LAB 8 : BARTURATES

Assist. Lecturer:
Safa Hameed Mohsin

Terms To Learn

Anxiolytic : is a drug that reduces anxiety.

Sedative: is a drug that decrease activity, moderate excitement & calms the patient.

Hypnotic : is a drug that produces sleep-resembling normal sleep.

General Anesthetic : a drug that causes loss of consciousness associated with absence of response to pain

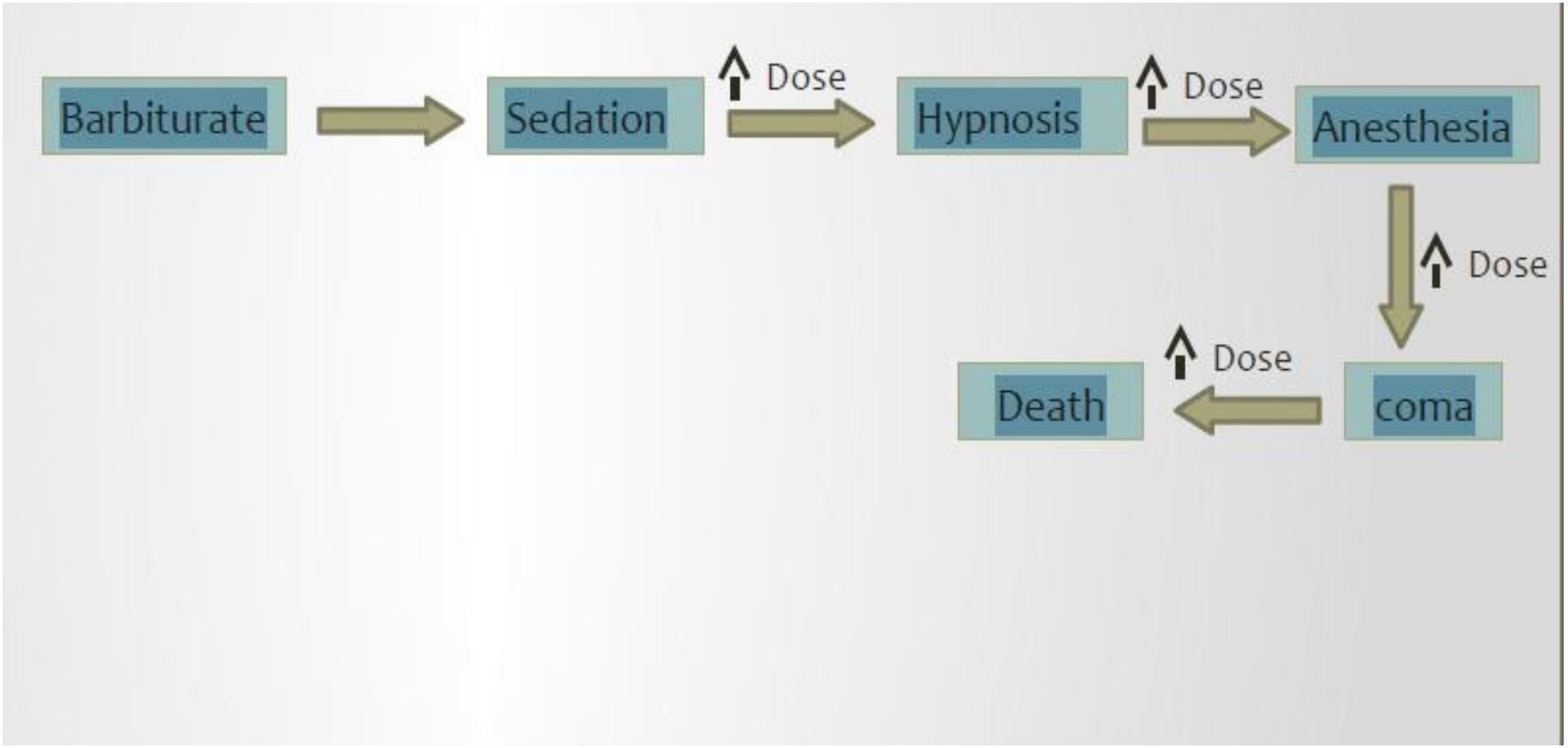
Sedative-Hypnotic Drugs

- **The sedative-hypnotics**: produce dose-dependent CNS depressant effects.

- **Sedative:** is a drug that decrease activity, moderate excitement & calms the patient.
- **Hypnotic drug:** is a drug that produces sleep-resembling normal sleep.

- EX: **Benzodiazepines**, **Barbiturates** &**miscellaneous agents**

CNS depressant effect of Barbiturates



Mechanism of Action

- **Barbiturates**: facilitating and prolonging the inhibitory effects of GABA receptor.
- **Barbiturates**: bind to multiple isoforms of the GABA A receptor
- **Barbiturates**: increase the duration of GABA-mediated chloride (influx of Cl ion) channel opening (hyperpolarization)
- **Barbiturates**: may also block the excitatory transmitter glutamic acid, and at high concentration, sodium channels.

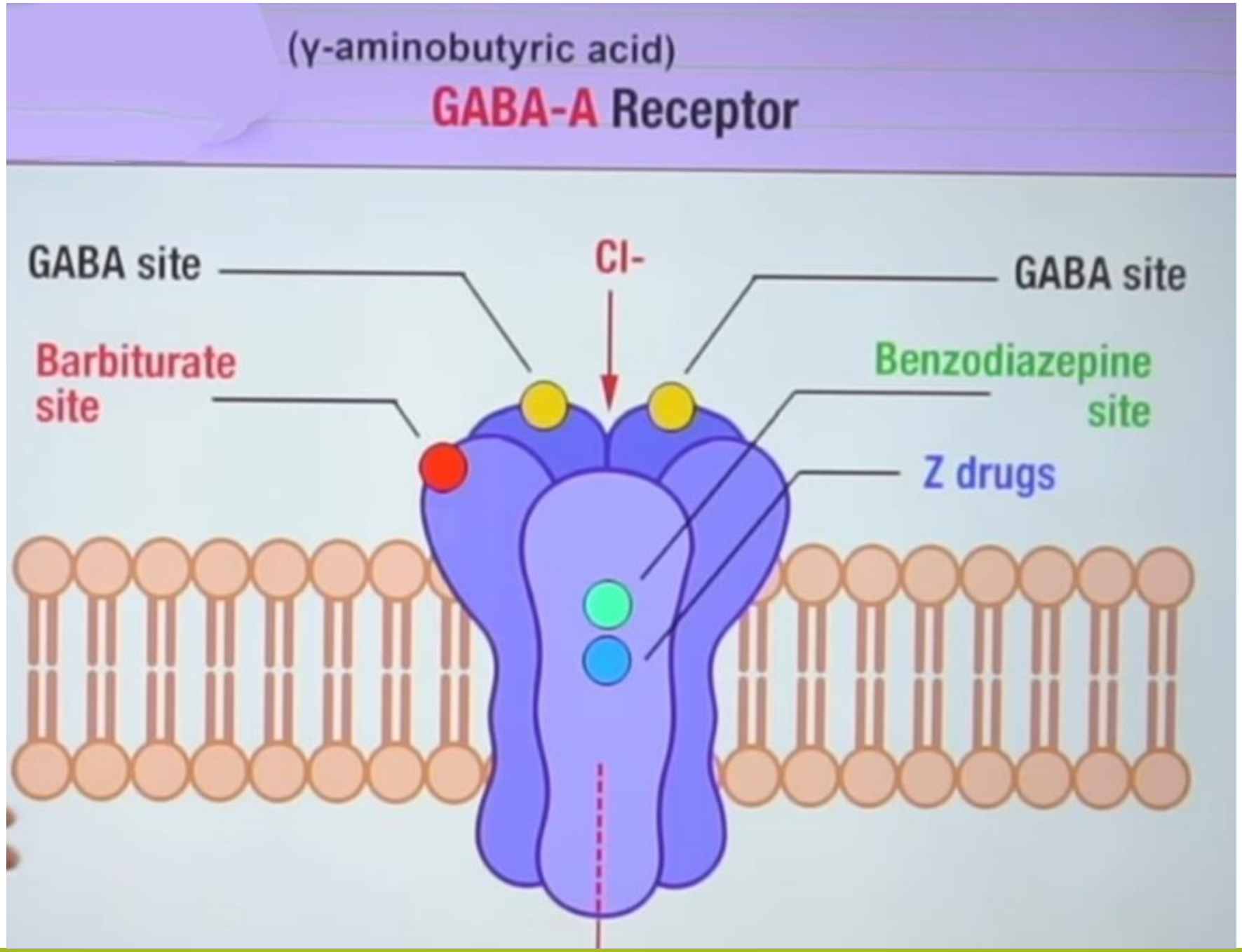
Barbiturates + GABA receptor

Activation of GABA receptor

Opening of Chloride channel
Increase the duration of GABA gated channel opening

Hyperpolarization of cells

CNS depression


(γ-aminobutyric acid)
GABA-A Receptor
GABA site
Cl-
GABA site
Barbiturate site
Benzodiazepine site
Z drugs

Barbiturates

Advantages:

- Rapid anesthetic onset;
- Provides a prolonged duration of surgical anesthesia.
- Can be a sedative.
- Anesthetic agent depending on the dose

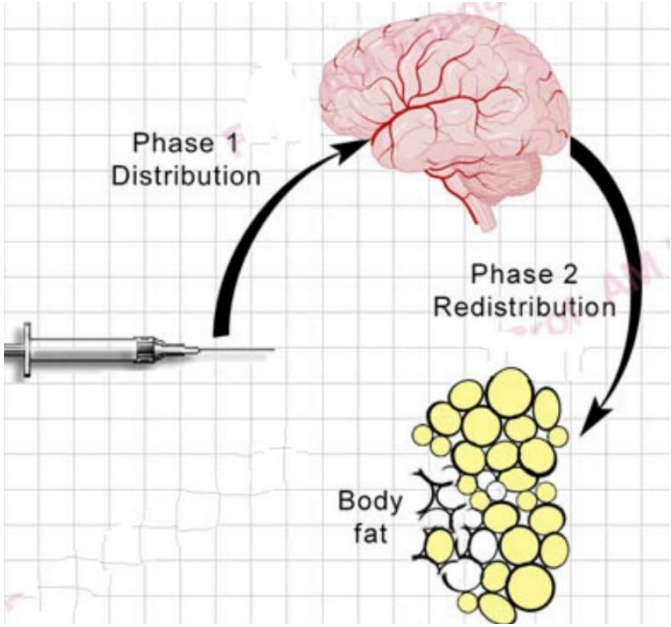
Disadvantages:

- Prolonged recovery time.
- inadequate analgesic properties.
- extremely expensive.
- narrow margin of safety.
- produces respiratory depression at higher dosages.
- Potent inducer for liver metabolizing enzymes.
- They have addiction potential, both physical and psychological.

Pharmacokinetics

- **High lipid solubility → Cross BBB → rapid onset**

- **Redistribution to other tissues → Short duration of action**

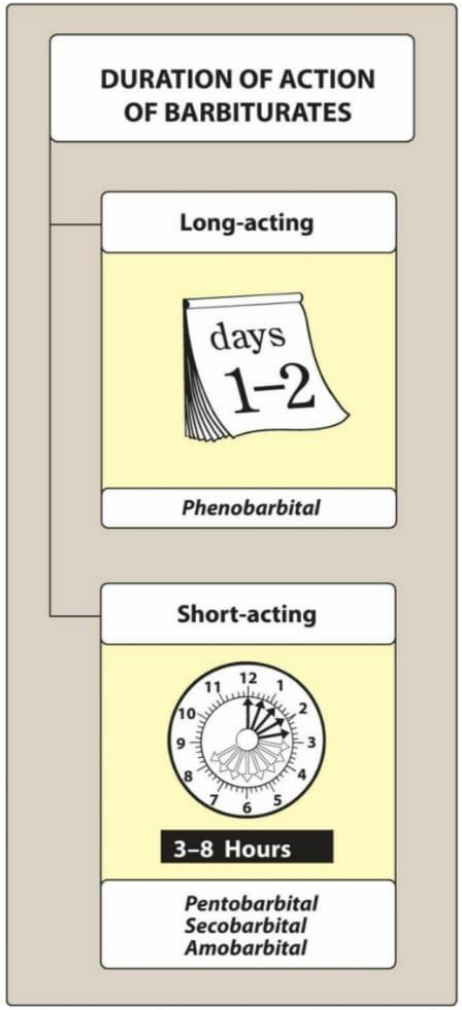


Barbiturates

Thiopental: ultra short acting

Secobarbital: short action

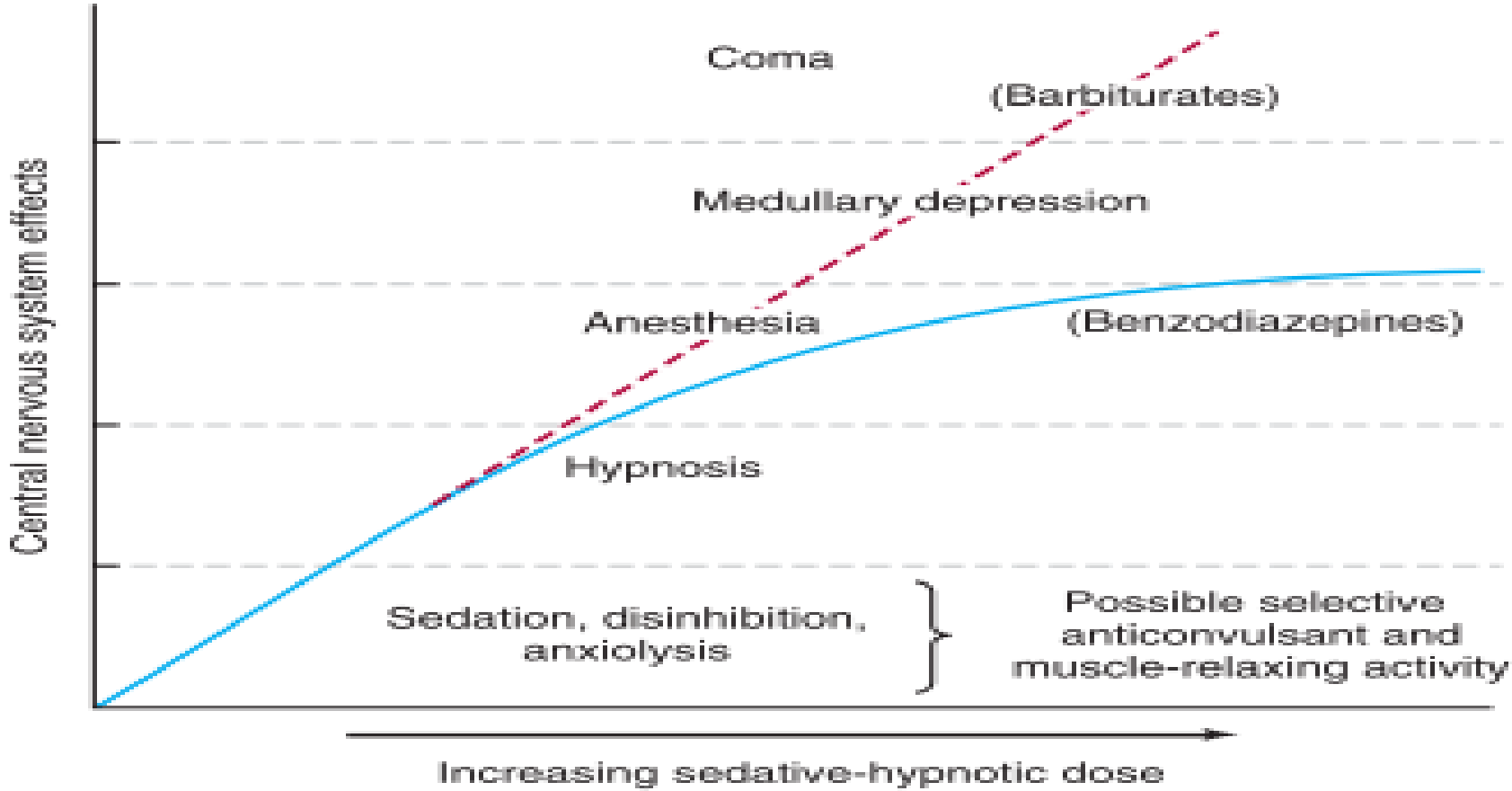
Phenobarbital: long acting



Clinical Applications

- Anesthesia (**thiopental**)
- Insomnia and sedation (**secobarbital**)
- Seizure disorders (**phenobarbital**)

CNS depressant



Adverse effects

- Drowsiness, severe respiratory & cardiovascular depression.
- Tolerance
- Dependence liability> benzodiazepine
- Enzyme induction may lead to multiple drug interactions
- Withdrawal symptoms is much more sever than opioid and can results in death (no antidote).
- C.I. in pregnancy

- **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**

1- 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 10gm/100ml, a 2% solution of Drug A is 2gm/100ml (20mg/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

2- 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

3- Dose rate of the drug

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

Practice

•For most applications the following formula is applicable:

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

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

(10 mg/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 15 - 3.75 =11.25 ml of diluent

•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: 10x0.3kg= 3mg of xylazine

2% xylazine is 20 mg/ml

3/20=0.15 ml of 2% xylazine

Methods

1- Check the weight of two mice / rats.

2- Inject one animal with normal saline I.P and mark it as control, and another animal with Phenobarbital I.P or S.C in a dose of 50 mg/kg.

3- Inject one animal with normal saline I.P and mark it as control, and another animal with Thiopental I.P or S.C in a dose of 30 mg/kg.

4- Record the observations and time of occurrence in a table form.

Group Number	Drug	IP (mouse #1)		Sc (mouse #2)	
		Onset of action (LORR)	Duration of action	Onset of action (LORR)	Duration of action
Subgroup 1	Thiopental				
Subgroup 2	Thiopental				
Subgroup 3	Thiopental				
Subgroup 4	Phenobarbital				
Subgroup 5	Phenobarbital				
Subgroup 6	Phenobarbital				

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.