General Anesthesia in Lab. animals

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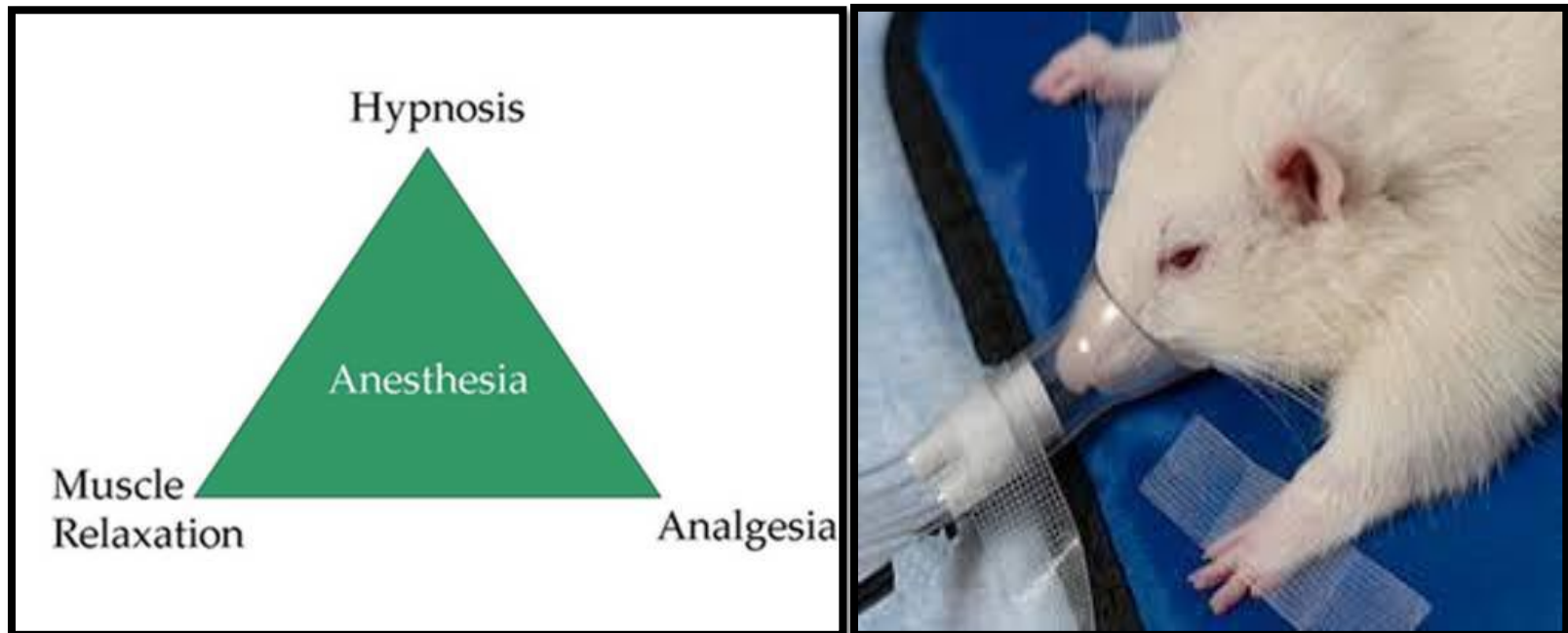
Anesthesia
WHAT DOES THE WORD MEAN?

- **Anesthesia** = **without** **sensation**

- an = without, aestos = sensation

- A <u>controllable and reversible condition</u> in which sensory perception and motor responses are **both** markedly depressed

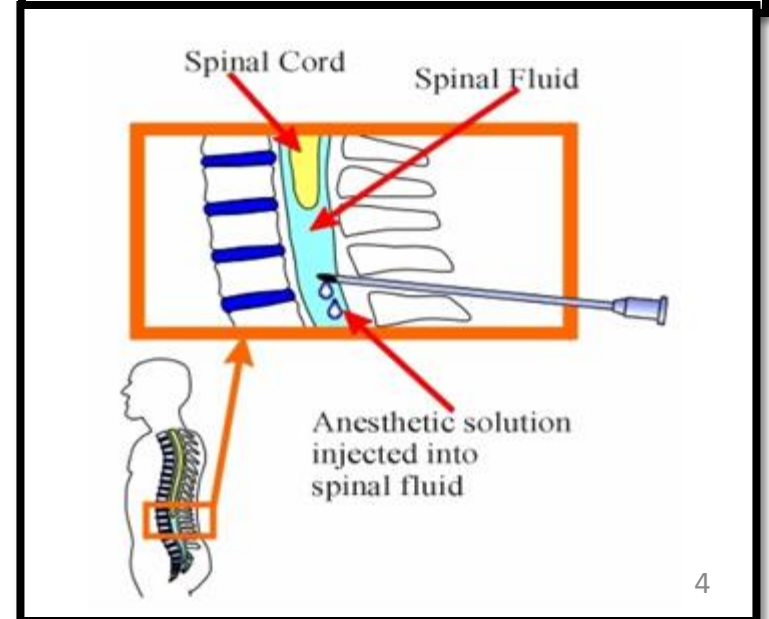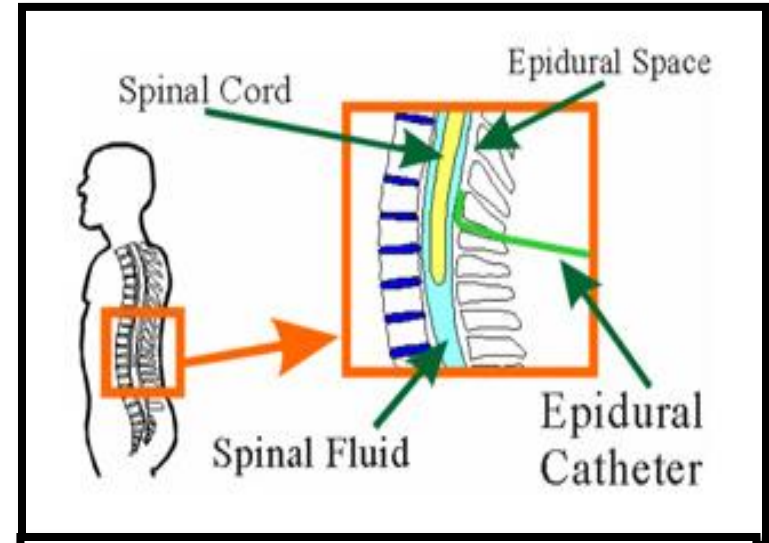**General Anesthesia**: **Loss of consciousness in addition to loss of sensation**

• **Analgesia**: **Loss of sensitivity to pain.**

•**Sedation:** A state of **mental calmness**, decreased response to environmental stimuli.

Types Of Anesthesia

1. **General Anesthesia**

2. **Regional Anesthesia** – Including

Epidural, **Spinal** and **Nerve Block** Anesthesia

3- Combined General and Epidural Anesthesia

4- Monitored Anesthesia Care with Conscious Sedation

https://www.macllp.com/patient-education/different-kinds-anesthesia#general

The Ideal Anesthesia

- ✓ Reversible and controlled - **loss of consciousness.**
- ✓ "No" mortality
- ✓ Undisturbed physiology/vital functions, Minimal homeostatic changes
- ✓ Optimal conditions for surgery
- ✓ Relief of pain, stress and discomfort
- ✓ Easily administered
- ✓ Economic

Inspection Before Anesthesia

- Check the animals (sick ,...

- Acclimatization (period of adaptation to anew climate is needed to allow animals to – Recover metabolic and hormonal changes caused by transport stress – adaptation to new environment, staff and routine)

- Fasting (not necessary need in mice and rat)

- Pre-medications

Pre- medication

- ↓Fear, provide sedation and stress free induction to anesthesia

- ↓ Reduce amount of anesthetic drug

- ↓ Volume of salivary and bronchial secretions

- ✖ Block " vaso-vagal effect"

- ↓ Preoperative pain and minimize post operative pain

Pre- medication

- **Anti-cholinergic drugs**: – Reduce bronchial and salivary secretions – No vagal reflexes, less gut motility – Correct slow heart rate. Ex : Atropine

- **Sedatives**: – Sedation, potentiate anesthetics EX: Phenothiazines , Benzodiazepines

- **Analgesic agent** –analgesic effect EX: Xylazine

Preanesthetic Considerations

Anesthesia of small laboratory animals is particularly challenging due to the following problems that relate to their small body size:

- ❖ Hypothermia
- ❖ High metabolic rate ، and lack of reliable clinical signs of respiratory and cardiovascular functions.

Because hypothermia is potentially lethal, **preservation of body heat is an integral part of anesthetic management** (Ex. use hot plate or warm blanket)

The sex of mice influences the pharmacokinetics and metabolism of anesthetics probably due to differences in **plasma corticosteroids ،**
hormones ،
or hepatic enzymes.
As an example, a higher dose of ketamine is recommended for female mice compared with that for males.
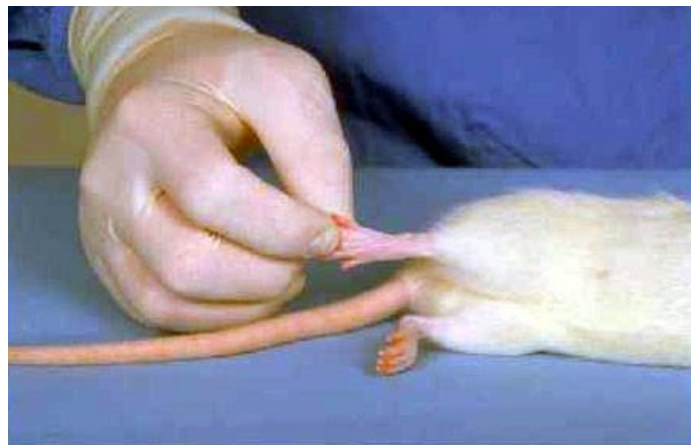
Injectable Anesthesia

- In mice, injectable anesthetics can best be administered via IP, IM, and IV routes.

- The injection volume should be carefully considered according to the available route:

- adequate volumes by

- range from **(0.1 to 1mL) IP**,

- (**0.05 to 0.2 mL) IV,**

Assessment of Anaesthetic

- Depth: assessment of anaesthetic depth
- Tail pinch and
- Pedal reflex
- Ear pinch

Barbiturate (anesthetic drug) Sedation ----hypnosis --- anesthesia

Class of drugs that act as CNS depressants, and can therefore produce a wide spectrum of effects, from mild sedation to total anesthesia

They are also effective as **anxiolytics, hypnotics, and anticonvulsants**

Barbiturates also have analgesic effects, however these effects are somewhat weak.

- **Long acting Barbiturates , ex.** **Phenobarbitone**

- **Short acting Barbiturates, ex.** **Pentobarbital**
- **3-8 hr.**

- **Ultra short acting Barbiturates, ex. Thiopental**
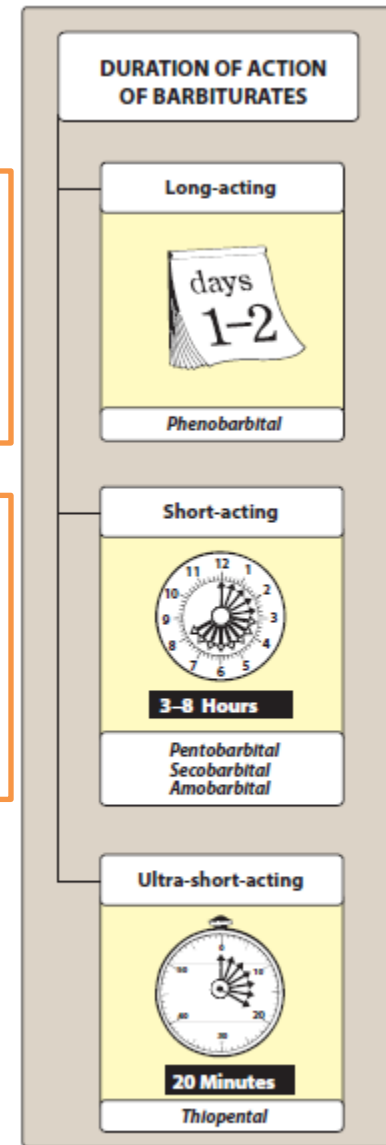- **10-20 min.**

DURATION OF ACTION OF BARBITURATES

Long-acting

days 1–2

Phenobarbital

Short-acting

3–8 Hours

Pentobarbital
Secobarbital
Amobarbital

Ultra-short-acting

20 Minutes

Thiopental

Figure 9.8
Barbiturates classified according to their durations of action.

Mechanism of action

Enhance binding of GABA (Gama -aminobutyric acid) with its receptors, prolonged opening
of the Chloride channel (influx of Cl) → **hyperpolarization**.

Block the AMPA receptor, a subtype of glutamate receptor,
Leading to decrease the activity of excitatory glutamate neurotransmitter.

GABA site

Barbiturate site

Cl⁻
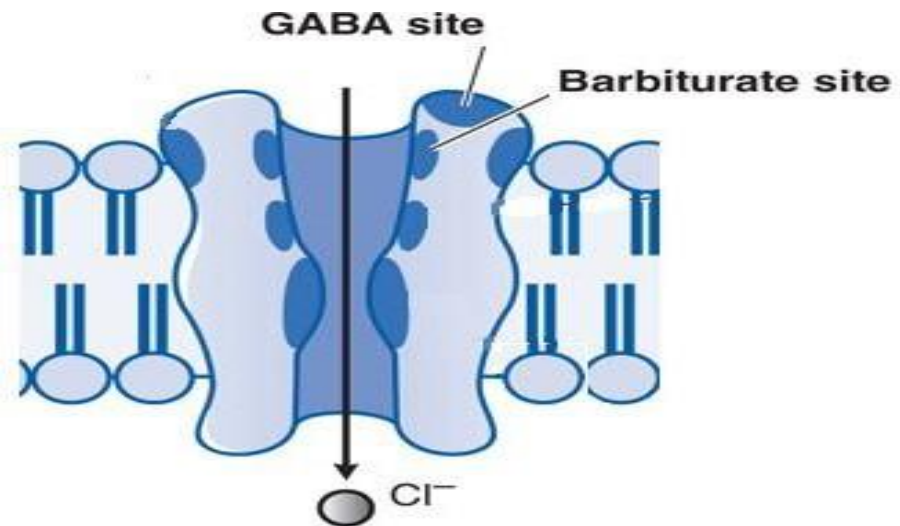
Pharmacokinetics High lipid solubility →Cross BBB
rapid onset Redistribution to other tissues Short duration of action

Experiment protocol

Six mice are injected with Thiopental (three of them By Sc. route and other three by IP route.

Thiopental dosage form :1 gm vial
Thiopental dose in mice:
Thiopental 30 – 40 mg/kg IP.

Pentobarbital dosage form:
1000mg/20ml ampoule
Pentobarbital dose in mice:
Pentobarbital 50-90 mg/kg IP

Calculate Your Dose

- The **dose** is the amount of drug taken at any one time .

- **Weight of drug**(e.g. 250 mg)

- **Volume of drug solution** e.g. 10 mL, 2 drops…

- **The number of dosage forms** (e.g. 1 capsule, ..

- **The dosage regimen** is the frequency at which the drug doses are given. Ex. 2.5 mL twice a day, one tablet three times a day …

- Accurate dosing is critical for the proper utilization of all pharmaceuticals.

- First you need to know what volume you want to inject into the animal with each treatment being administered, then you need to know how much drug should be in that given volume

To calculate the correct dose of drug you need to know

- The **concentration** of the drug
- The **weight** of the animal
- The recommended **dose rate** of the drug for each specific animal model

Concentration of the drug

•mg/ml: Manufacturers usually provide concentrations of their product in milligrams (mg) of drug per (ml) of solvent.

10 % ➡ solution of Drug A is **10 gm/100ml،**

2 % ➡ solution of Drug A is **2gm/100ml = 20 mg /ml**

• IU/ml: International Units per ml of, like some of the fat soluble

vitamins

•powders: The mg of active drug in the vial. For example, Drug B comes in powdered form with 500mg per vial:

•If you add 5ml of sterile water for injection to the vial thus providing 5ml of 100mg/ml drug

•If you add 2.5ml of sterile water for injection, will make 2.5ml of a 200mg/ml solution

Weight of the animal

• It is always best to use a scale and get an accurate weight

• If you cannot weigh the animal prior to injection, you need to be experienced in estimating the weight.

Dose rate of the drug

• Always look up the drug dose for the species you are working with -it often varies

Calculate Your Dose Practice

•For most applications the following formula is applicable :

$(C1)(V1) = (C2)(V2)$

•Q- Ex. You have 20 ml of a 10 mg/ml solution and you want to make
 15ml of a 2.5 mg/ml solution.

Set up the math as follows:

C1 = 10 mg/ml C2 = 2.5 mg/ml V1 = unknown V2 = 15 ml

(10mg/ml) (V1) = (2.5 mg/ml) (15 ml)V1 = 3.75 ml

So you dilute 3.75 ml of C1 to a final volume of 15 ml therefore you need to add =11.25 ml of diluent

Q- How to administer xylazine at a dose rate of 10mg/kg to a 300 g rat?

You are using 2% xylazine.

The proper dose for a 300g rat is: 10mg/kg x 0.3kg= 3mg of xylazine2% xylazine is 20 mg/ml

3mg /20 mg/ml = 0.15 ml of 2% xylazine

Experimental protocol

- Barbiturates are hypnotic drugs

- Onset of action is the time required to loss the righting reflex

- Duration of action in mice can be measured by the 'sleeping time' (i.e. the time from the loss of righting reflex to recovery of reflex)

Parameters	
General Activity	
Characteristics of Breathing	
Onset of Sleep (min.)	
Duration of Sleep (min.)	

Experimental protocol

The **loss of righting reflex (LORR) assay** was used to evaluate sedative/hypnotic effects Righting reflex the ability to assume an optimal position when there has been a departure from it

The onset time of sleep was noted for all animals. After induction of sleep, mice were placed in the inverted position and when sedation was over, the mice came to **normal posture** and time was noted Record:

• LORR was recorded as the time at which the animal was unable to turn itself (onset of action)

• The time to regain the righting reflex (duration of action)

Results
Report

Discussion: mention and discuss your results, for example:
•From the results obtained, we noted that onset of action was faster in IP than SC route. This is due to…..etc.