of **dopaminergic receptors** in the limbic system.
24. Chlorpromazine **depresses CTZ** in the medulla and acts as a powerful antiemetic.
25. Chlorpromazine is adrug of choice in the treatment of **'schizophrenia'**.
26. Chlorpromazine is contraindicated in **pheochromocytoma**.
27. Reserpine is a principle alkaloid of '*Rauwolfia serpentina*' used in **snakebite**.
28. Reserpine produces depletion of **5-HT and catecholamines** from the brain and peripheral sites.
29. **Promethazine** is a drug used in the treatment of **motion sickness**.
30. Mania is a **bipolar** disorder.
31. Chlorpromazine is not effective in the vomiting of **motion sickness**.
32. Chlorpromazine produces **tranquillizing** effect.
33. **Reserpine** is not useful in immediate quietening or manic patients.
34. **Nootropics** are the supplementary drugs/substances.
35. Nootropics are called **'smart drugs'** that can boost brain performance.
36. Nootropics are sometimes called **'cognitive enhancers'**.
37. *Panax ginseng* and *Bacopa monnieri* are natural phytoconstituents used as **nootropics**.
38. Piracetam is a nootropic agent which is a derivative of **GABA (γ-amino-butyric acid)**.
39. Nootropics probably act by **changing the levels of neurotransmitters, hormones or enzymes**.
40. **Mephenesin, methacarbamol and chlorsoxazone** are central acting muscle relaxants.
41. **Mephenesin** was the first drug found to cause muscle relaxation without producing unconsciousness.
42. **Nystagmus** is an adverse effect of mephenesin.
43. Dolomed and Dolopar are the brand names of **mephenesin**.
44. The muscle relaxant properly of methocarbamol is due to its **sedative property**.
45. **Opioid analgesics** are also known as narcotic analgesics/true analgesics.
46. **Morphine** was the first opioid analgesic discovered.
47. Morphine has a **biphasic** effect.
48. Morphine produce **miosis (constriction of pupils)**.
49. **Morphine** decreases peristaltic movements and produce constipation.
50. Dryness of mouth and constipation are the major drawbacks of **morphine**.
51. **Naloxone and nalorphine** are the antidotes/antagonists used in the treatment of morphine poisoning/opium poisoning.
52. Methylmorphine is a chemical name of **codeine**.

53. The usual dose of codeine is **10–30 mg per day orally**.
54. Heroin is a **diacetylmorphine**.
55. Heroin is a **semi-synthetic** derivative of **morphine**.
56. **Pethidine** is a synthetic narcotic analgesic.
57. Pethidine depresses pain impulses by interacting with **opioid receptors** at the spinal cord level.
58. Constipation is the major adverse effect of **morphine**.
59. Morphine is contraindicated in **pregnancy and lactation**.
60. **Morphine** is used in the treatment of renal, biliary and intestinal colics.
61. The condition of feeling of well-being is called **euphoria**.
62. Glycodin is a popular brand name of **codeine**.
63. **Tincture of opium** is used in diarrhoea.
64. In biliary colic, morphine is used along with **atropine**.
65. Nalorphine or naloxone is used in **morphine poisoning**.
66. **Methadone** is a substitute of morphine.
67. **Morphine** is contraindicated in head injury.
68. Pethidine is used as an **obstetric analgesic**.
69. The dose of naloxone is **0.4–0.8 mg** repeated every 10–15 minutes as required.
70. Morphine stimulates **CTZ** and produces vomiting.