

Al-Mustaqbal University College
Department of Pharmacy
4th stage
Practical Pharmacology II
Lab: 2



PRECLINICAL STUDIES & LABORATORY ANIMALS

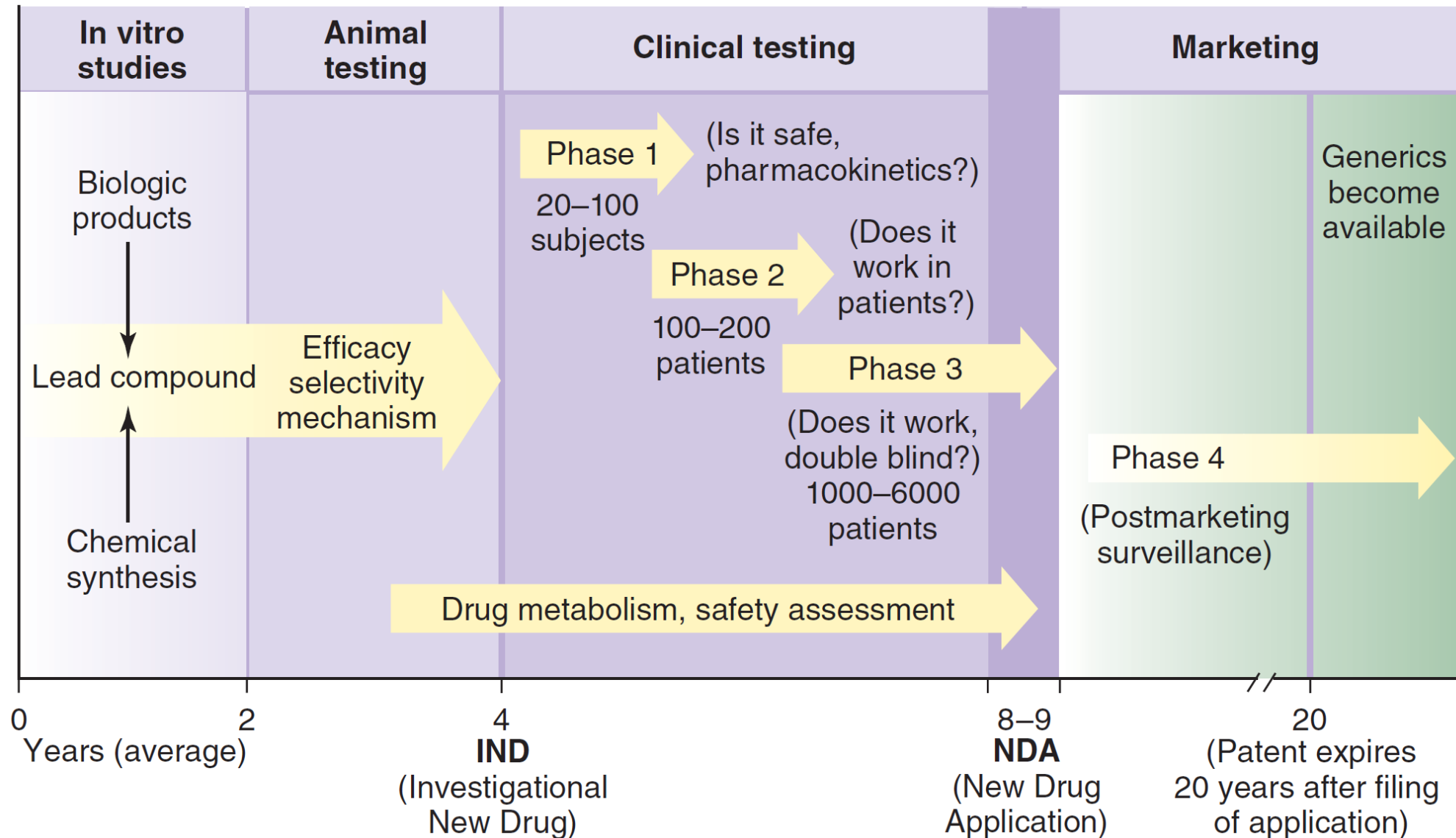
Dr Qassim A zigam

PRECLINICAL STUDIES

- The studies which are conducted to define **pharmacological** and **toxicological** effects.
- These studies were done with a **specific approach** to development and testing that is required to bring a drug to **market**.
- Some of the **requirements** may be **different** for drugs used in **life-threatening** diseases.



DEVELOPMENT PROCESS OF DRUG



ANIMAL TESTING

A. Acute Toxicity

- Acute toxicity studies are required for all **new drugs**.
- These studies involve the administration of incrementing doses of the agent up to the lethal level in at least **2 species** (eg, 1 rodent and 1 nonrodent).

B. Subacute and Chronic Toxicity

- These testing are required for **most agents**, especially those intended for **chronic use**.
- Tests are usually conducted for **2–4 weeks (subacute)** and **6–24 months (chronic)**, in at least **2 species**.

TYPES OF ANIMAL TESTS

A. Pharmacologic Profile

- It is a **description** of all the **pharmacologic effects** of a drug (eg, effects on cardiovascular function, gastrointestinal activity, respiration, renal function, endocrine function, CNS).
- Both **graded** and **quantal** dose-response data are gathered.

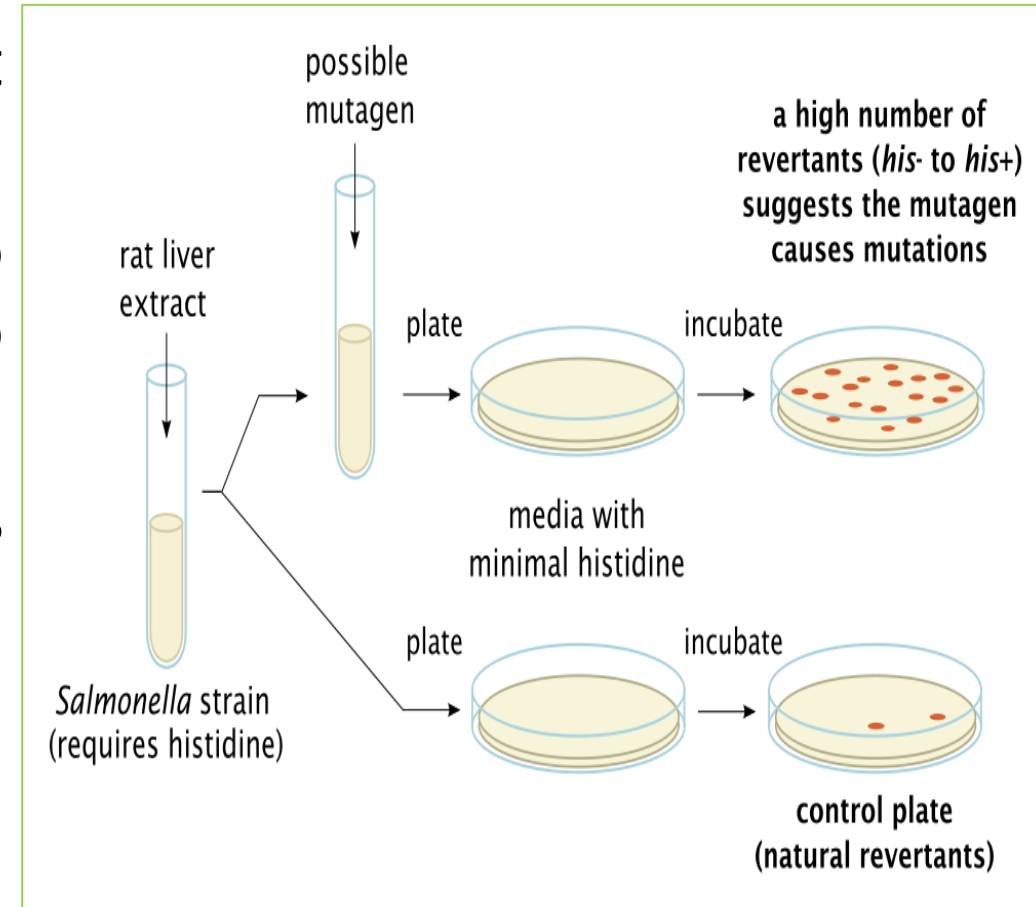
B. Reproductive Toxicity

- It involves the study of the **fertility** effects as well as **teratogenic** and **mutagenic** toxicity.
- **Teratogenesis** can be defined as the induction of developmental defects in the somatic tissues of the fetus (eg, by exposure of the fetus to a chemical, infection, or radiation).

TYPES OF ANIMAL TESTS

C. Carcinogenesis

- **Carcinogenesis** is the induction of malignant characteristics in cells.
- Carcinogenicity is **difficult** and **expensive** to study, and the **Ames test** is often used to screen chemicals.
- Agents with known **carcinogenic effects** include coal tar, aflatoxin, nitrosamines, and the polycyclic aromatic hydrocarbons in tobacco smoke (eg, benzopyrene).



ANIMALS SHARING DNA SEQUENCES

- Humans share (98.8%) of their DNA with **chimpanzees**, while **mice** share nearly (90%).
- This is **important** because mice have been used in laboratories as experimental animals for research into human disease processes for years.
- Also, **Rats** have since been used to answer a wide range of **basic science questions** related to common human diseases in the fields of physiology, immunology, pharmacology, toxicology, nutrition, behavior, and learning.



ANIMALS SHARING DNA SEQUENCES



Pig 98%



Chimps % 98.8



Zebra fish
73%



Cat 90%



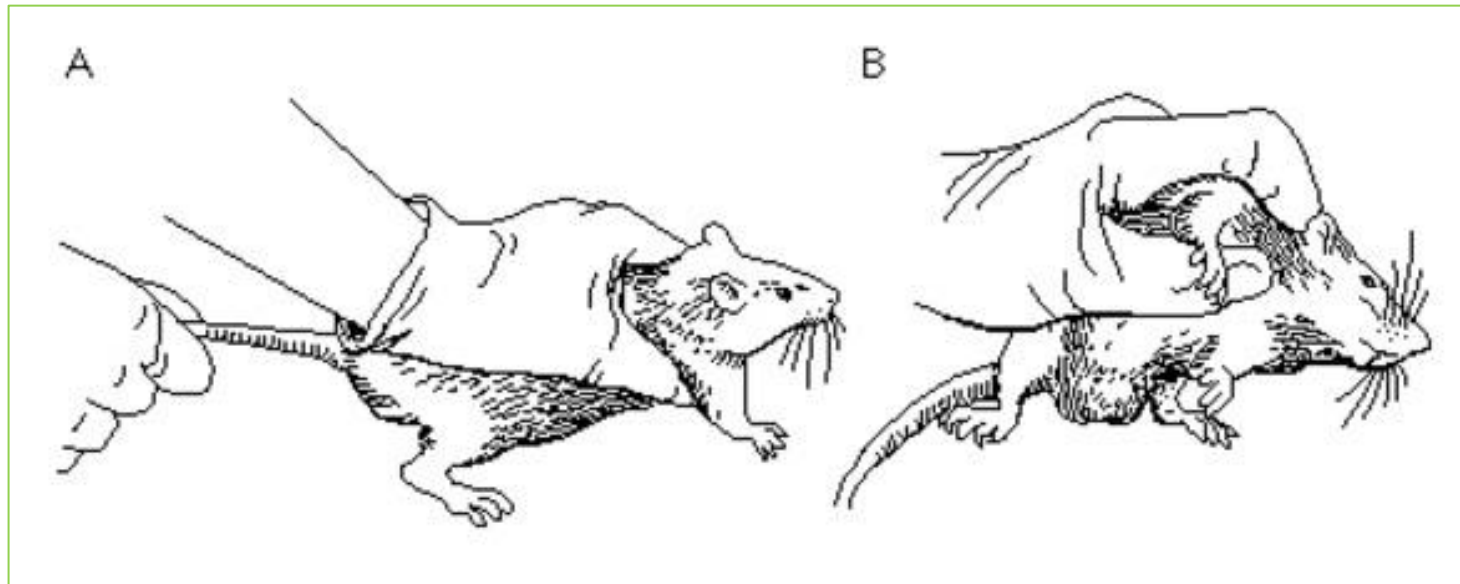
Mouse % 85



Dog 84%

LAB. ANIMALS HANDLING AND RESTRAINT

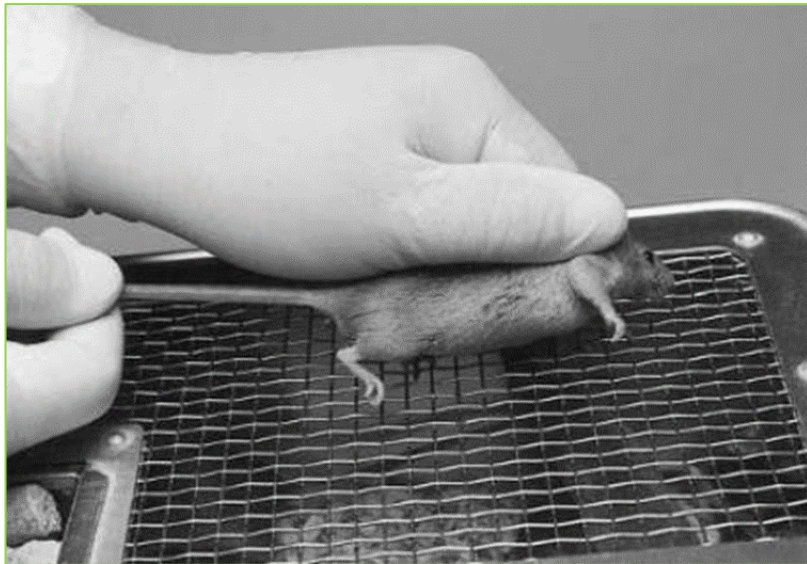
- **Good** handling and restraint is the most important technique for correct **administration**.
- **Proper restraining** leads to successful administration and varies with the routes of administration.
- There are **two styles** of manual restraint, one uses **both hands** and the other is **single-handed**.



LAB. ANIMALS HANDLING AND RESTRAINT

Double-handed manual restraint:

- **Handling** It is **quickly** and **firmly** picked up by the **scruff** of the neck behind the ears with the **thumb and index** finger of the other hand.
- The **tail** is transferred from the **first hand** to between the palm and little or ring finger of the **other hand**, then **fixed**



LAB. ANIMALS HANDLING AND RESTRAINT

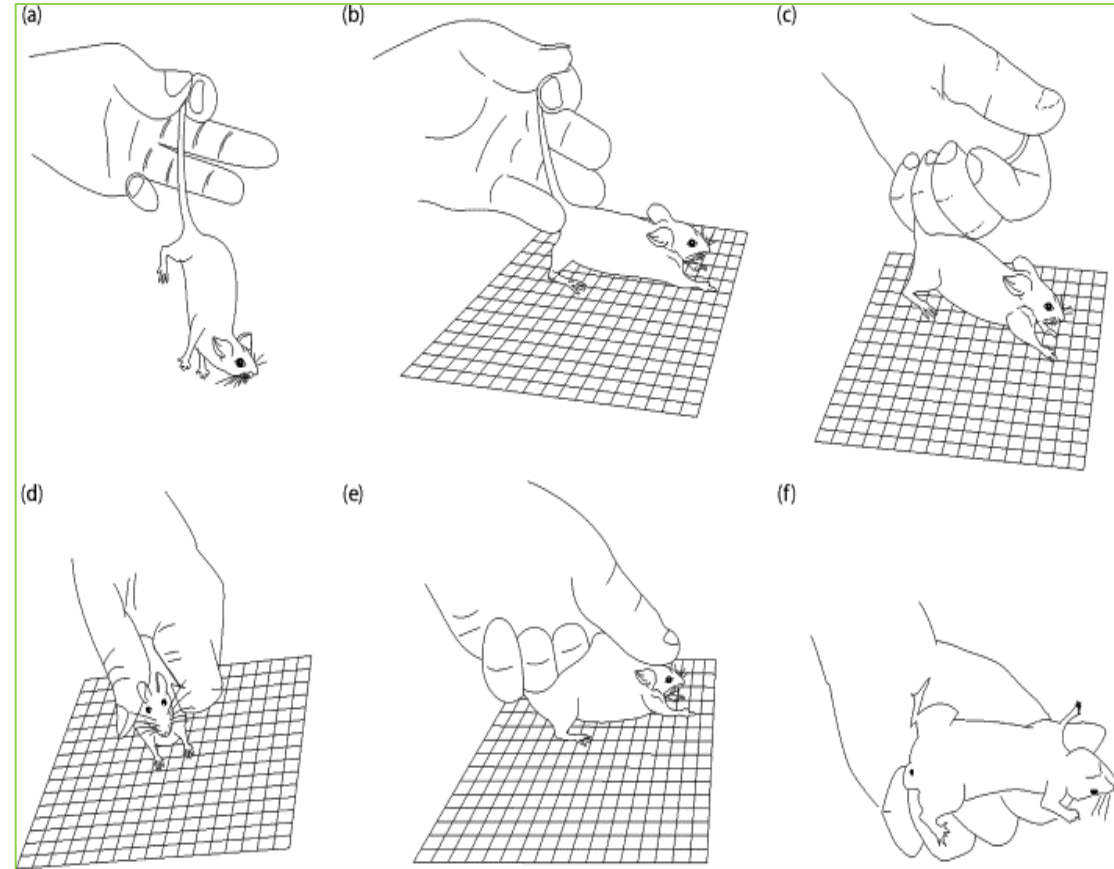
Double-handed manual restraint:



LAB. ANIMALS HANDLING AND RESTRAINT

Single-handed restraint:

1. The tail is picked up using the thumb and forefinger of the chosen hand.
2. Then the mouse is placed on the cage lid or other solid surface.
3. The tail is immediately grasped by the palm and middle finger, ring finger and/or little finger, and the thumb and forefinger released.
4. The fold of skin from the scruff of the neck down the back is immediately gripped using the thumb and forefinger.



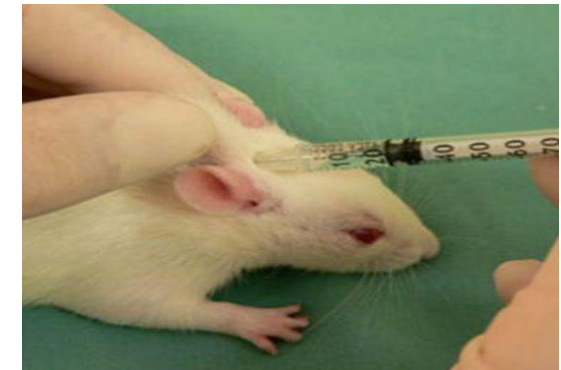
LAB. ANIMALS HANDLING AND RESTRAINT

Single-handed restraint:



ADMINISTRATION ROUTES

- There are **several** possibilities for the administration of substances to **mice**.
- The most **common** routes are **oral**, **subcutaneous**, **intraperitoneal**, or **intravenous** injection.
- **Intramuscular** administration is **not recommended**, as the muscle of the mouse is too **small**.



FACTORS AFFECTING ADMINISTRATION

1. Concentration of substances

- The concentration can **vary** over a fairly **wide range** without greatly influencing the end result of the experiment.
- **Lower** concentrations are clearly **desirable**.

2. PH of the injected solution

- For most routes of administration, providing the solutions are not highly buffered, a pH range of **4.5–8.0** is satisfactory.

3. Volume and frequency of administration

- The injection volume is **limited** by any **toxicity** of the substance and by **the size** of the mouse.
- It should be kept as **small** as possible.



**THANK YOU FOR
YOUR ATTENTION**

