Introduction to Laboratory of Pharmacology

Routes Of Drug Administration

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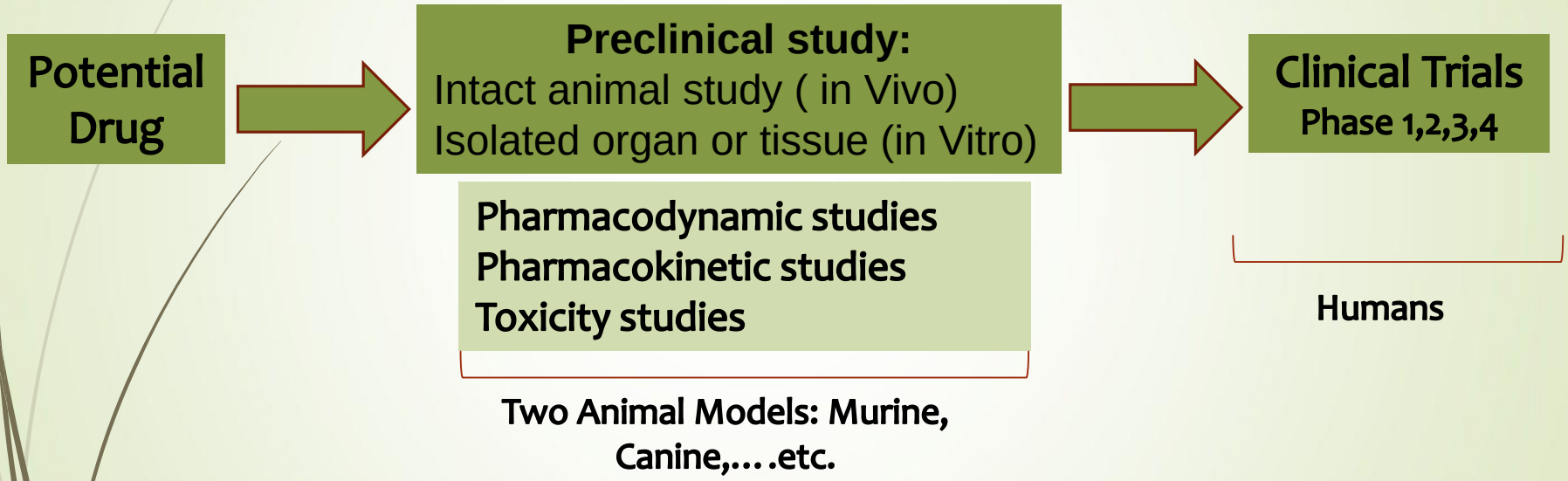
Laboratory of Pharmacology

- Pharmacological experiments are designed to study the effects of drugs on tissues, organs, and other living subjects
- Find out new therapeutic agents
- Study the mechanism(s) by which the drug interact and affect the targets
- Clinical Trials: Study the effect (s)/side effect (s) of drugs on humans

Significance of Pharmacological studies

- **Drug Development:**



- **Evaluating and Exploring doses, mechanisms, side effects,… etc.**

The Institutional Animal Care and Use Committee (IACUC)

- are centrally important in applying laws about animal research in the United States
- The NIH Office of Laboratory Animal Welfare (OLAW) has been directed by law to develop policies that describe the role of Institutional Animal Care and Use Committees.

Laboratory Animals

Rats were first used for experimental purposes in the mid 1800s

Carefully bred rats are used in animal testing for a number of reasons, including their frequent reproduction, genetic purity and similarities to human biology

Lifespan	2.5-3.5 years
Adult weight	M 300-500g, F 250-300g
Birth weight	5-6g
Heart rate	330-480 beats/minute
Respiratory rate	85 breaths/minute
Body temp.	35.9-37.5°C

Rats

Rats are generally fed a diet containing low fiber, protein and fat

Rat rooms are usually maintained at 30-70% relative humidity and a temperature of 18-26°C

Rats should be adapted to handling to reduce stress

Blood can be collected from several sites in the rat including tail vein, retro-orbital sinus, vena cava or cardiac puncture

Can receive oral, IP, IM, and IV

Laboratory Animals

Mice

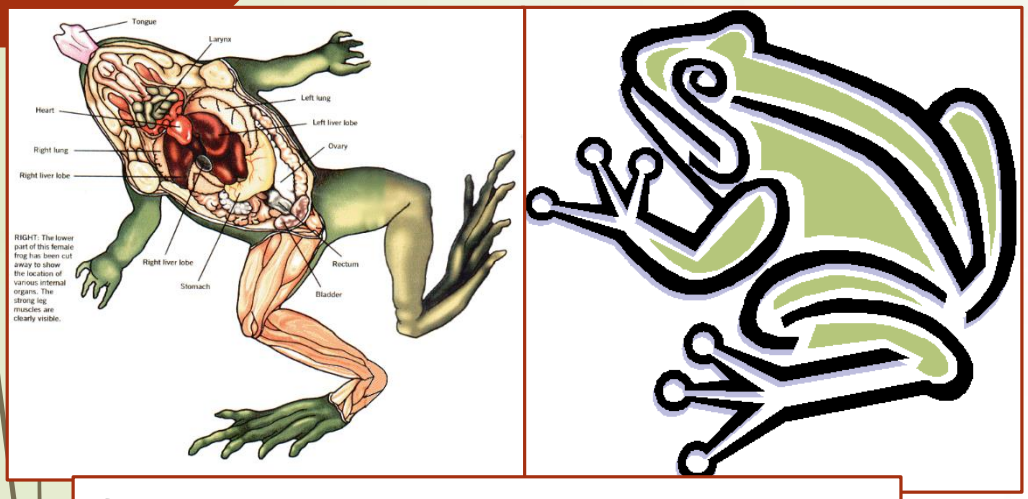
The mouse and human genomes are about 85 percent the same, and those similarities have made the mouse a powerful model for studying human biology and disease

Handling, blood collection, and drug administration: same as rats

Lifespan	1-3 years
Adult weight	M 20-30 g, F 18-35g
Birth weight	1-2 g
Heart rate	310-840 beats/minute
Respiratory rate	80-230 breaths/minute
Body temp.	36.5-38°C

Easy to make disease models

Laboratory Animals



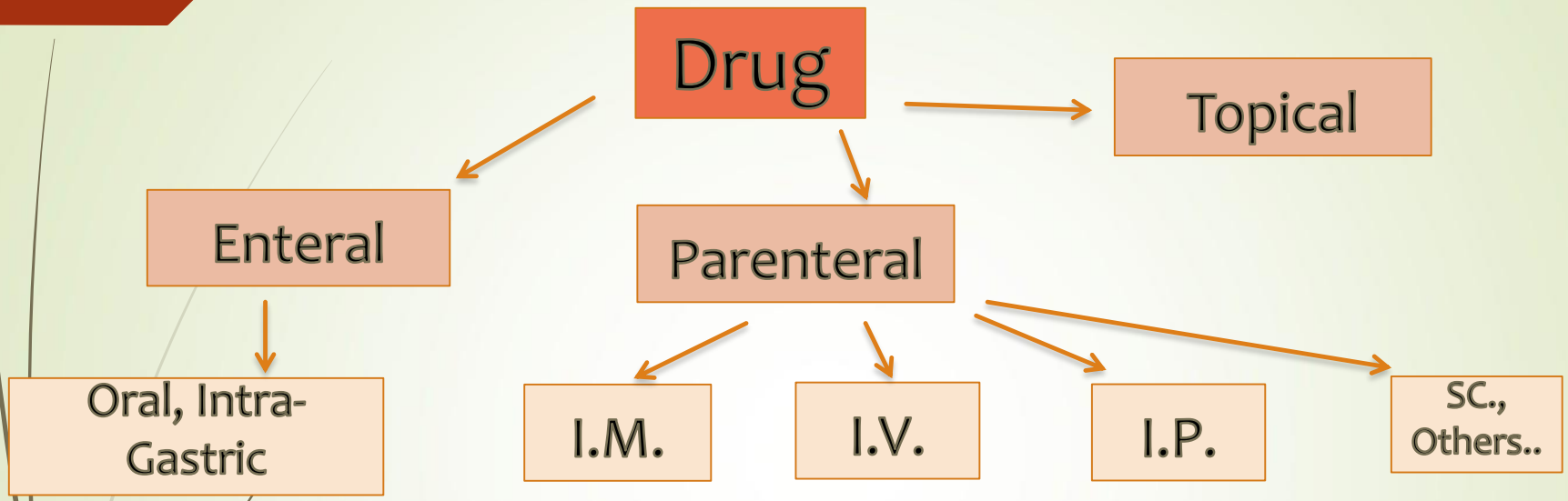
frog or toad: physiological studies

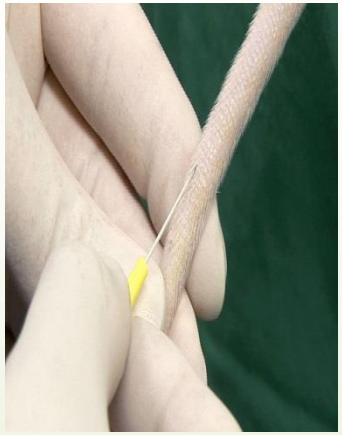
guinea pig: hypersensitive test (allergic reaction) or the screening of anti-asthmatic drug

Rabbit: Expensive, the effect of some drug

Other: Cat, Dog, pig, and Monkey

Routes of Drug Administration





Enteral Route of administration

Placement of drug directly into any part of the GIT

It could be Oral, Sublingual ,Intragastric gavage, or Rectal.

1- Oral : Swallowing a drug through mouth, It may be done by adding desired drug to the drinking water or to the food

- The oral route is economical, convenient, relatively safe, and some animals can be trained to cooperate voluntarily, depending on the compound being administered
- This route is not preferable since it inaccurate

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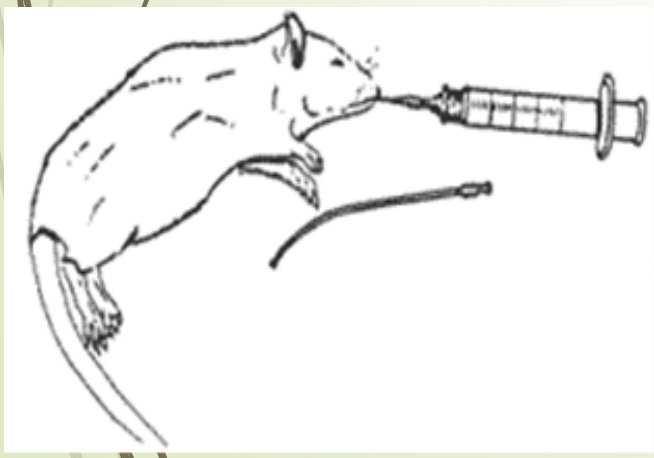
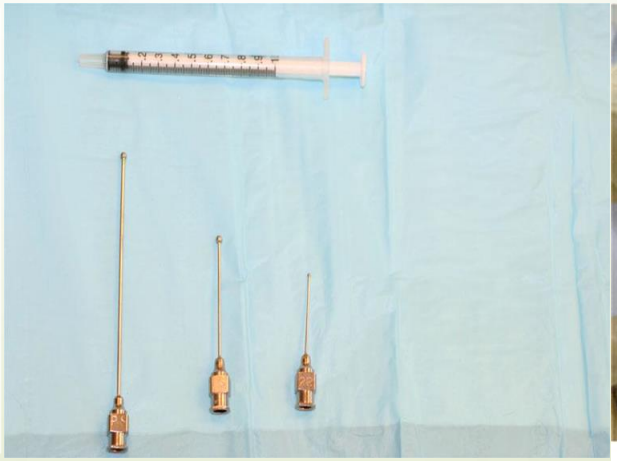
Routes of Drug Administration

Enteral Route of administration

2- Intra-gastric gavage: is the administration of fluids directly into the lower esophageal or stomach.

- Gavage is often used in research settings, instead of mixing substances in water or food, to ensure accurate dosing of animals.
- A small, curved, metal tube, usually with a ball on the end (feeding needle) is often used with small rodents. Entrance may normally be obtained without anesthesia using ordinary hand restraint and the ball prevents trauma to the esophagus and oral cavity.





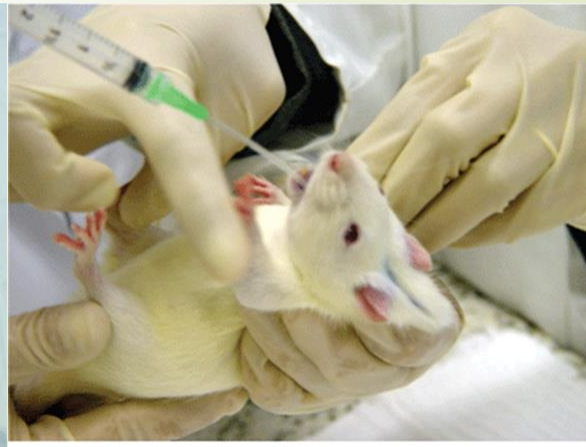


Figure 1 - Administration of DMBA by gavage.

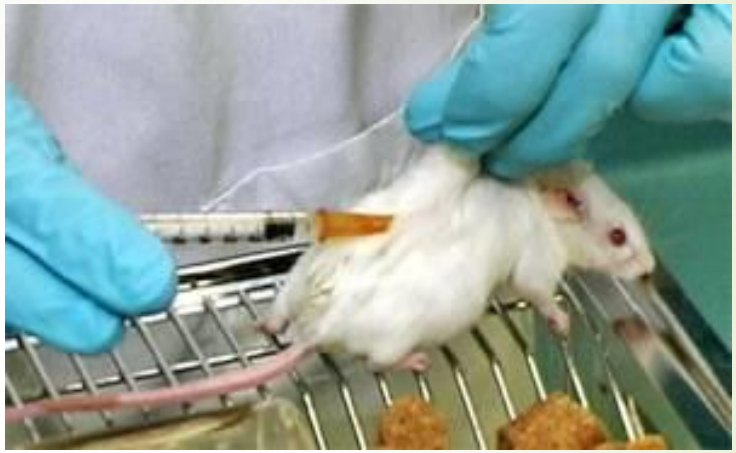
Parenteral routes of administration

- Routes other than Enteral are called Parenteral routes of administration
- Parenteral administration methods typically produce the highest bioavailability of substances because these methods avoid the first-pass effect of hepatic metabolism.

- **1- Intravenous (IV**) directly in the vascular system through a vein
- **2- Intraperitoneal (IP**) - injected into the abdominal cavity
- **3- Intramuscular (IM)** injected into a muscle
- **4- Subcutaneous (SC**) injected under the skin
- **5- Intradermal (ID**) - injected between the layers of the skin
- **6- intracerebral(IC)-** injected into the brain
- **7-Epidural :** injected into the epidural space of the spinal cord
- **8-Intranasal:** sprayed into the nose for absorption across the nasal mucou
- **9- Inhalation:** Inspiration through nose or mouth
- **10-Intra-articular:** injection directly into the joint space

1-Subcutaneous (SC) injections

- The best spot to inject Subcutaneously is the loose skin on the back of the neck
- A mouse may easily be injected by one person, whereas a rat may require restraint by one person and injection by the other
- Not suitable for large volumes. Suitable for some insoluble suspensions



Procedure

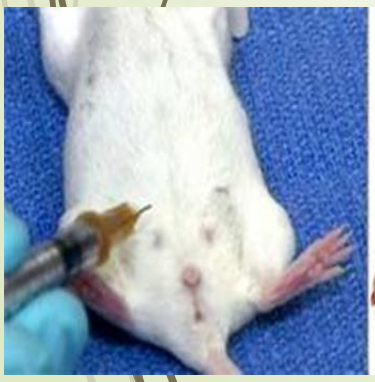
- Lift the skin over the back to form a tent.
- place the mouse on the wire lid so it can hang on . Scruff the skin over the back and tent it up.
- Insert the needle at the tent base, Hold the needle parallel to the animal's body to also avoid puncturing underlying structures.
- Aspirate to ensure that the needle has not entered a blood vessel.
- Withdraw the needle and then press the skin to seal the needle's exit hole in the skin and to prevent the fluid from leaking out.

2-Intraperitoneal (IP) injections

- Commonly used in rats and mice since muscle mass is so small and veins are difficult to find
- Rapid absorption (almost as fast as IV) due to large peritoneal surface
- IP administration results in a faster absorption into the vasculature than SC administration l
- A mouse may easily be injected by one person, whereas a rat might require restraint by one person and injection by the other
- Volume of vehicle ranging between 2 ml/kg to 10 ml/kg

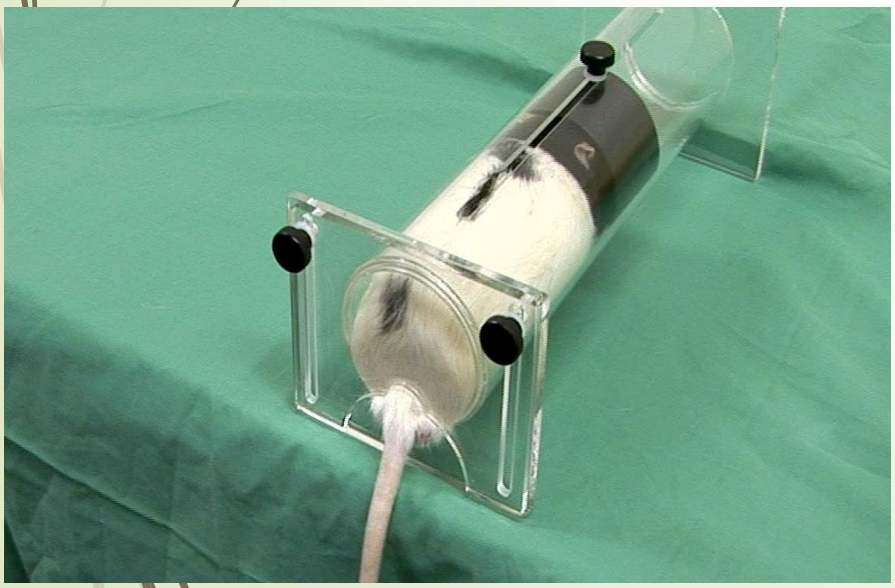
Intraperitoneal (IP) injections

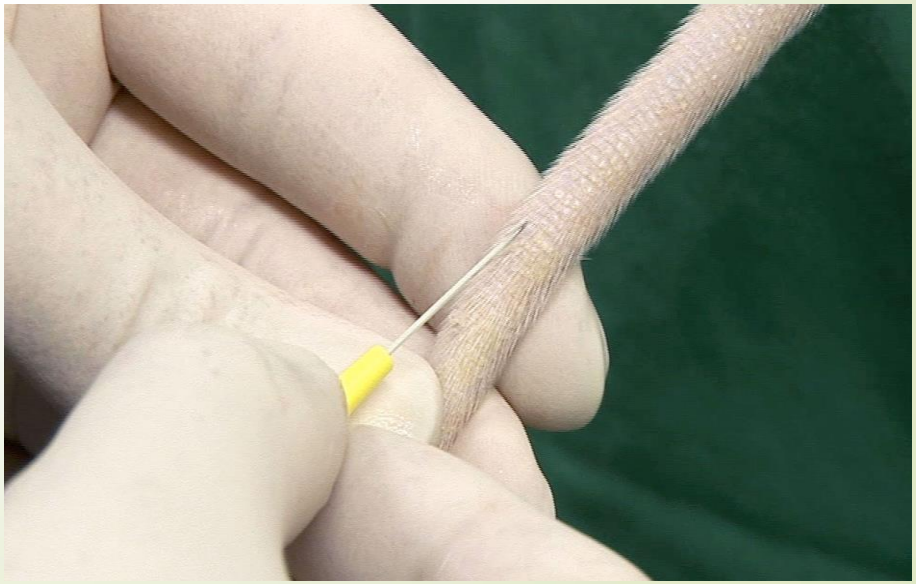
- The injection site is usually on the animal's right lower abdominal quadrant
- Insert the needle at approximately 45 degree angle
- There are three points that you need to pay attention: **position/ angel / draw back.**
- first the position of injection is in the abdomen, not too high, not too low, if too high, liver may be hurt, if too low, bladder may be hurt.
- Second, the angle should be about 45 degree.
- Third, after the syringe needle has been in the abdomen, before injection, you should draw back the stylet to see if can draw out something, if not , you can go on. If draw out blood or urine, that shows you have fail



3- Intravenous (IV) injections

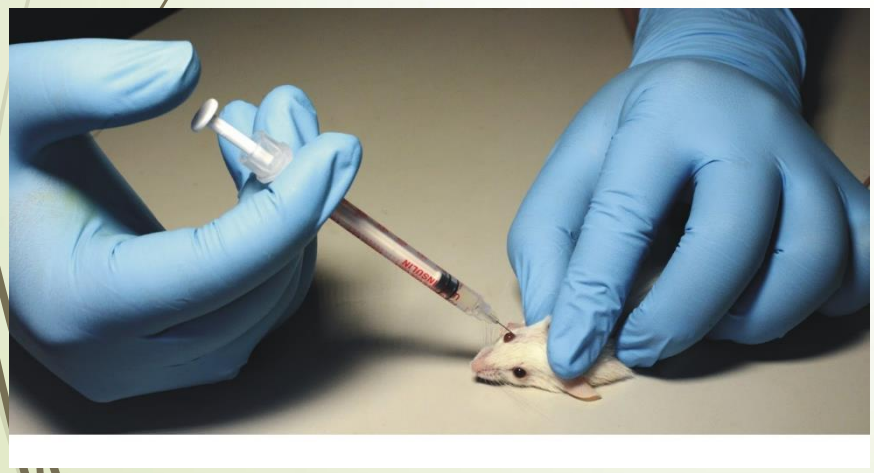
- is the most efficient means of delivering substances to animals because it bypasses the need for solute absorption
- Technically difficult, and the use of a restraining device with appropriate size for the animal to be injected, is often required
- Performed in mice and rats, use the lateral tail vein located on either side of the tail
- The tail vein is difficult to find that's why mouse is often placed under a heat lamp to promote peripheral vasodilation
- Suitable for large volumes. Must inject slowly.

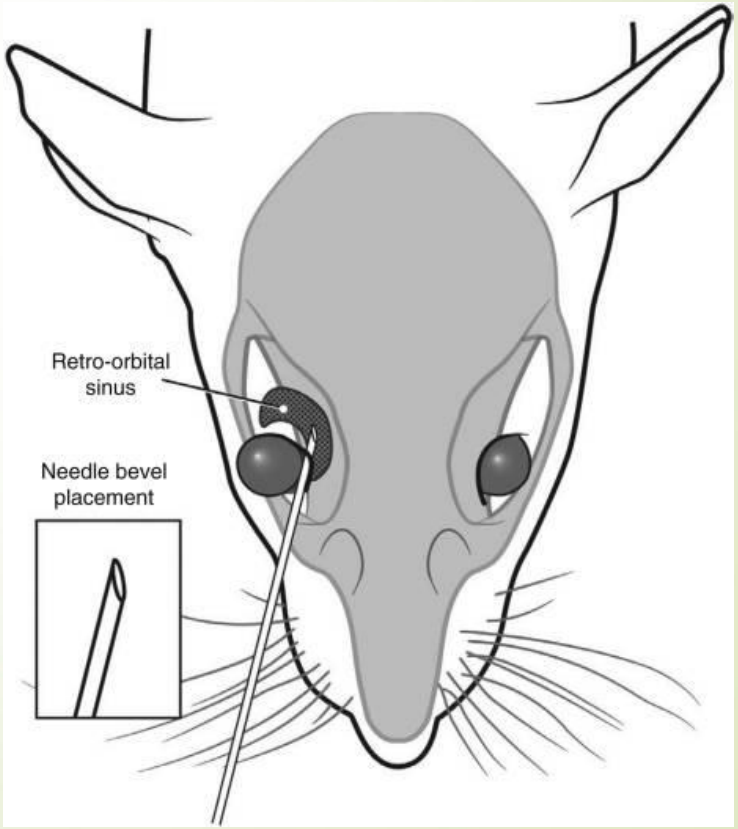




Retro-orbital injections in mice

- This technique is a useful alternative to tail vein injection.
- The mouse should be anesthetized so that it remains still during the procedure (inhalant anesthetic)
- The needle is being placed in the retro-bulbar space (the region behind the globe of the eye).





4-Intramuscular (IM) injections

- intramuscular injections result in uniform and rapid absorption of substances, because of the rich vascular supply
- Not recommended in mice and small species due to their small muscle mass
- Smaller volumes are administered intramuscularly than for subcutaneous delivery
- Suitable for aqueous or specialized depot preparations

Intramuscular (IM) injections

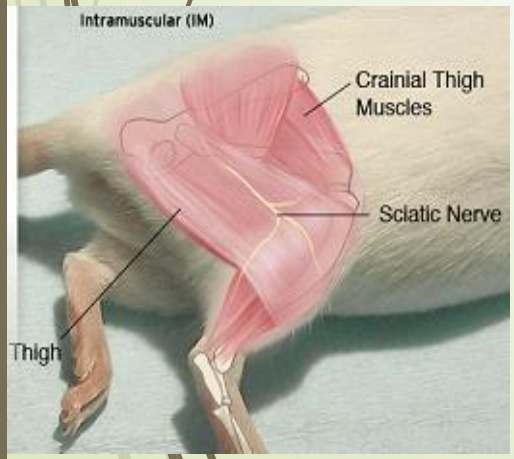
Procedure

1- One person restrains the mouse by the scruff method with one hand and steadies the leg to be injected with the other.

2- The second person , aspirates and , bevel up. Direct the needle caudally (toward tail) if using the caudal thigh muscles or cranially (toward head) if using the quadriceps It is very important to avoid injuring the sciatic nerve.

2- Aspirate to ensure that you have not entered a blood vessel.

3- If no blood is seen, slowly inject the material



Injection site and volume in Rodents

Route	Maximum needle size	Optimal volume	Site
Gavage	Mice: 20 Gauge, (3.8cm) length Rat: 16 Gauge, (7.6cm) length	5 mL/kg (to 20 mL/kg)	intragastric
IV	25	Up to 5 mL/kg	tail or Retro-orbital vein
Sc.	22	Maximum of 5 mL/kg per site	Intrascapular (Scruff), neck, Flank
IM	25	Maximum of 0.05 mL/kg per site	caudal thigh , quadriceps muscles
IP	25	Maximum of 10 mL/kg	Lower ventral quadrants

Aim of the experiment

1. Learn how to handling, treating and preparing animals for the experiments and the ethical guidelines during treatments with animal being .
2. Measure the required volume of a drug in a syringe using aseptic techniques.
3. Learn how to give different types of routes of administration in this lab which includes: Intraperitonial, intramuscular and subcutaneous.

Handling and restraint

Good handling and restraint is the most important technique for correct administration .There are two styles of manual restraint:

a- Double handed manual restraint

b- Single handed restraint


BE KIND TO
ANIMALS