

**A WELL ILLUSTRATED PRACTICAL TEXT ON
SYSTEMIC PHARMACOLOGY AND THERAPEUTICS
(PHARM 302)**

Note Book

**Systemic Pharmacology and Therapeutics
(PHARM 302)**

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INTRODUCTION TO ANAESTHESIA (Reversible loss of consciousness)

Anaesthesia can be defined as:

1. The condition of having sensation block or temporary taken away.
2. Reversible lack of awareness (general anaesthesia) or a lack of awareness of a part of body (spinal/local anaesthesia).
3. Anaesthesia is a pharmacologically induced reversible state of amnesia, analgesia, loss of consciousness, loss of skeletal muscle reflexes and decreased stress response.

BRIEF HISTORY

- Anaesthesia came into use first time in 1840's when people start using morphine and opium in order to get the effects similar to the anaesthetics.
- In 1846's, Oliver Wendle Holmes – named the sedative agents as anaesthetics. He was the man who used this word first time.
- In the same era (1846's), William Mortin (a dentist) – used ether as anaesthetic first time.
- In 1847's, James Simpson used chloroform to get the anaesthetic effect and he succeeded.
- Local anaesthesia came on seen first time in 1877.
- Intravenous (IV) anaesthesia came on seen first time in 1920.
- Muscle relaxants were came on seen first time in 1920.

TERMINOLOGY

1. Analgesia:

It refers to the blocking of sensation of pain.

2. Amnesia:

It refers to the loss of memory.

3. Hypnosis:

Induction of sleep in order to produce a state of unconsciousness.

4. Paralysis:

It refers to preventing unwanted movements of muscle tone.

5. General Anaesthesia:

Drug induced loss of consciousness during which patients are not arousable even by a painful stimulation.

6. Deep sedation:

Drug induced depression of consciousness during which patients can not be easily aroused but can be respond to a painful stimuli.

7. Moderate sedation:

Drug induced depression of consciousness during which patient respond to verbal communication.

8. Minimal sedation:

Drug induced state during which patient respond to verbal commands but memory and coordination may be impaired.

9. Regional Anaesthesia

It can be defined as “the loss of pain sensation with varying degree of muscle relaxation in certain regions of the body”. E.g. spinal, epidural

10. Spinal Anaesthesia:

It is also known as “sub-arachnoid block”.

It refers to “ a regional block resulting from small volume of local anaesthetic being injected into the spinal cord”. The spinal cord is covered by dura meter and it contains CSF (cerebrospinal fluid) and spinal cord.

The sub-arachnoid block is usually injected between the 4th and 5th lumber vertebrae.

11. Epidural Anaesthesia:

It refers to “ a regional block resulting from an injection of a large volume of local anaesthetic into the epidural space”. The epidural space lies outside the dura meter.

12. Local Anaesthesia:

These are similar to the regional anaesthetics but they exert their effect on a smaller area of the body.

OBJECTIVES OF ANAESTHESIA

There are few fundamental objectived of clinical anaesthesia.

- a) Narcosis – depression of central nervous system (CNS)

- b) Analgesia – loss of pain sensation
 - c) Muscular relaxation – particularly of skeletal muscles.
 - d) Hypo-reflexia – loss of all reflexes.
-

CHARACTERISTICS OF AN IDEAL ANAESTHETIC

Some of the outstanding characteristics of an ideal anaesthetic are as follows:

- i) Rapid induction and rapid recovery
 - ii) High margin of safety
 - iii) Less irritant particularly to the respiratory system
 - iv) Free from toxic effects on vital organs
 - v) No explosion hazards
 - vi) It should fulfill all properties of anaesthesia.
-

SELECTION CRITERIA FOR AN ANAESTHETIC

- i. Type and duration of surgery
 - ii. Anatomical and physiological status of the animal
 - iii. Susceptibility: whether animal show desired response or over response
 - iv. Drug interaction
 - v. Respiratory status of the animal
-

INHALATION ANAESTHESIA

For inhalation anaesthesia, various kinds of gases and vapours of volatile substances are used.

Mode of action:

Inhalation anaesthesia → Alveolar level → Blood → Brain → crosses Blood Brain Barrier (BBB) → depress the CNS

Desired Properties:

1. Less irritant and less toxic
2. Free from bad smell
3. It should not promote capillary bleeding.

4. It must have greater margin of safety
5. It should be less explosive.

ADMINISTRATION OF INHALED ANAESTHETICS

Requirements:

- i. Compressed gas source
- ii. Pressure reducing valves
- iii. High pressure bearing tubes
- iv. Flow meter
- v. Vaporizer
- vi. Tubing for connection to patient
- vii. Endotracheal intubation

Techniques to administer Anaesthetic Agent

Basically, there are four techniques for the administration of anaesthesia:-

1. Open method
2. Semi-open method
3. Closed method
4. Semi-closed method

1. Open Method:

In this method, cotton swab is soaked in an anaesthetic agent and placed closed to the nostrils of the animal.

This method is usually used in small animals like rabbit, cat, rat etc.

Advantage:

- a) Easy to administer
- b) Simple instruments are required
- c) Minimal resistance in respiration and minimal rebreathing

Disadvantage:

- a) Wastage of anaesthetic agent
- b) Environmental pollution
- c) Not applicable for large animals

2. Semi-Open Method

In this method, animal exhale gas into the atmosphere, there could be partial rebreathing of exhaled gas and there is no CO₂ absorption in the exhaled gas.

It is used in the large animals.

3. **Semi-Close Method**

In this method, gases are partially exhaled to the atmosphere and partially are rebreathed. But there is chemical separation of CO₂ from the exhaled gas.

4. **Closed Method:**

In this method, the animal is cut off from the environment for respiration. The exhaled air is directed towards a separate chamber filled with CO₂ absorbing agent. CO₂ is reabsorbed and remaining air is circulated.

Advantages:

- a) No wastage of anaesthetic agent
- b) No environmental pollution
- c) Minimum gas flow is required

Disadvantage:

- a) Require advanced machinery
- b) There is a need to monitor animal very closely.
- c) Resistance to inhalation is more as compared to that in fresh air.
- d) There is conservation of heat in system so the temperature of the body is increased.
- e) There are chances of inhalation of CO₂ absorbing agent which can cause respiratory problems.

PREPARATION OF ANIMAL FOR ANAESTHESIA

1. History of the patient
2. Physical Examination of the patient
3. Biochemical and lab tests
4. Be prepare for untoward effects
5. You must know the duration of surgery
6. Fasting to the animal / patient
 - a. In small animals: 6-8 hours

b. In large animals: 10-12 hours

7. Pre-anaesthetic medication

Advantages:

- a) Helps in restraining of animal
- b) Useful to minimize the surgical pain.
- c) Used to decrease the quantity of general anaesthesia
- d) Helps in safe, easy induction and recovery
- e) Useful to minimize the autonomic reflexes of the body.

CLASSES OF PRE-ANAESTHETIC MEDICATION

1. Anti-cholinergic drugs:
e.g. Atropine, Hyosine etc.
2. Tranquilizers:
e.g. i) Phenothiazine derivatives like chlorpromazine (LARGACTIL)
ii) Propenidol derivatives iii) Benzodiapin derivatives
3. Morphine derivatives
4. Miscellaneous drugs
e.g. Ketamine etc.

LOCAL ANAESTHESIA

Local anaesthesia desensitizes a specific part of the body and not the whole body.

- o Cocaine was the agent which was used as local anaesthetic but later on banned due to its addictive properties.
- o Now a days, xylocaine, lignocaine, and procaine are commonly used local anaesthetics.

CLASSIFICATION OF

LOCAL ANAESTHETICS BASED ON MODE OF APPLICATION

1. Surface / Topical anaesthetics
2. Infiltration anaesthetics
3. Conduction or Nerve block
4. Para-vertebral anaesthetics

5. Epidural anaesthetics
 6. Refrigeration
 7. Potentiation → synergistic effect (adrenaline + 2% atropine)
-

Experiment No. 1

DEMONSTRATION OF SURFACE ANAESTHESIA IN RABBIT

Requirements:

Rabbit, local anaesthetic, scissors, cotton swab

Procedure:

- Take a rabbit and restrain it properly.
- Clip the eye lashes of both the eyes.
- Mark one as “A” and the other as “B”.
- Mark eye “A” as control eye and eye “B” as experimental eye.
- Put 2 drops of local anaesthetic i.e. xylocaine in experimental eye.
- Hold both eyelids together so that drug may absorb maximally.
- After two minutes, check the reflexes of experimental eye with cotton swab by touching cornea.

Observations:-

- Onset of anaesthesia = 3 minutes after putting the drops
 - Duration of anaesthesia = 8 minutes
-

Experiment No. 2

DEMONSTRATION OF INFILTRATION ANAESTHESIA IN RABBIT

Requirements:-

Rabbit, local anaesthetic, syringe, needle and common pin

Procedure:-

- Take a rabbit, clip hairs from back of the rabbit on the both sides.
- Mark two circular areas on the back of the rabbit.
- Keep area “A” as control area and “B” as experimental area.
- Inject local anaesthetic i.e. xylocaine subcutaneously in experimental area “B”.

- Two to three (2-3) minutes are given to drug to absorb completely and after that check the pricking response.

Observations:-

- Onset of anaesthesia = 2-3 minutes
 - Duration of anaesthesia = 25 minutes
-

STAGES OF ANAESTHESIA

There are four stages of anaesthesia as follows:-

Stage No. 1:- Voluntary Excitement / Stage of analgesia

- This stage lasts for initial administration of anaesthetic agent to the loss of consciousness. Epinephrine is released in this stage so various states occur that are excessive salivation, urination and defecation may occur.

Stage No. 2:- Involuntary Excitement / Stage of hallucination

- This stage lasts from the loss of consciousness to the onset of regular pattern of breathing. Crying in dogs and neighing in horses may occur in this stage.

Stage No. 3:- Surgical stage

- This stage is characterized by unconsciousness and progressive depression of reflexes. There would be muscular relaxation, respiration is slow down and regular (deep anaesthesia).

Stage No. 4:- Medullary paralysis

- In this stage, respiration centre which is located in the medulla depressed, so respiration can stop completely.
-

STAGES AND SIGNS OF GENERAL ANAESTHESIA IN ANIMALS

(Table 7; P:49)

Stages	I	II	III (Surgical Anaesthesia)				IV
Symptoms	Analgesia (Vol. struggling and excitement)	Delirium (Invol. struggling and Narcosis)	Plane I	Plane II	Plane III	Plane III	Medullary paralysis
Part of CNS depressed	Sensory cortex	Motor cortex	Midbrain & S.C.	S.C. depressed	S.C. more depressed	Medulla paralyze slightly	Medulla paralyzed
Respiration	Rapid deep with vol. holdings	Irregular invol. holding	Irregular, slower and shallower	Regular, shallow	Mostly abnormal	Abnormal	No respiration
Ocular Movements	Voluntary	++++	++++	Fixed	Fixed	Fixed	Fixed
Pupil size *	Dilated	Dilated	Slightly constricted	Dilated (+)	++	+++	++++
Conjunctiva	Normal	Normal	Normal	Normal	Normal or pale	Pale	Cynotic
Reflexes:							
- Conjunctival	+	+	-	-	-	-	-
- Corneal	+	+	+	+	-	-	-
- Pharyngeal	+	+	+	-	-	-	-
- Laryngeal	+	-	-	-	-	-	-
Muscle tone	Normal	Increased	Relaxation (+)	++	+++	++++	Nil

- = Total absence

+ = Slight action

++ = Moderate action

+++ = Strong action

++++ = Very strong action

S.C. = Spinal cord

* = No Pre-medication

ISOLATED HEART ACTIVITY OF RABBIT AND EFFECTS OF DIFFERENT DRUGS

Requirements:

There are four basic requirements to keep the heart alive outside the body.

- a) Energy
 - b) Electrolytes
 - c) Oxygen
 - d) Temperature
- Energy and electrolytes are provided via “Lock’s solution”.
 - Oxygen is provided by a oxygen cylinder.

Apparatus Name:

Heart perfusion apparatus

Technique Name:

Lagendroff’s technique

Procedure:-

- Prepare fresh “Lock’s solution and maintain it at 37 C and make it sure that sufficient oxygen has been diffused into it.
- Take a 200 ml beaker and pour sufficient amount of “Lock’s solution” into it and add few drops of heparin(anticoagulant) into it.
- Stun the rabbit by a forceful blow on the head & quickly open the chest cavity.
- The heart is then removed quickly and placed in a beaker containing heparinized Lock’s solution.
- Take the heart out of the beaker and insert glass canula of the apparatus into the lumen of the aorta.
- Tie a thread around the aorta to keep heart hanging from the aorta
- Wait for some time to set the heart again into its normal contraction and relaxation and then pass the common pin through the ventricles and connect it with chymograph.

EFFECTS OF DRUGS ON HEART

Four types of effects usually observed on the heart as follows;-

1. Inotropic Effect

- This refers to the increasing or decreasing the forceful contraction of the heart.
- Any drug which increases the force of contraction of the heart, has +ve inotropic effects and if it leads to decrease in force of contraction of heart, has -ve inotropic effect.

2. Chronotropic Effect

- This phenomenon related to the “speed of the heart beat or rate of contraction”.
- If any drug increases the rate of contraction then it has +ve chronotropic effect; but if a drug decreases the rate of contraction, then it said to be has -ve chronotropic effect.

3. Dromotropic Effect

- This phenomenon is related to “ the conduction velocity of the heart”.
- Heart intrinsically beat via electrical signal produced from the A.V node
- So, if any drug increases electrical signals to the heart, then we can say that it has +ve dromotropic effect and vice versa.

4. Lucitropic Effect

- This phenomenon is related with the relaxation of heart muscles. If any drug increases the relaxation in the heart muscles, then it have =ve lucitropic effect but if drug has suppressed effect on relaxation of the heart, then it said to be has -ve lucitropic effect.

Precautions:-

- i) Heart being a very delicate organ, requires gentle handling.
 - ii) Extra care should be made / taken while inserting a pin into ventricles.
 - iii) The pin should be inserted only when the experiment is to be started.
 - iv) Ringer’s solution should be used very frequently to prevent heart from drying.
 - v) The components of Lock’s solution should be measured accurately and prepared freshly.
 - vi) Oxygen supply should be continuous.
 - vii) The perfusion fluid going to heart should be free from air bubbles.
 - viii) There will be sufficient length aorta (1-2 cm) which will facilitate to tie the aorta with the glass canula.
-

EFFECT OF AUTONOMIC DRUGS ON THE EYE OF A RABBIT

Requirements:-

Autonomic drugs, rabbit, dropper, scissors, cotton swab.

Procedure:-

- Clip the eye lashes of both eyes and observe the size of the pupil of both eyes.
- Keep one eye as “control” and the other as “experimental”.
- Put 1-2 drops of drug in the conjunctival sac of “experimental eye” and close it for 1-2 minutes for proper absorption of the drug.
- Observe the size of the pupil of experimental eye and compare it with that of control eye.

Observation

- i) Cholinergic drug (e.g. pilocarpine) causes constriction of the pupil
 - ii) Anti-cholinergic drug (e.g. atropine) causes dilatation of the pupil.
-

EFFECT OF AUTONOMIC DRUGS ON

1. Respiration rate of the dog

2. Blood pressure (BP) of the dog

Requirements:-

Surgical table, surgical kit, pentothal Na⁺ (General Anaesthetic), normal saline, Na⁺ citrate (5% sol.), syringe, needle, thread, chymograph, autonomic drugs, mercury manometer, pressure bottle, bull dog clamp, rubber tubing, animal (i.e. dog)

Procedure:-

- Anaesthetized the animal by Pentothal Na⁺ (dosage: 18-20 mg/kg b.wt)
- Put the animal on dorsal recumbency on table.
- Tie the legs of the dog on table and perform cannulation.

1. Tracheal Cannulation:-

- Find the trachea by just palpating the ventral aspect of the neck of the dog.
- Expose it by cutting subcutaneous muscles and skin. Retract the trachea and pull it little upward.
- Give V-shape cut between two cartilaginous rings of trachea.

- Insert the pointed end of canula by removing the flap and tie the canula to fix it in the trachea.

Significance:-

- i) To facilitate the breathing
- ii) To record the respiration rate

2. Femoral vein Cannulation:-

- Femoral vein is located on medial aspect of the thigh.
- Place the finger and feel the pulse.
- Give incision and cut the sub-cutaneous muscles.
- Artery is found superficial and vein is just below it. Take the vein and put ligations at the upper and lower part just to make the region blood-free.
- Cut the one wall of the vein and insert the canula in it and pass the thread underneath the vein and tie the canula and then open the ligations.

Significance:-

- i) To administer intravenous (IV) compensatory fluid if blood has been lost
- ii) IV anaesthetic agent could be given.
- iii) IV drugs could be given and we can note the blood pressure of animal (dog)

3. Carotid Artery Cannulation

- Carotid sheath contains carotid artery, which is present along side of trachea.
- From the same cut which was made for the tracheal cannulation will be used to locate the carotid artery.
- For locating carotid artery, insert the finger deep in the throat region. Feel the pulse and palpate the structures around the trachea.
- As it is a major artery, thus has a stronger pulse.
- Alongside of the trachea, carotid sheath is present which is composed of carotid artery, vein and a nerve.
- Tear the sheath, and separate the artery, vein and the nerve.
- Give permanent ligation on artery towards the head side and temporary ligation by bull dog clamp on the lower side.
- With the help of a scalpel, cut one wall of the artery and insert canula into it.

- Fix it with the help of a thread.

Significance:-

- i) To record the direct blood pressure

Reference Fig. Set apparatus for Recordings of Blood Pressure via C.A. cannulation

<Here a fig. must be drawn>

How to Record Blood Pressure?

- After cannulation, fill the U-tube with the mercury. One side of the tube is attached with the writing device (or recorder)
- Now, fill the Na-citrate 5% solution in the pressure bottle.
- Apply it to wash the system, 2-3 times to ensure that there is no air bubble.
- Blood exerts pressure, then writing device will move up (systolic pressure) and down (diastolic pressure) as clamp is moved.
- The results will be in graphical form.

-----THE END

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