1 - Drug preparations and route of drug administration

- There are many ways to administer drugs

1. Enteral —> drugs taken into gastro-intestinal (GI) tract, e.g. swallowing a pill
2. Parenteral —> drugs administered by routes other than the GI tract, e.g. injection via needle

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Tablets and Capsules

- The most common and usually the easiest way of taking medications is through the mouth (Orally)
- Drugs designed to be taken orally are presented in a number of forms:
  - Compressed tablet —> most frequently dispensed form of a drug and may be engraved with a company symbol or code and may also be scored for dividing the dose
  - Sugar-coated capsules —> improves palatability of the drug
  - Enteric-coated tablet —> designed to be released in the small intestine and not the stomach, this type of drug can be used for patients who cannot tolerate the non-enteric-coated tablets due to gastric irritation (e.g. Aspirin)
  - Sustained-release tablet —> the coating on the tablet slows down the rate of drug dissolution, thus, the drug is released over a period of time, this form of drug minimises multiple dosing

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Sublingual and Buccal routes

- Some tablets are intended to dissolve in the mouth (not swallowed)
  - this way, the drug enters the systemic circulation before passing through the liver, thus delaying drug degradation
- Sublingual involves placing the drug under the tongue (absorbed through the mucous membranes of the mouth)
- Buccal involves placing the drug between the cheeks and gums

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Injection

- Administration of drugs by injection is called parenteral administration; generally produces a faster response
  - drawbacks: (1) needle must be sterile, (2) may be painful, (3) cannot be readily administered by patients themselves
- There are various parenteral routes:
  - Subcutaneous —> injected into the later of fat that lies immediately under the skin later
  - Intramuscular —> directly injected into a muscle mass
  - Intravenous —> injecting the drug directly into the vein

Suppositories

- Drugs can also be given rectally in the form of suppositories and melt at body temperature
- The rouse is useful for the unconscious patient or when vomiting precludes the oral route
- Like the sublingual route, the absorbed drug enters the systemic circulation before passing through the liver

Skin and Respiratory tract

SKIN

This route of drug administration is usually used when the local effects on the skin are desired. Drugs may be applied in the form of ointments, liniments, lotions, creams and pastes. More recently, drugs requiring systemic effects are using this route of administration. An example is nitroglycerin paste; used for its anti-anginal properties.

RESPIRATORY TRACT

Drug preparations designed to be given via this route are in the form of aerosol sprays or gas. A number of medications used to treat lung problems (e.g. asthma, chronic bronchitis) are manufactured in the form of aerosol sprays (e.g. salbutamol, ipratropium bromide) to maximise the localised effects in the respiratory tract and to minimise the systemic undesired effects.

Other Routes

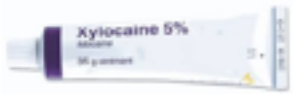
- Nose, vaginal and eyes are routes often used for localised effects
- Spinal route (Intrafecal) is used for its systemic effects

Iontophoresis

- Iontophoresis is a potential alternative drug delivery route to the parenteral route. It is a useful form of delivering drugs that are poorly absorbed through the skin or that are extensively degraded by the enzymes in the gastro-intestinal tract.
- It's an effective and painless method of delivering ionic drug compounds to a localised tissue area by applying electrical current to a solution of the drug.
  - a positive current is applied, driving positively charged drug molecules away from the electrode into the tissues, and similarly, a negative current will drive negatively charged drug molecules into the tissues
- This mode enhances drug delivery by:
  - increasing the penetration of drug molecules through the skin
  - increasing drug absorption rate
- This method has been shown to be beneficial in treatment of localised skin disorders, e.g. nail disease and psoriasis

- There are 3 types of regulatory receptors

1. **Ion channels**
   - some drugs act by mimicking or blocking the action of natural substances that regulate the flow of ions through plasma membrane channels
     - e.g. local anaesthetics, such as Lignocaine (Xylocaine) block voltage-gated sodium channels causing loss of pain perception (anaesthesia) in the area where the drug is administered

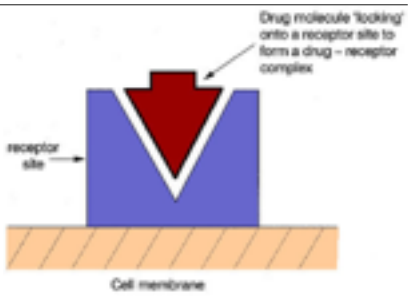


2. **Enzymes**
   - enzymes promote or speed up chemical reactions in the body; some drugs interact with enzymatic reactions in the body by increasing, decreasing or blocking the biochemical reactions
     - e.g. Aspirin (Disprin) blocks the enzyme cyclooxygenase, thus causing platelets to become less sticky

3. **Transport proteins**
   - drugs can also affect the normal transport processes in the body
   - Insulin, a natural substance produced in the body, and a drug that is sometimes given to individuals with diabetes mellitus, is an example of a protein that promotes the transport of glucose from the blood into the cells, causing blood glucose levels to fall

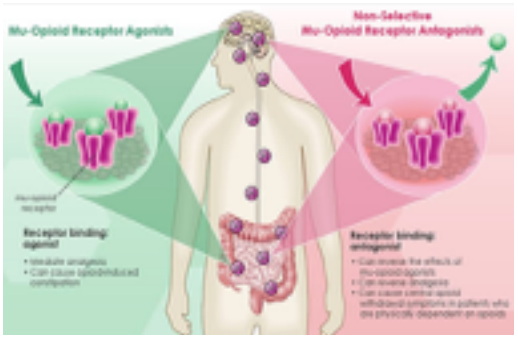
Drug-Receptor Interactions

- The drug-receptor interaction is similar to the relationship between a lock and key
- The intensity of the body's response to the drug is usually proportional to the number of receptors that are occupied by the drug

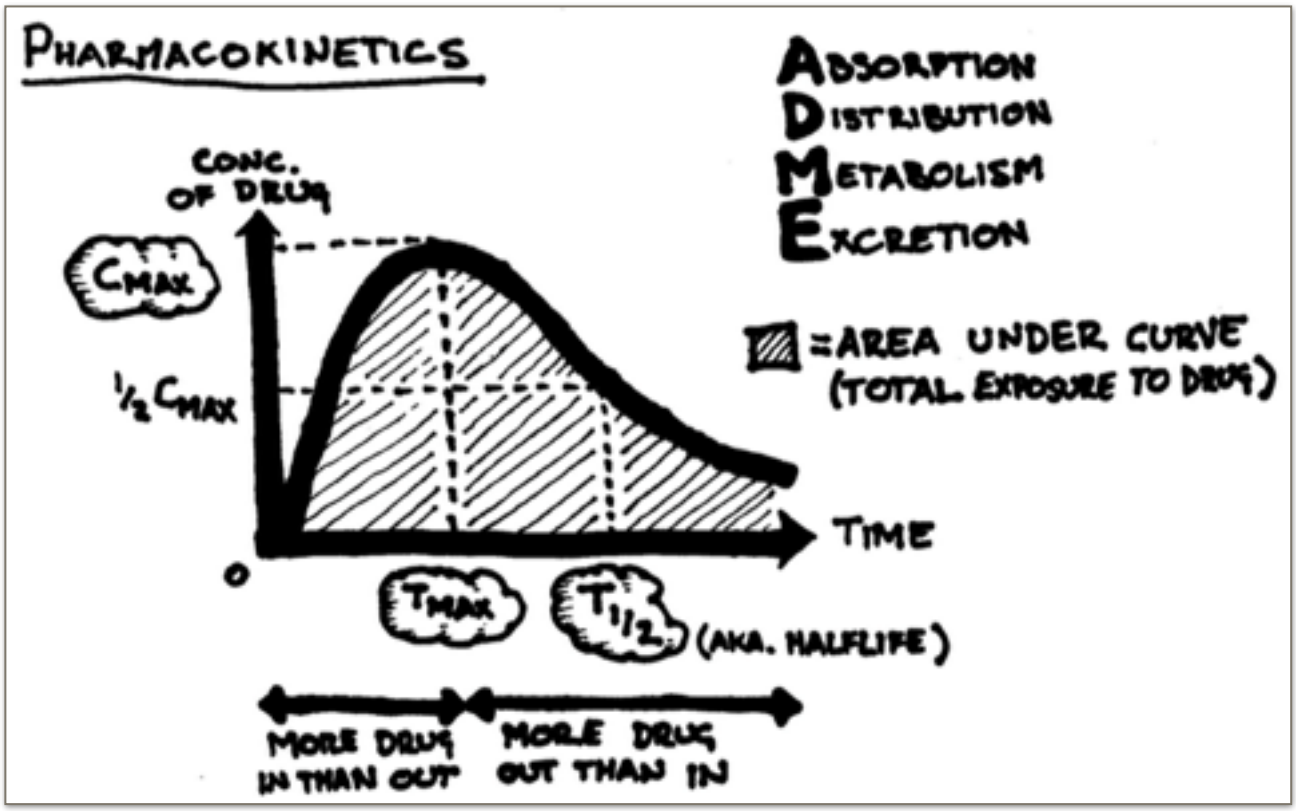


Agonists & Antagonists

- **Agonist** —> drugs that stimulate and mimic the effects of natural substances in the body
  - activates receptors by binding to the specific receptor type in the body and produces some kind of cellular response
- **Antagonist** —> inhibit or block receptor activity
  - they may be reversible, competitive or irreversible; reversible competitive antagonists bind reversibly with receptors



Pharmacokinetics 1 - Introduction



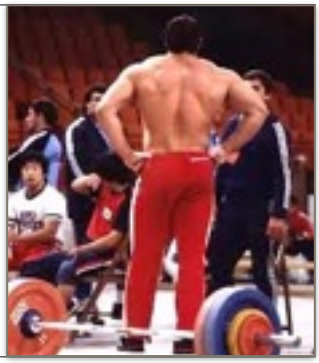
- **Pharmacokinetics** —> the study of the effect the body has on drugs
- **Pharmacodynamics** —> the study of the effects of drugs on the body

- **Absorption** —> how then drug gets into the body
- **Distribution** —> where the drug goes in the body
- **Metabolism** —> how the body chemically modifies the drug
- **Excretion** —> how the body gets rid of the drug

- C_{MAX} —> where the concentration of the drug is at its peak in the body
- T_{MAX} —> the time at which the maximum concentration occurs
- $T_{1/2}$ —> the time it takes to remove half of the current concentration of the drug from the body

- The area under the curve represents the total exposure of the drug to the body

Peptide Hormones and Analogus



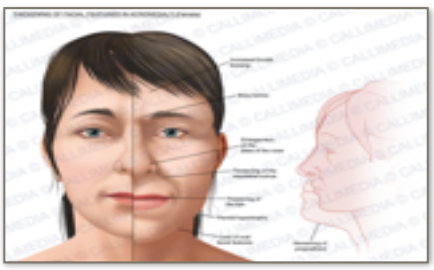
- Growth hormone is produced by the anterior lobe of the pea sized **pituitary gland**
- Although it stimulates most body cells to increase in size and number, its major targets are the bones and skeletal muscles (particularly muscle mass)

Erythropoietin (EPO)

- Erythrocytes (RBCs) primarily take oxygen in the blood to all cells in the body
- More than 2 million RBCs are produced per second in a healthy person, promoted by the action of erythropoietin (EPO), a glycoprotein hormone produced by the kidneys that regulates the production of RBCs in the bone marrow
- Erythrocytes normally constitute about 45% of the total volume of a blood sample
- Excessive RBCs can lead to polycythemia (an abnormally increased concentration of haemoglobin in the blood)
- **Symptoms**:
  - trouble breathing when lying down
  - dizziness
  - excess bleeding
  - headache
  - itchiness, especially after a warm bath
- **Treatment**: (goal is to reduce blood thickness and prevent bleeding & clotting
  - a method called phlebotomy is used to decrease blood thickness; one unit of blood (about 1 pint) is removed each week until the number of RBCs drops. (The treatment is continued as needed)
  - chemotherapy to reduce RBCs made in bone marrow
- **Outlook** (prognosis):
  - the disease usually develops slowly; most patients don't have problems related to the disease after being diagnosed
  - the condition is often diagnosed before severe symptoms occur

Growth Hormone (GH)

- While GH is important for growth, its overproduction by the pituitary gland can result in acromegaly
- The signs of hyper-secretion of GH in an adult:
  - change in the face, jaw or tongue
    - cheekbones & forehead are more prominent
    - inability to bite or teeth have become more widely spread
  - enlarged hands and feed (often requiring larger rings or shoe sizes)



Drugs in Pharmacokinetics & Pharmacodynamics

Drug	Context	Description / Info
Warfarin	Distribution (protein binding)	- Warfarin is 99% bounds to plasma; only 1% is free
Acetaminophen (paracetamol)	Metabolism (drug toxicity)	- There's an ↑ in toxicity when the liver converts this drug to an intermediate hepatotoxic metabolite, ∴ resulting in the depletion of glutathione
Aspirin	Excretion (pH dependent ionisation)	- By ↑pH of urine, more aspirin is ionised, ∴ resulting in a reduction of passive reabsorption of aspirin, ∴↑excretion
Penicillin & **Probenecid**	Excretion (competition)	- The excretion of penicillin is delayed if it's given with probenecid, since the 2 drugs compete for the same transport mechanism for excretion
Salbutamol (Ventolin)	Agonist	- Binds to β2-adrenergic receptors in the bronchioles, causing smooth muscle relaxation, ∴ often used in an acute asthma attack
Metoprolol (Betaloc)	Antagonist	- Also classified as a β1-adrenergic antagonist, binds to the β1-receptors and prevents the natural substances in the body (e.g. adrenaline) from activating the β1-receptors
Lignocaine (Xylocaine)	Regulatory receptors (ion channels)	- Blocks voltage-gated sodium channels causing loss of pain perception (anaesthesia) in the area where the drug is administered
Aspirin	Regulatory receptors (enzymes)	- Blocks the enzyme cyclooxyrgenase, thus causing platelets to become sticky
Insulin	Regulatory receptors (transport proteins)	- Promotes the uptake of glucose into cells, thus causing blood glucose levels to fall
Morphine & **Pethidine**	Affinity	- Morphine is a more potent pain-killer (analgesic) than pethidine - There 2 are from the group opioids - Morphine has a stronger affinity for the opioid receptor site that modify pain when compared to the drug pethidine
Minoxidil	Side effects	- Minoxidil, an anti-hypertensive drug, is sometimes given for its secondary effect; the promotion of hair growth