Methods of Drug Administration and Drug Metabolism

Drug Administration

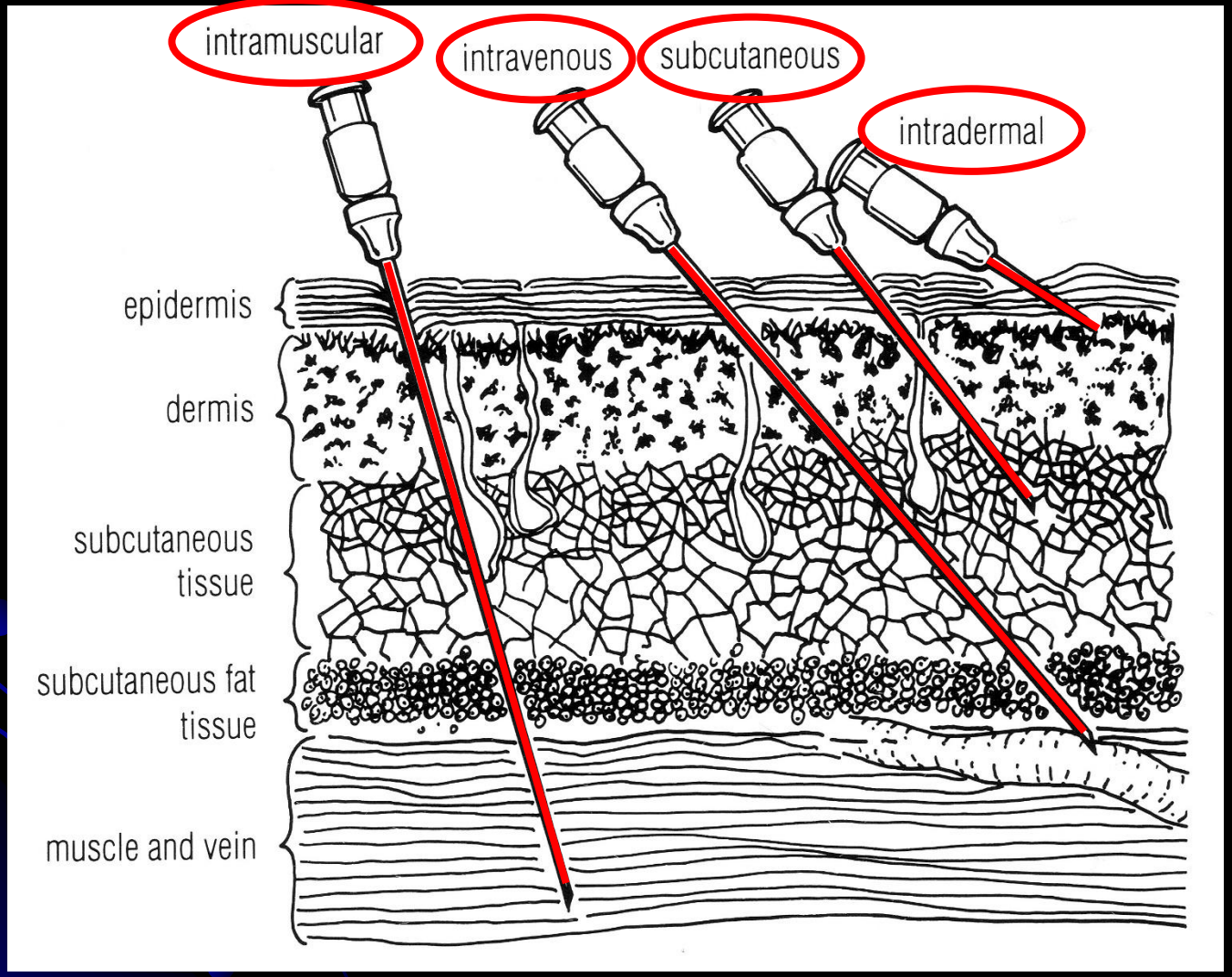
Drug Administration

Injection

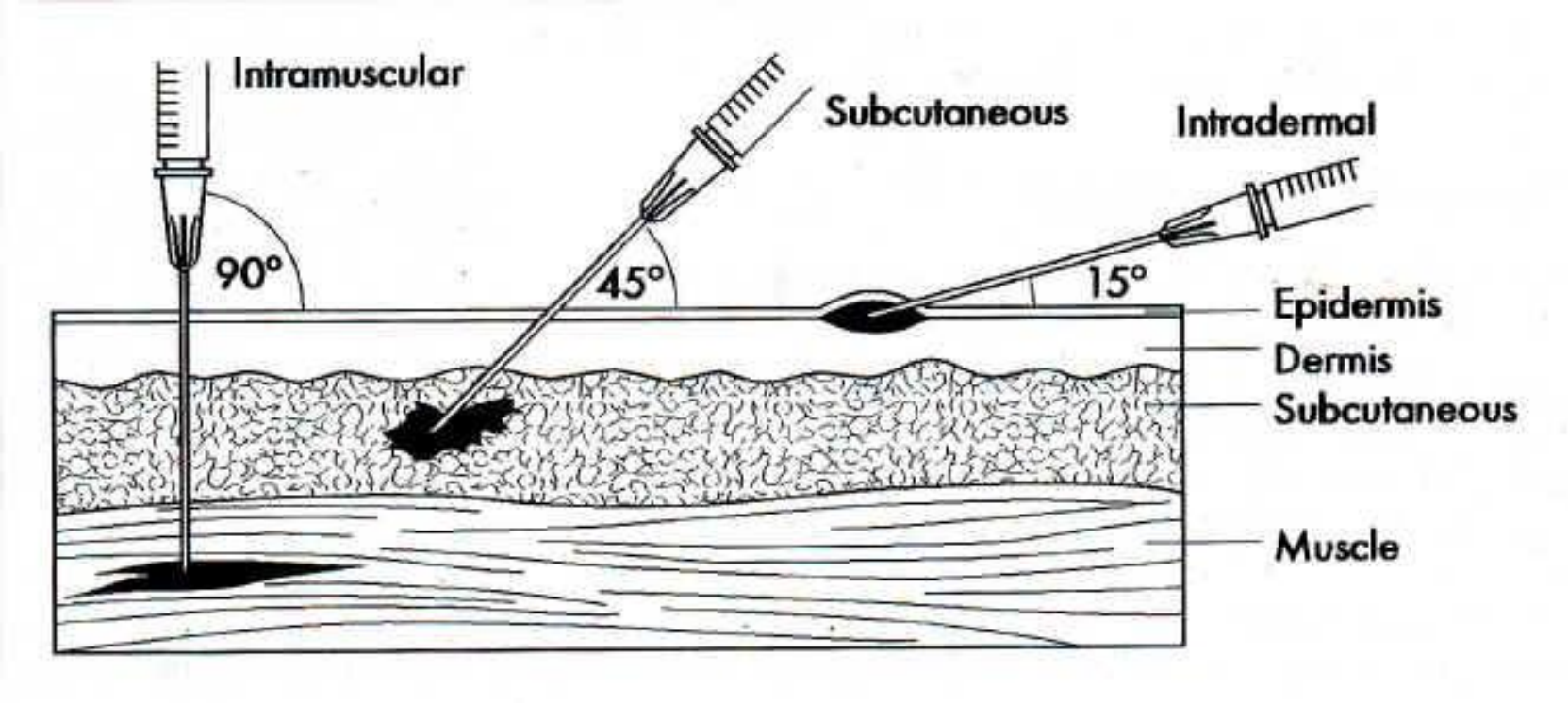
Injection

- Intravenous Injection.
- Intramuscular Injection.
- Subcutaneous Injection.

Injection

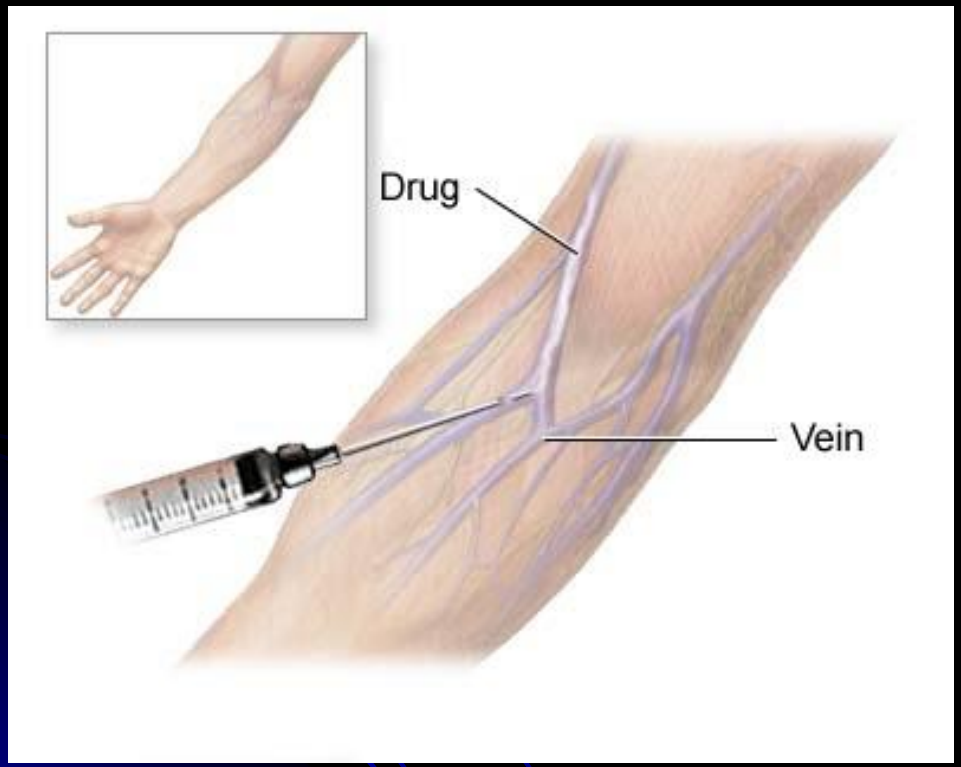

intramuscular
intravenous
subcutaneous
intradermal
epidermis
dermis
subcutaneous tissue
subcutaneous fat tissue
muscle and vein

Injection


Intramuscular
Subcutaneous
Intradermal
90°
45°
15°
Epidermis
Dermis
Subcutaneous
Muscle

Injection

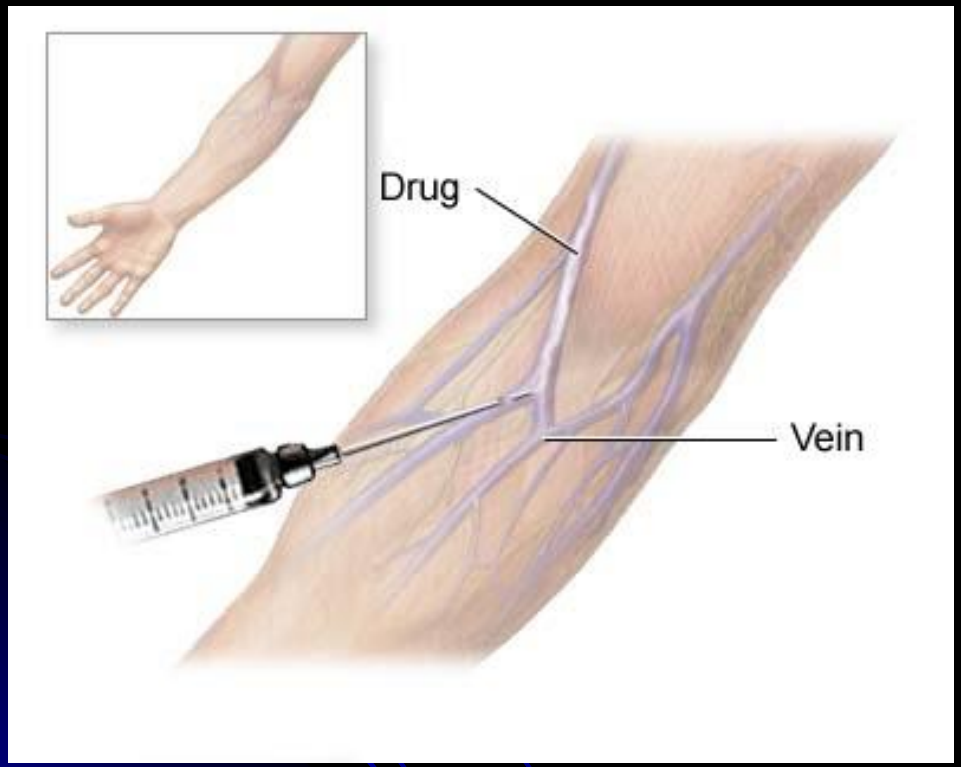
Intravenous Injection:



- The drug directly enters the circulation, bypassing any absorption barriers.

Injection

Intravenous Injection:

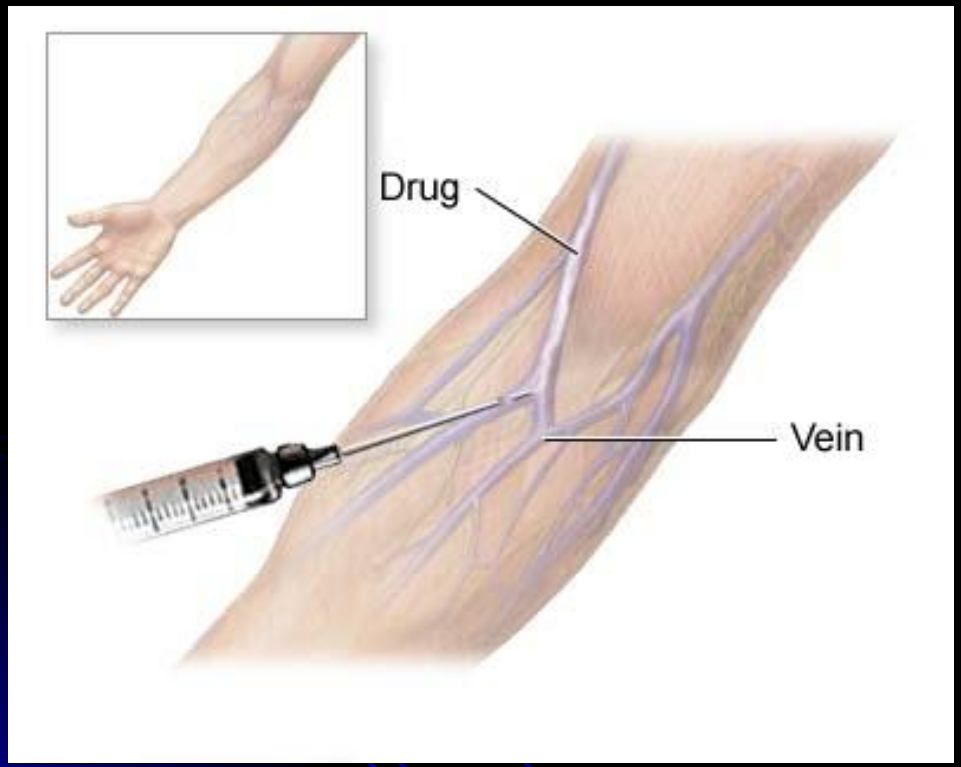


- Used to administer drugs which are poorly absorbed across the surface of the gastro-intestinal tract or which are destroyed by the enzymes / low pH of the gastro-intestinal tract.

- Used where a rapid effect is required.

Injection

Intravenous Injection:



- Can be used for continuous administration (*infusion*) of a drug.
- Used to administer large volumes of a drug.
- Used to administer drugs that could cause local tissue damage if administered by other routed, e.g. *cytotoxic* drugs.

Injection

Why Inject Into Veins and Not Arteries?

Arteries	Veins
• Carry oxygenated blood.	• Carry deoxygenated blood.
• Carry blood away from the heart.	• Carry blood towards the heart.
• Holds bright red blood.	• Holds dark red blood.
• Holds blood at a high pressure.	• Holds blood at a low pressure.
• Bleed profusely.	• Do not bleed profusely.
• Served by many nerves.	• Served by few nerves.
• Thick walled.	• Thin walled.
• Very elastic and muscular.	• Not elastic or muscular.
• No valves.	• Valves.
• Less numerous than veins.	• More numerous than arteries.
• Recognisable pulse.	• No recognisable pulse.
• Mostly deep.	• Can be deep or superficial.

Injection

The Procedure for Giving an Intravenous Injection:

1) Identify the vein to be used in some people this is straightforward, others may have to palpate (feel for) veins.

2) Choose the smallest possible bore and length of needle for the site of injection.

3) Clean the site with an alcohol swab.

Injection

The Procedure for Giving an Intravenous Injection:

4) Introduce the needle into the vein at a shallow angle, a change in resistance is felt as the needle enters the vein.

5) Always inject with the blood flow, *i.e.* towards the heart.

6) Pull back the plunger to identify that the needle is in a vein a small amount of dark red venous blood should trickle into the syringe. If a tourniquet is used it should be loosened immediately after accessing the vein.

Injection

The Procedure for Giving an Intravenous Injection:

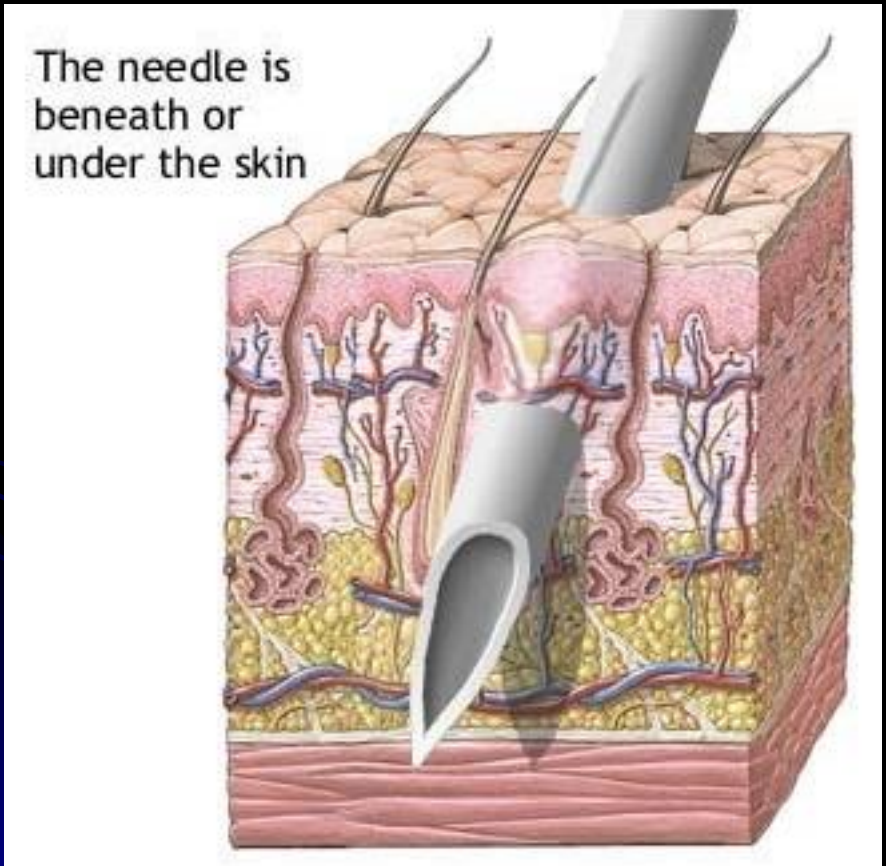
7) Inject slowly to reduce the likelihood of damage to the vein and to lower the fisk of overdose. Do not flush out this will significantly increase trauma to the vein.

8) Remove the needle slowly if the needle is removed too quickly, the vein may collapse.

9) Immediately apply pressure to the site bruising is caused by bleeding into the surrounding tissues. Immediate firm pressure will limit the amount of bruising caused.

Injection

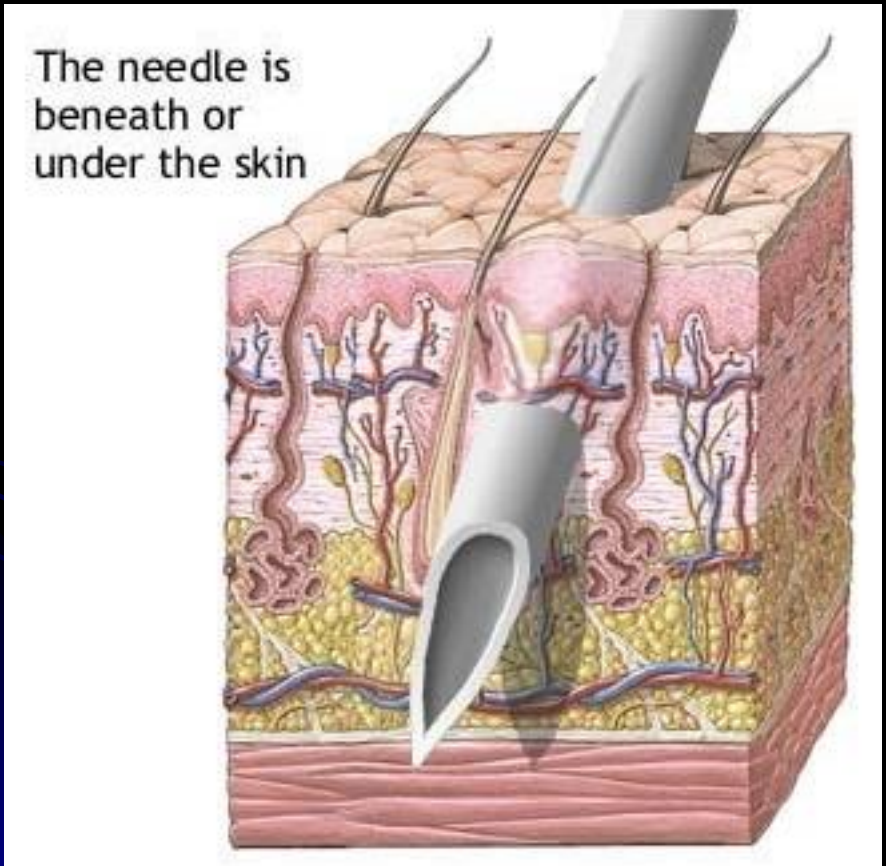
Intramuscular Injection:



- Used to administer a relatively large volume of a drug which is not required to have a rapid therapeutic effect.

Injection

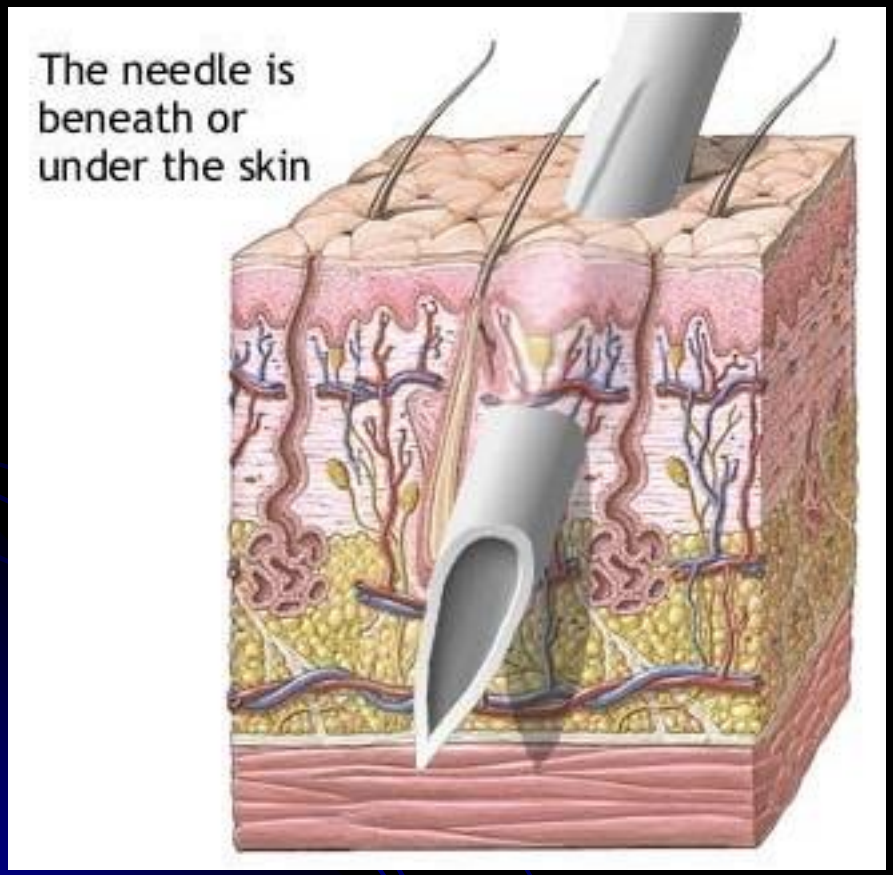
Intramuscular Injection:



- Can be administered in conjunction with the enzyme *hyaluronidase* which causes hydrolysis of muscle tissue and therefore increases the rate at which the drug diffuses into the bloodstream.

Injection

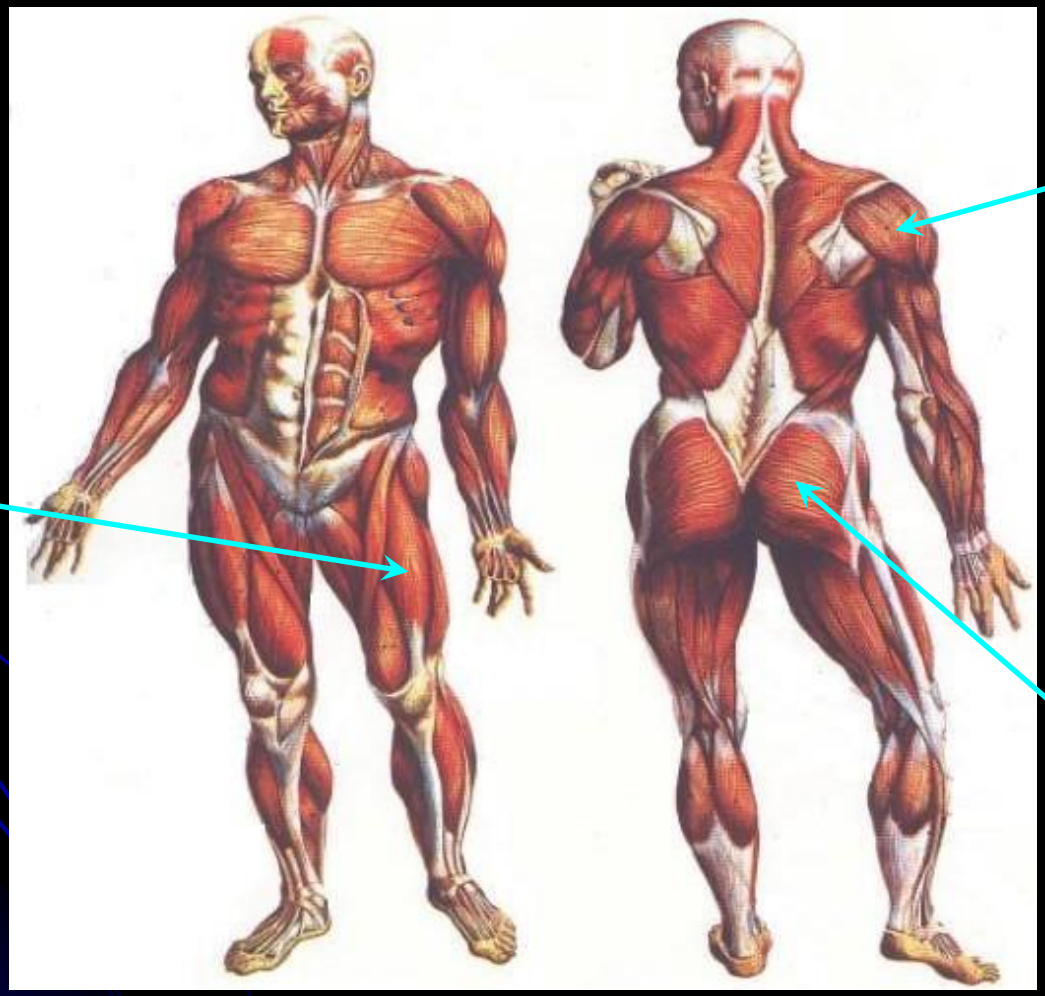
Intramuscular Injection:



- The main sites for intramuscular injection are the *deltoids*, *gluteus maximus* and *vastus lateralis*.

Injection

Intramuscular Injection Sites:



Deltoid

Vastus Lateralis

Gluteus Maximus

Injection

Obesity Stops Jabs Hitting Target

Story from BBC News: http://news.bbc.co.uk/go/pr/fr/-/2/hi/health/4477716.stm

Injecting drugs into the buttocks may not be a reliable way of administering medicine, research suggests. Doctors from a hospital in Dublin found many patients had so much fleshy tissue on their buttocks that jabs could not properly penetrate to the muscle. They found women, and in particular obese women, were most likely not to get the full intended dose.

Injection

Obesity Stops Jabs Hitting Target

Story from BBC News: http://news.bbc.co.uk/go/pr/fr/-/2/hi/health/4477716.stm

Dr Victoria Cha, based the Adelaide and Meath Hospital, summarised the situation by saying:

"*The amount of fat tissue overlying the muscles exceeds the length of the needles commonly used for these injections*."

Injection

Obesity Stops Jabs Hitting Target

Story from BBC News: http://news.bbc.co.uk/go/pr/fr/-/2/hi/health/4477716.stm

Professor Richard Guy, based at Bath University, identified one obvious drawback of using longer needles:

"*Whether using longer needles is a practical solution, I'm not sure, as these are unlikely to be terribly popular*."

Injection

Intramuscular Injection Sites:

Injection

Intramuscular Injection Sites:

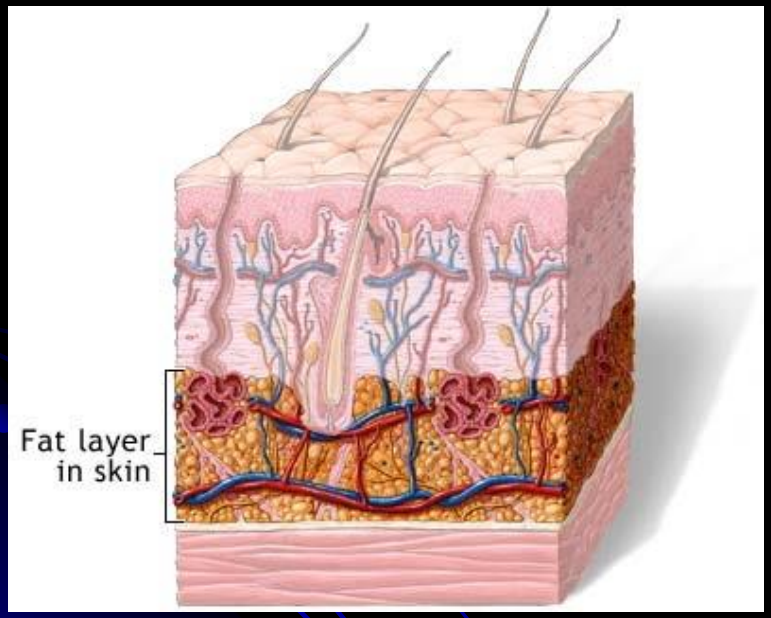
Injection

Intramuscular Injection Sites:

Gluteus Maximus

Injection

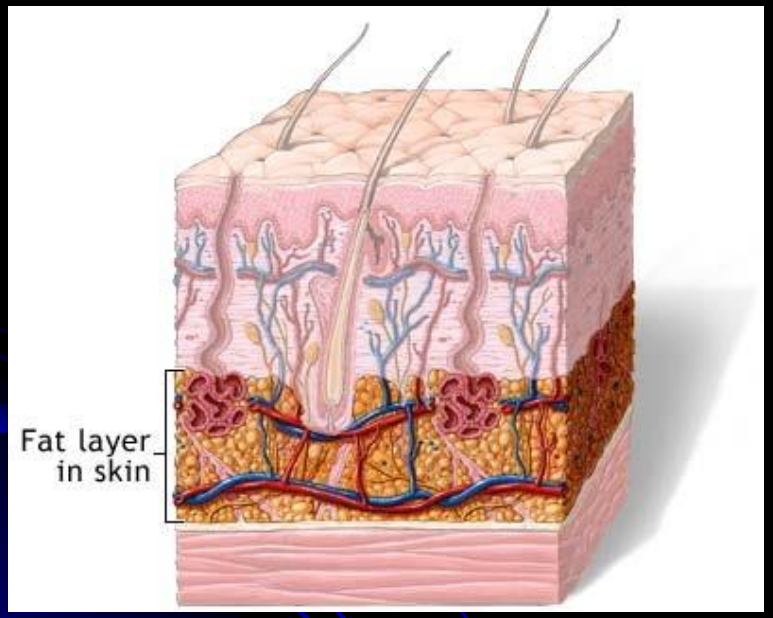
Subcutaneous Injection:



- Used to administer lipid soluble drugs.
- *Insulin* is probably the most common drug that is administered by subcutaneous injection.

Injection

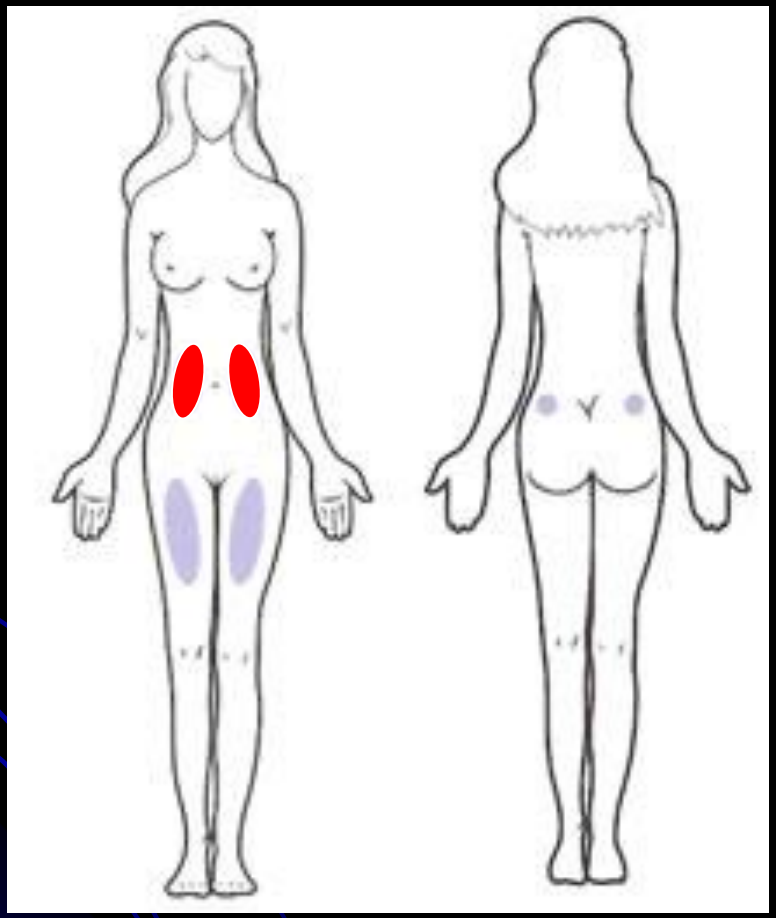
Subcutaneous Injection:



- Drugs in aqueous solution are usually absorbed quite rapidly, but absorption can be slowed by reducing the *hydrophilic* nature of the drug, e.g. through *esterification* of a polar alcohol or carboxylic acid group. The modified drug can then be injected into a muscle or the subcutaneous layer.

Injection

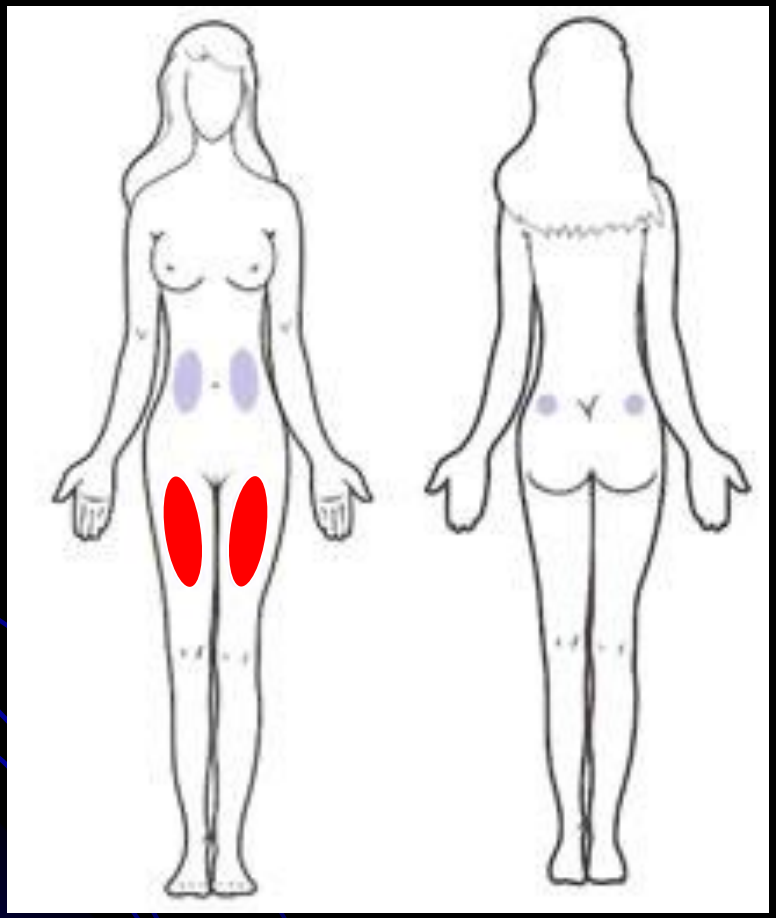
Subcutaneous Injection Sites:



Left and right sides of the abdomen.

Injection

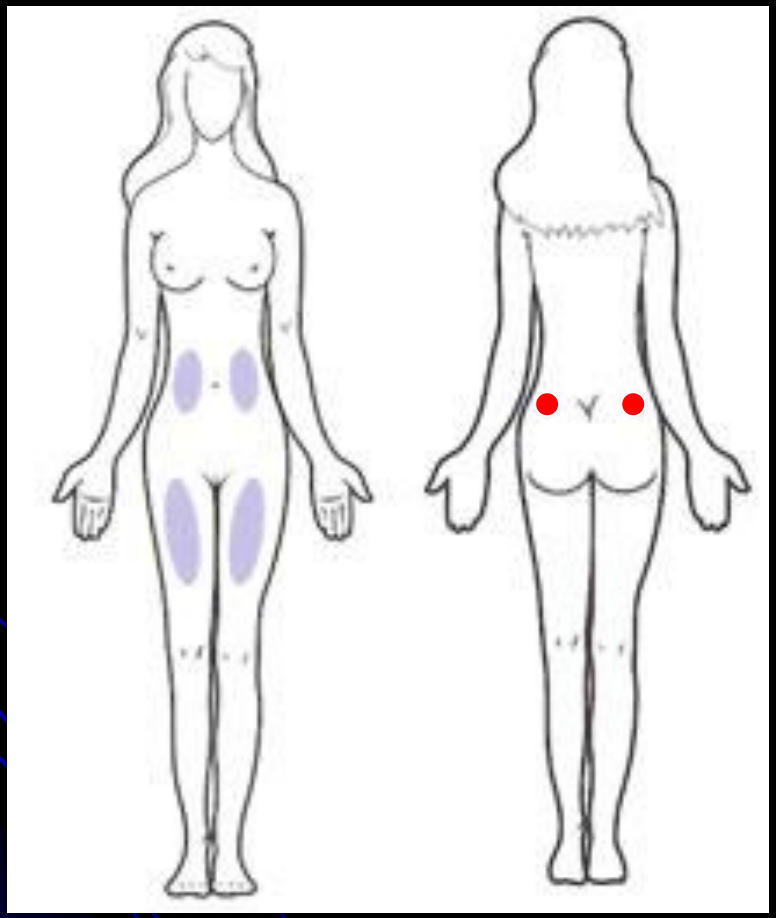
Subcutaneous Injection Sites:



Left and right thigh.

Injection

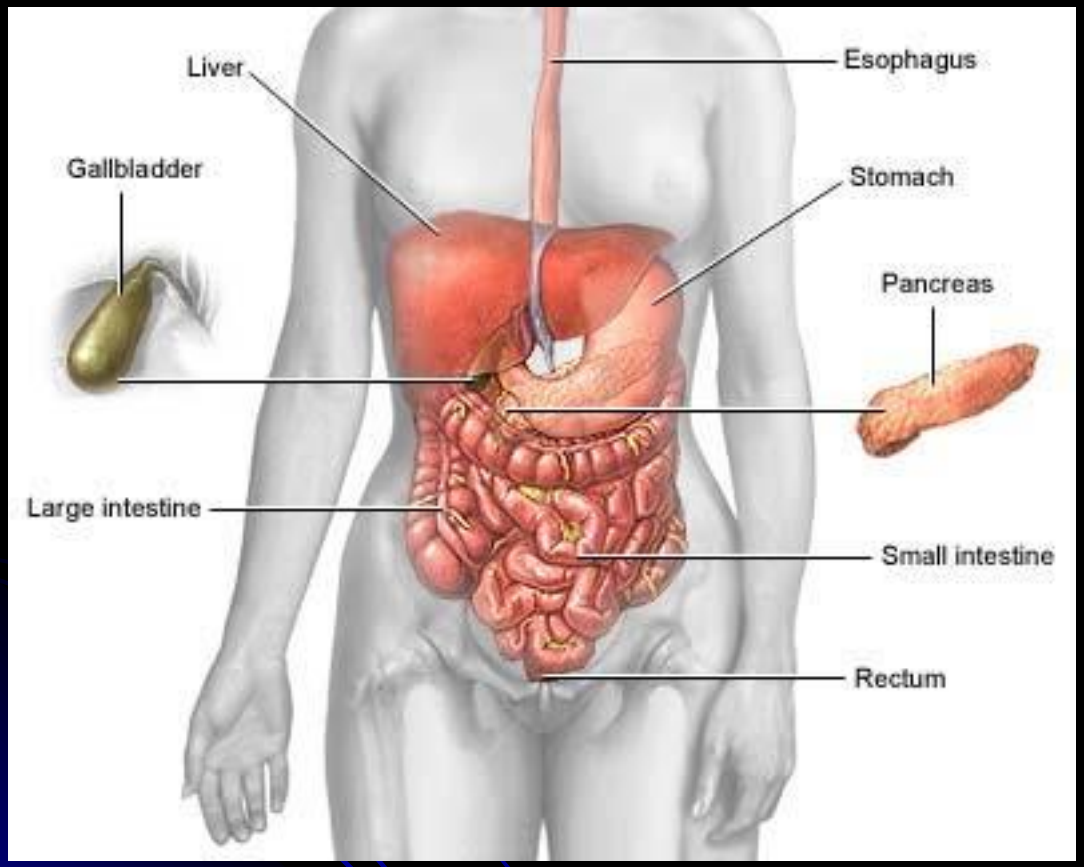
Subcutaneous Injection Sites:



Left and right sides of the lower back.

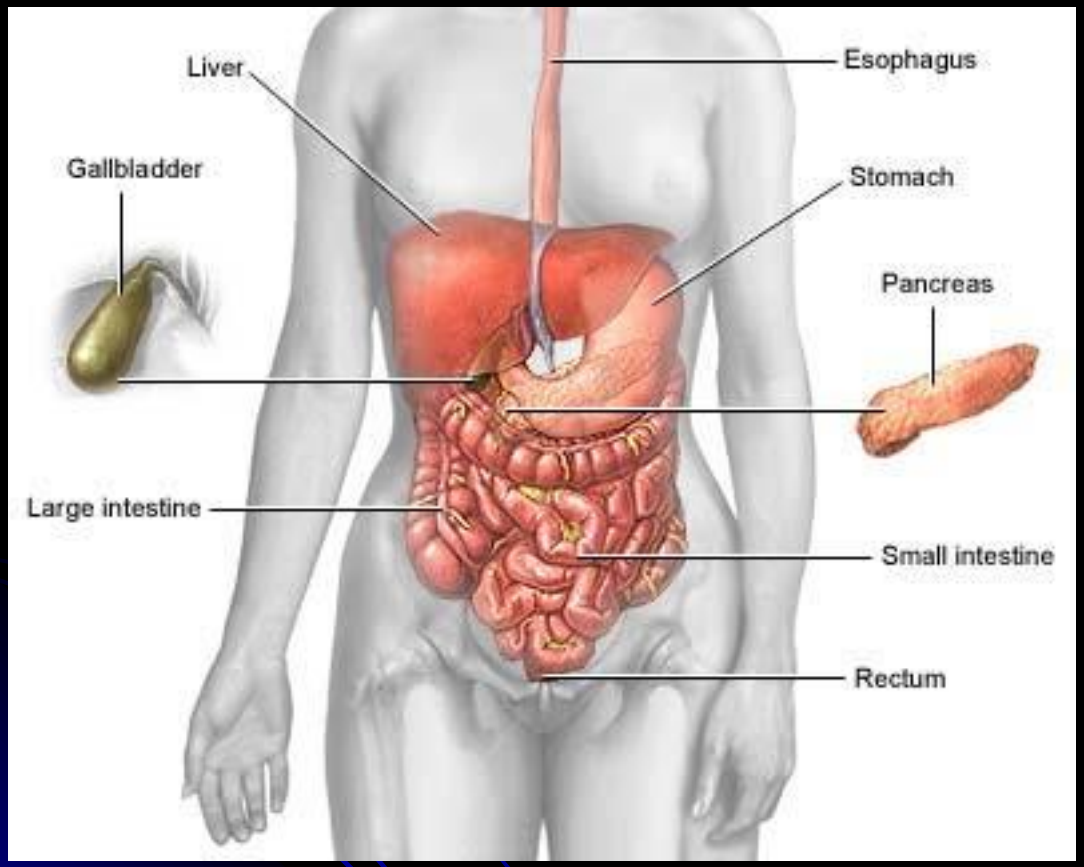
Oral Administration

Oral Administration



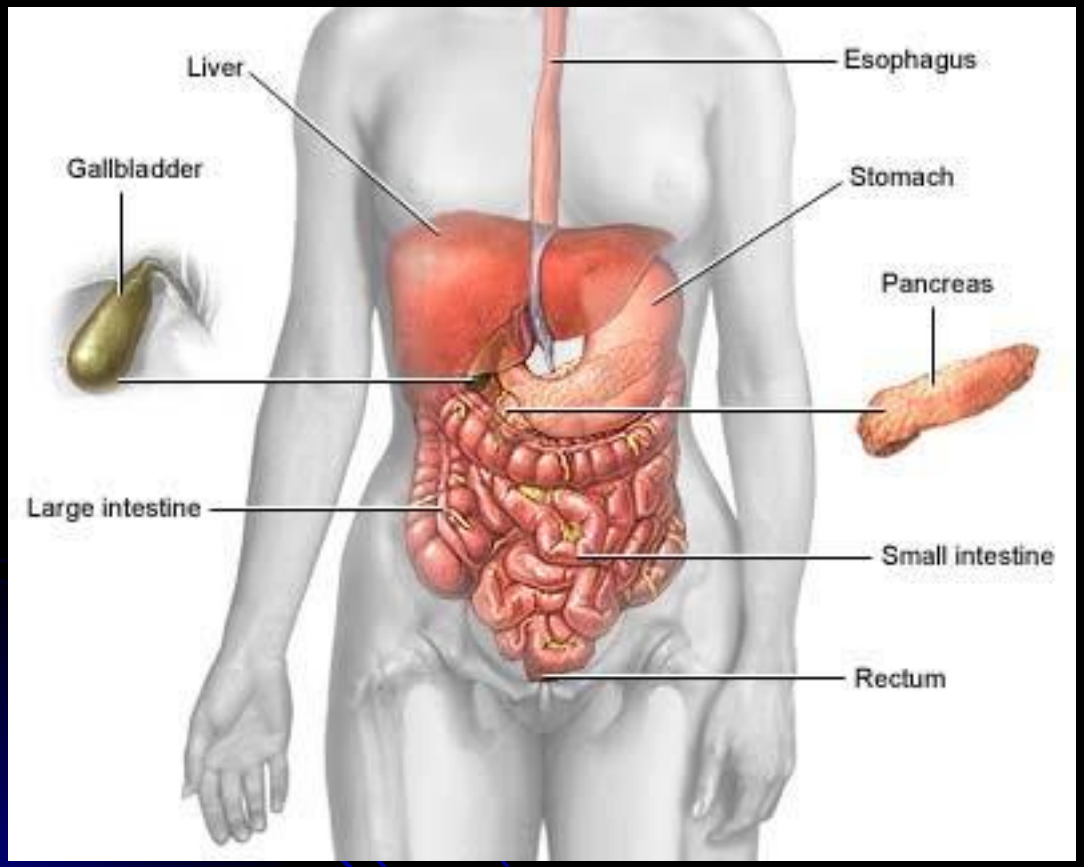
- Most drugs can be absorbed across the surface of the *gastro-intestinal tract*. This, in addition to its convenience, makes it the most widely used method for administering drugs.

Oral Administration



- Some drugs, e.g. *penicillin*, are destroyed by enzymes / low pH of the gastro-intestinal tract and so have to be administered by injection.

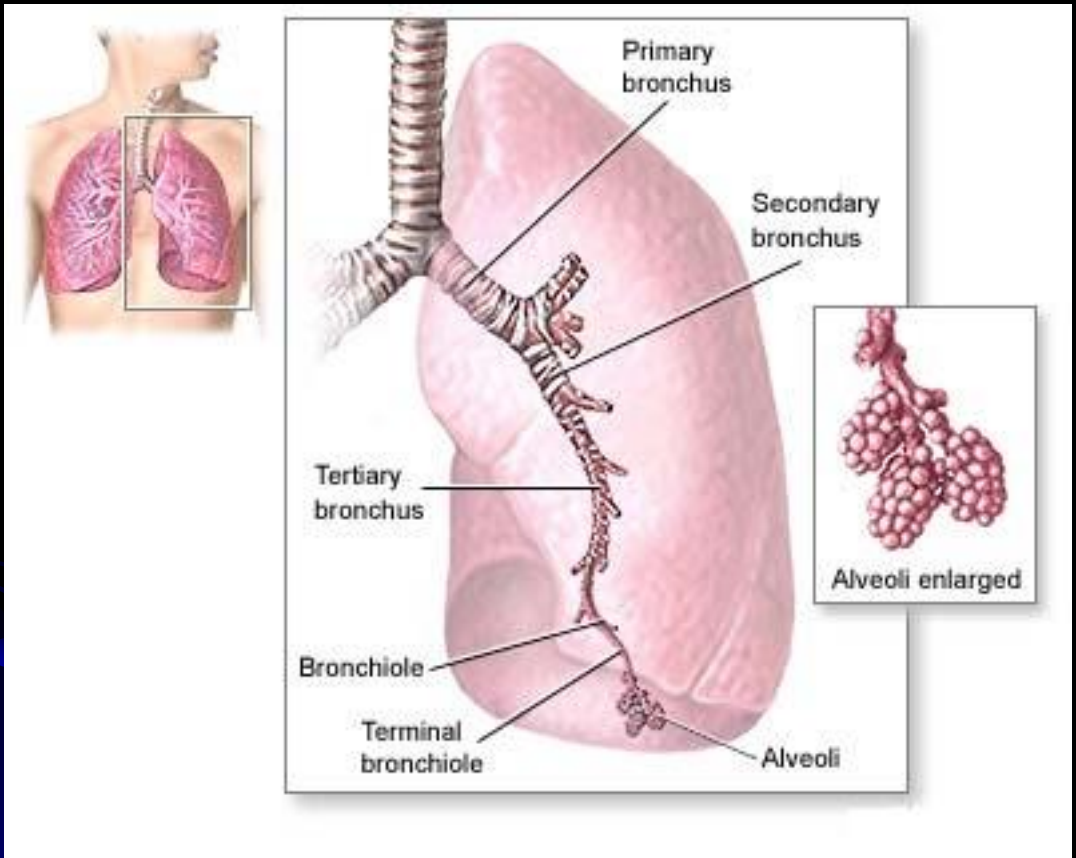
Oral Administration



- Once drugs that have been administered orally are absorbed into the blood, they pass directly through the *liver* where enzymes subject them to first *pass metabolism*. Metabolism of the drug by the liver will render a small portion of the drug inactive.

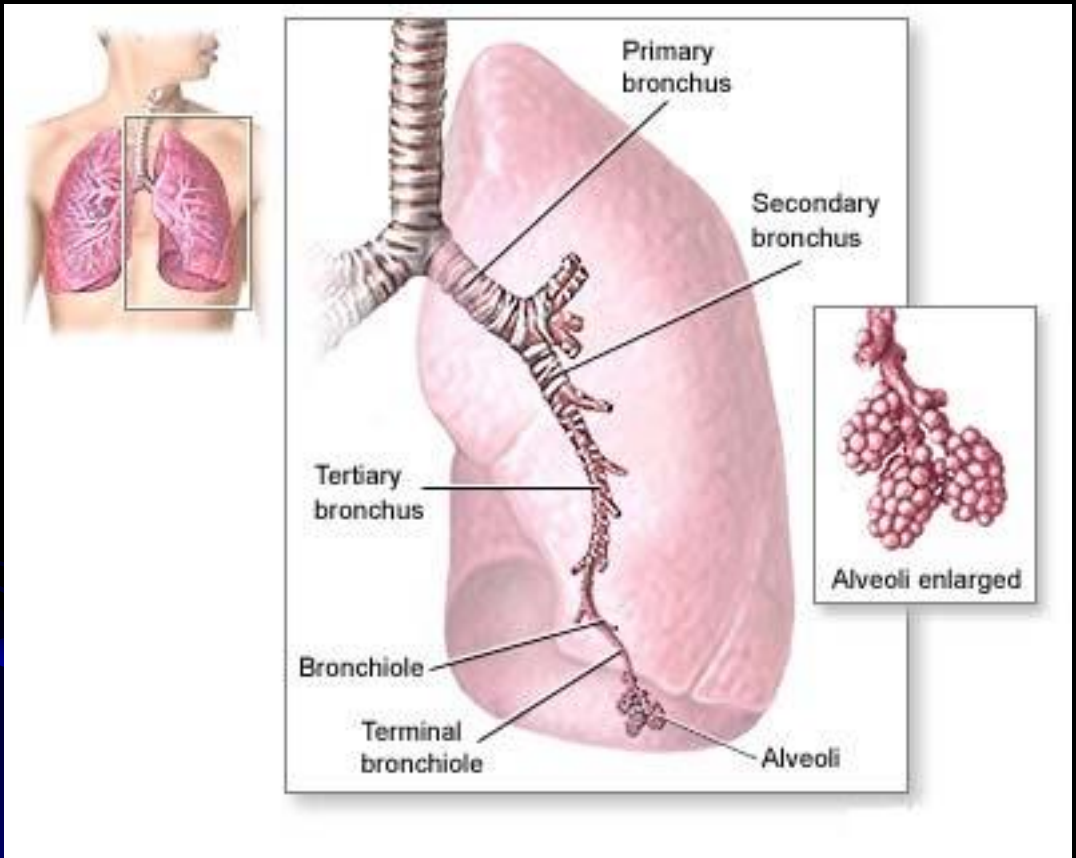
Inhalation

Inhalation



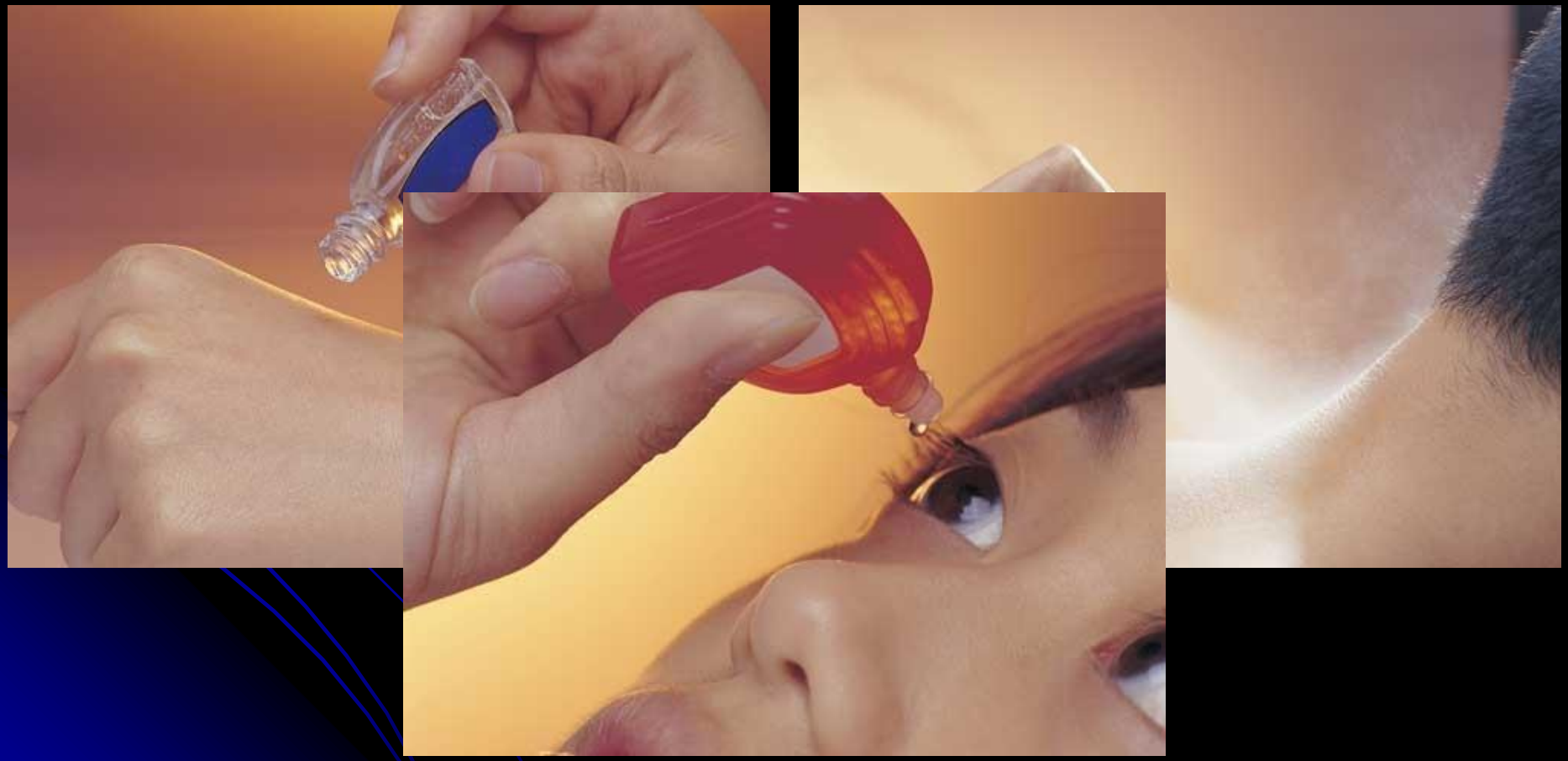
- This is used to administer volatile anaesthetics and some drugs that are used to treat asthma, e.g. *salbutamol*.

Inhalation



- Volatile anaesthetics are absorbed into the blood across the surface of the *alveoli*, while drugs that are used to treat asthma cause the smooth muscle of the airway (*bronchioles*) to relax, thus causing dilation of the airway (*bronchiodilation*).

External Application



External Application

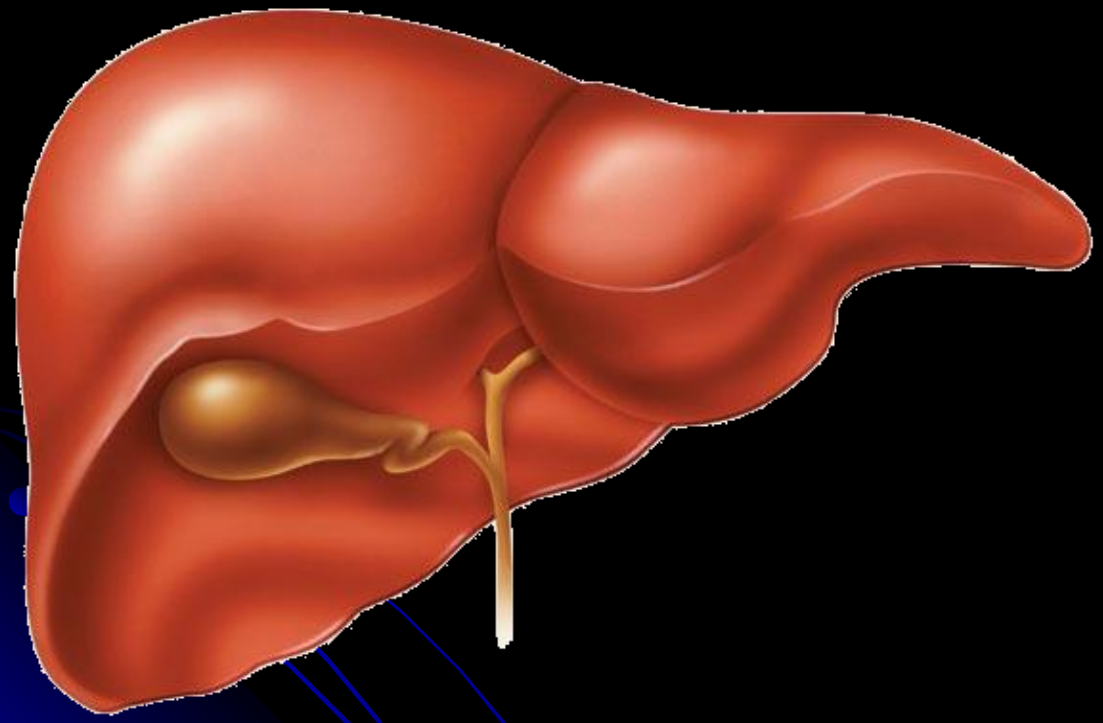
- Eye infections are usually treated by applying an antibiotic directly to the eye.

- Eczema is usually treated by applying an anti-inflammatory drug, e.g. *hydrocortisone*, directly to the area of inflammation.

Drug Metabolism

Liver Form and Function

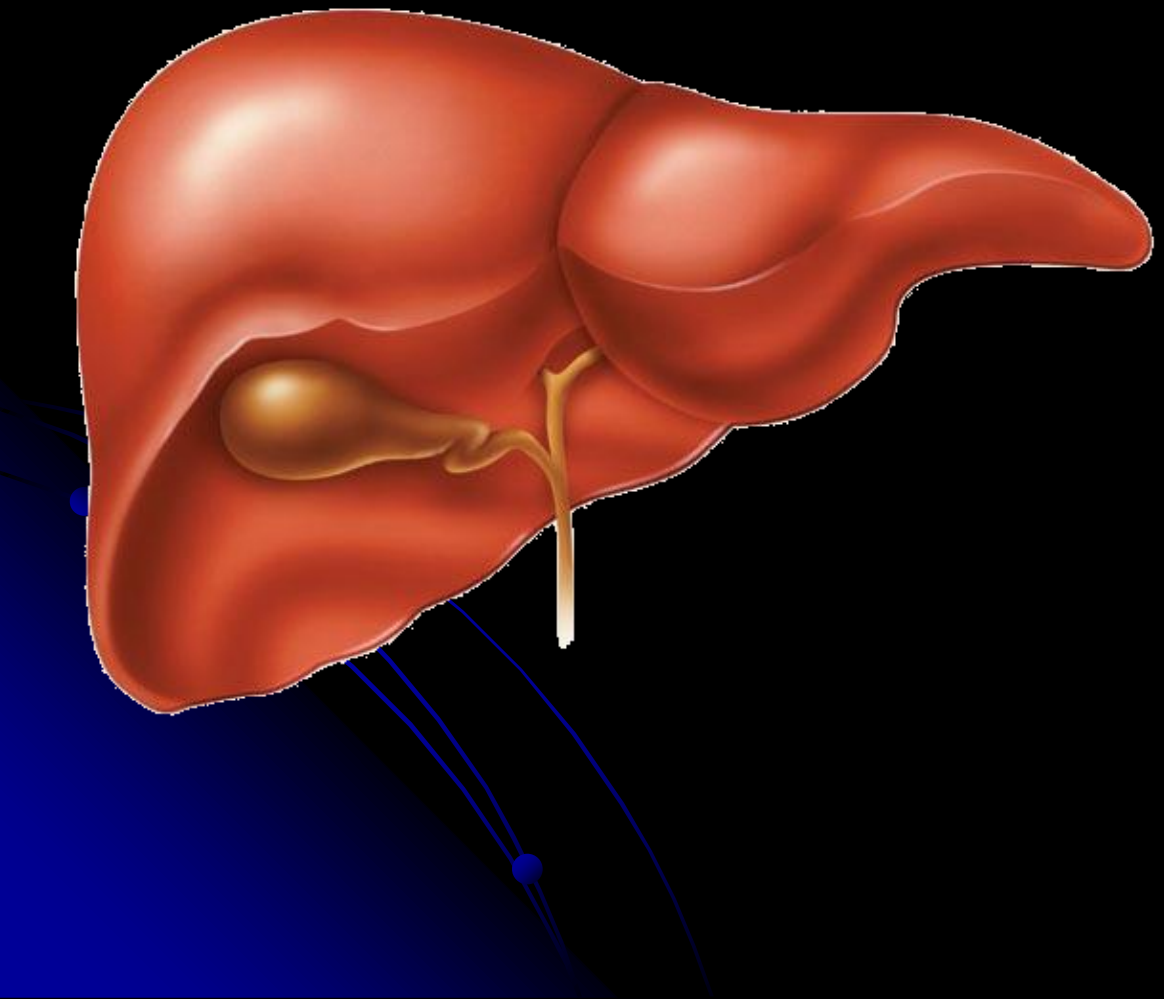
Phase One Metabolism:



Drugs are metabolised in the liver to make them more *polar* and hence increase their *solubility in water* so that they can be *excreted in the urine*.

Liver Form and Function

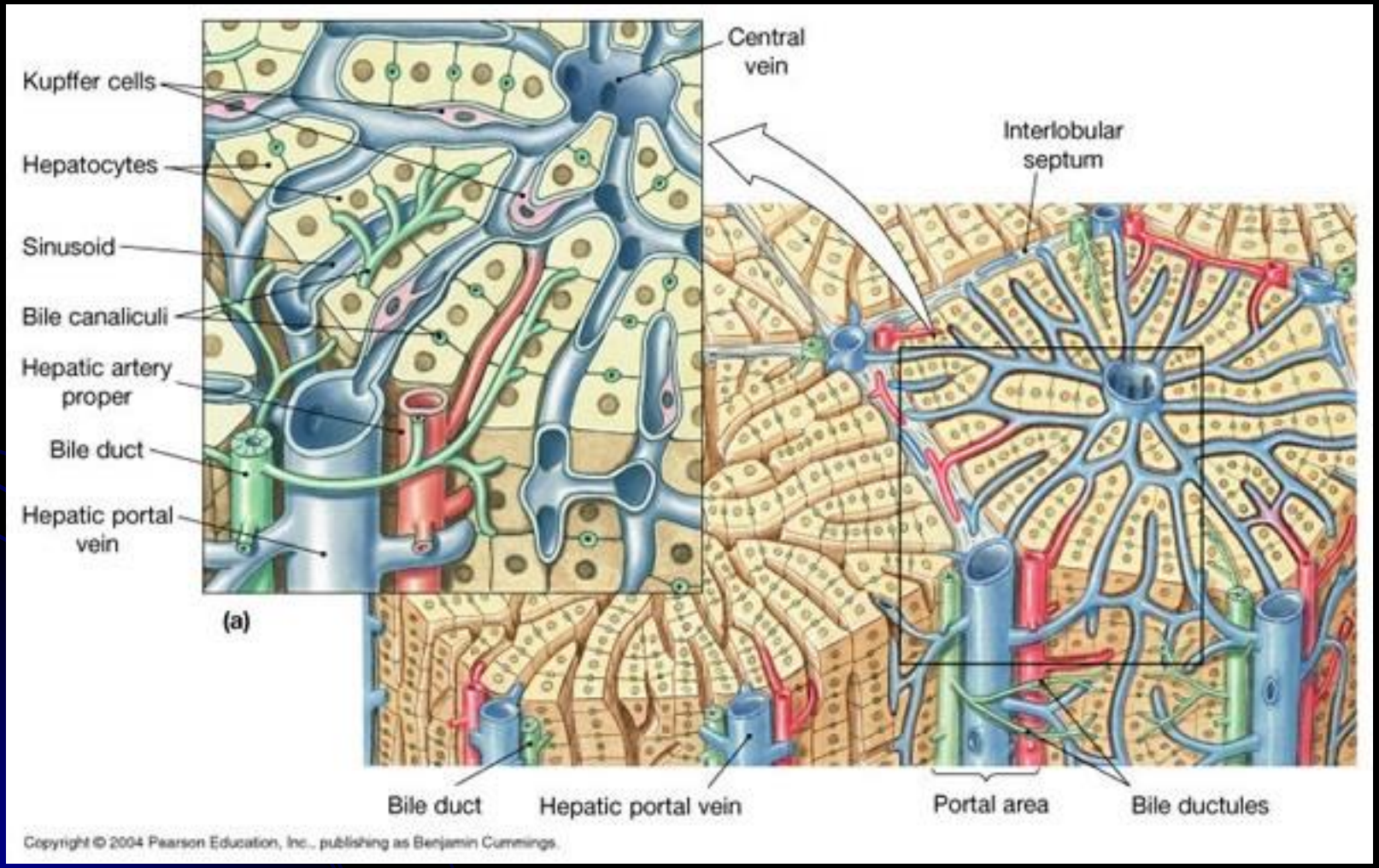
Phase One Metabolism:



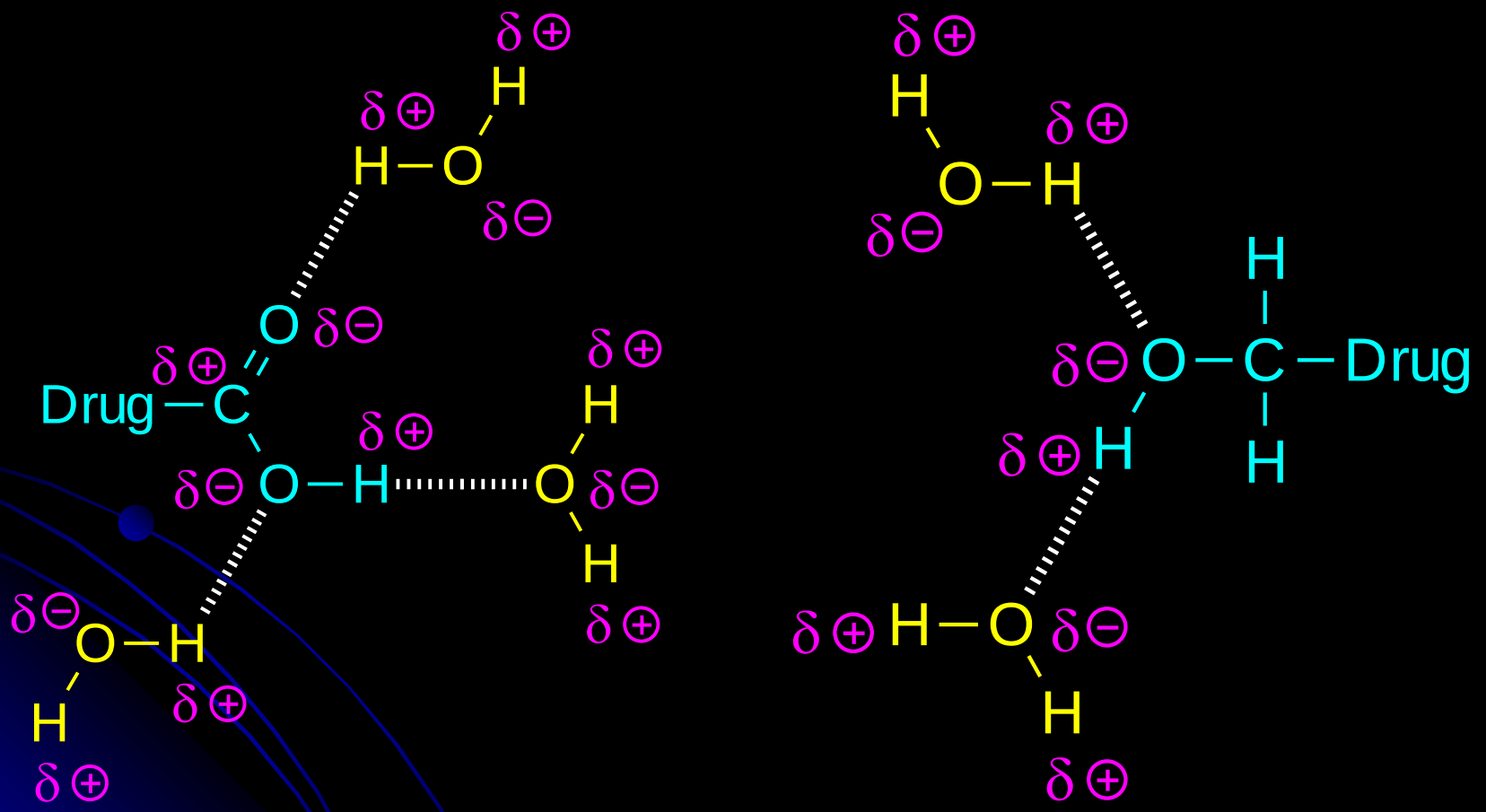
Oxidations are the most important reactions and these are catalysed by an important class of enzymes called the *mixed function oxidases* or *cytochrome P450s*. This enzyme complex is not very substrate specific and consequently, many drugs can be oxidised.

Liver Form and Function

A Detailed View of the Structure of the Liver:

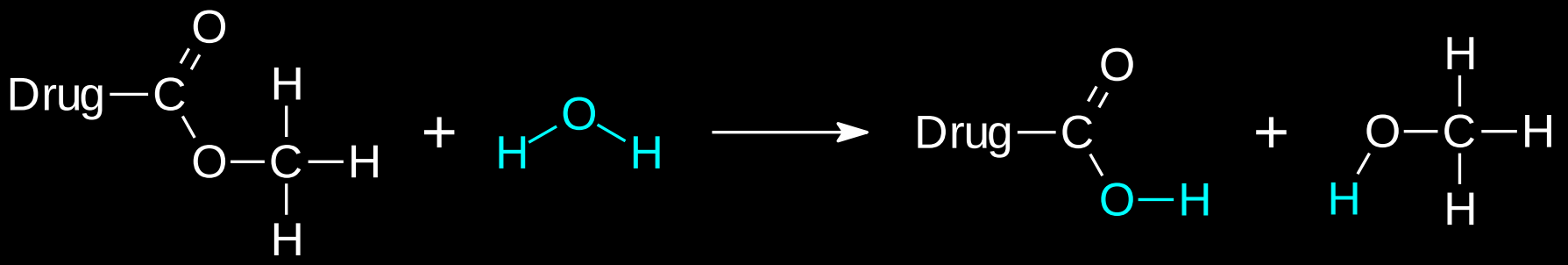


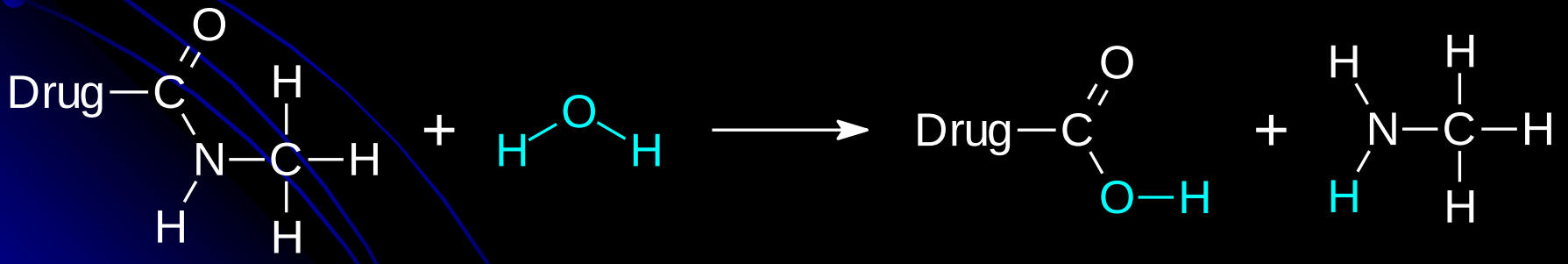
Solubility of Organic Compounds in Water



Phase One Metabolism

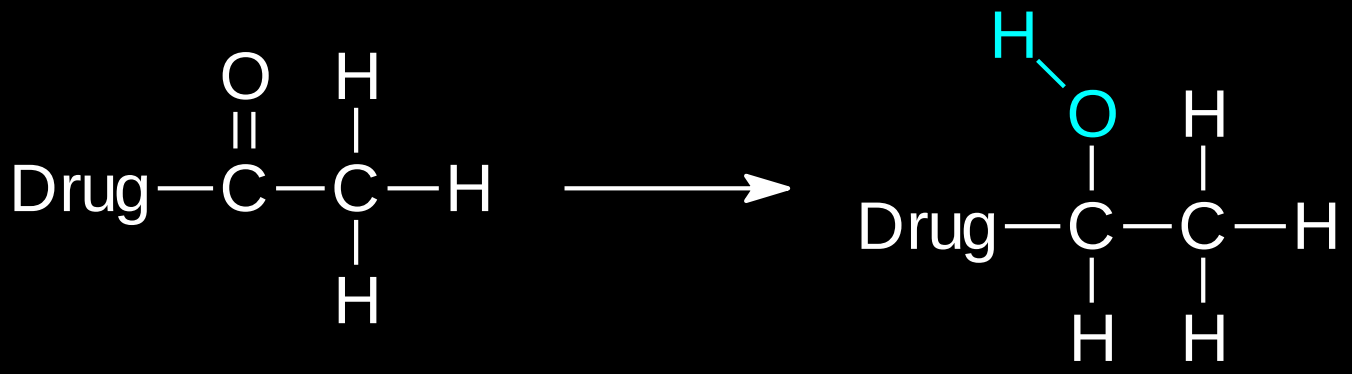
Hydrolysis

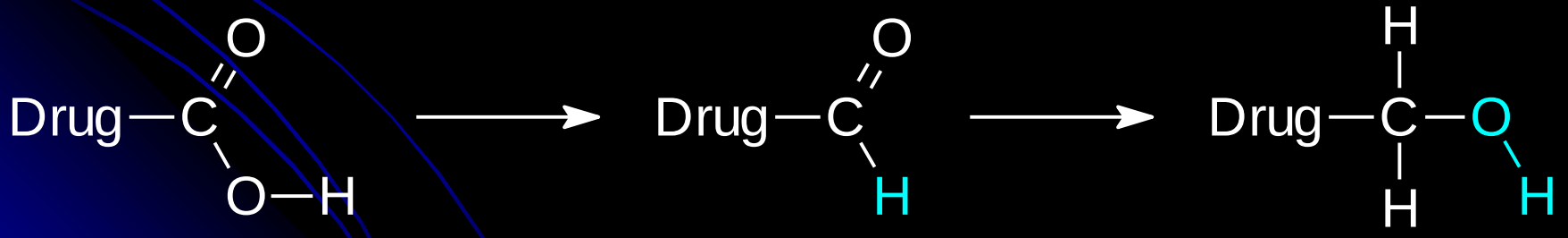




Phase One Metabolism

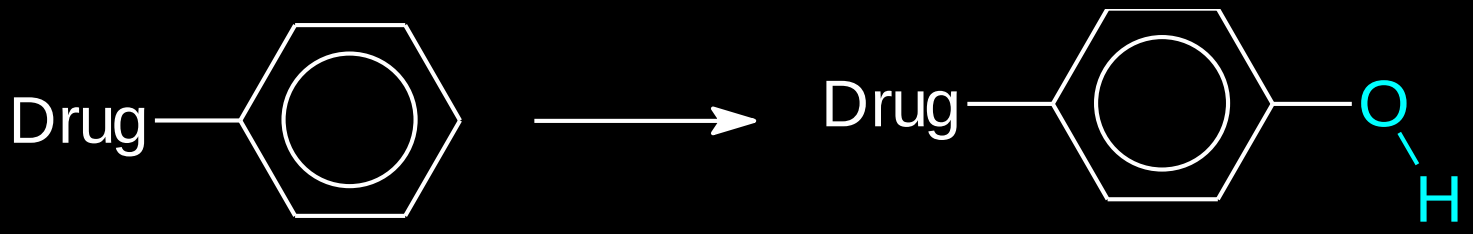
Reduction

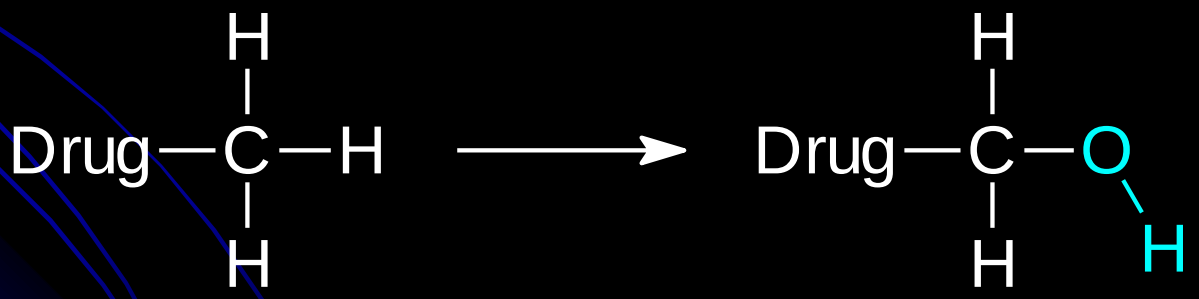




Phase One Metabolism

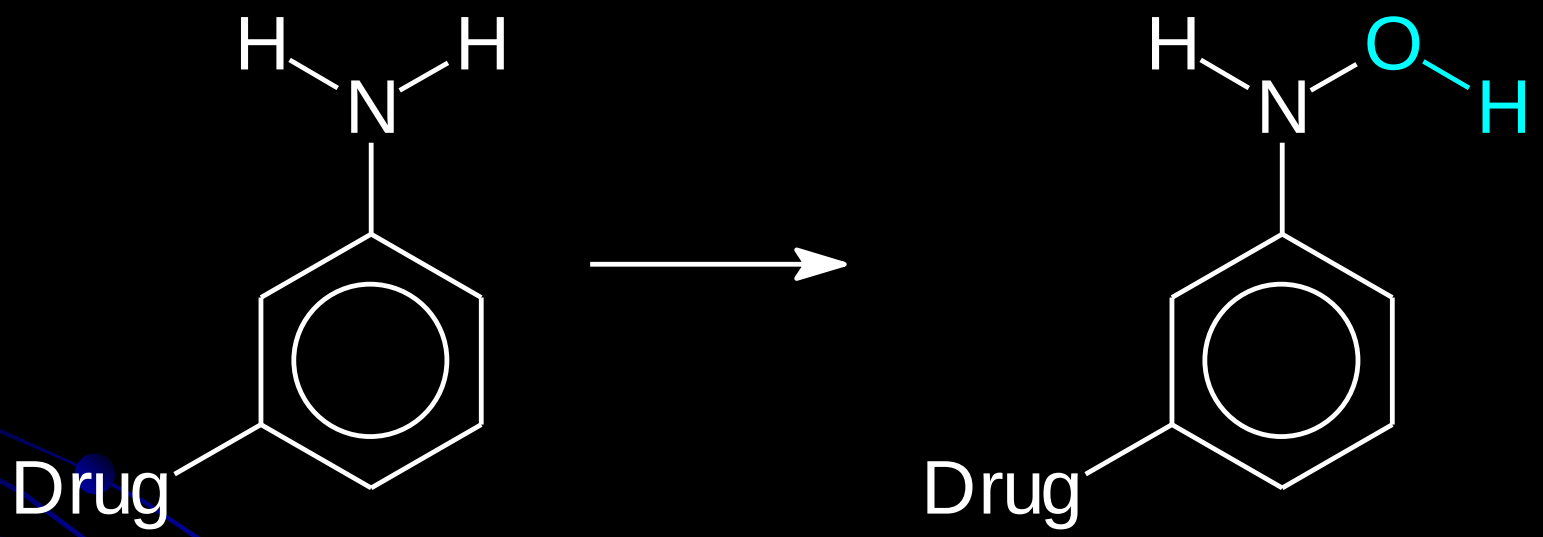
Hydroxylation





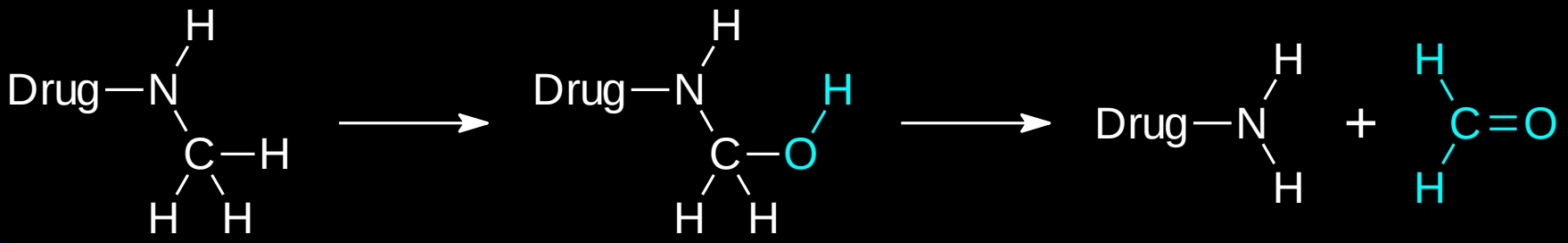
Phase One Metabolism

N-hydroxylation



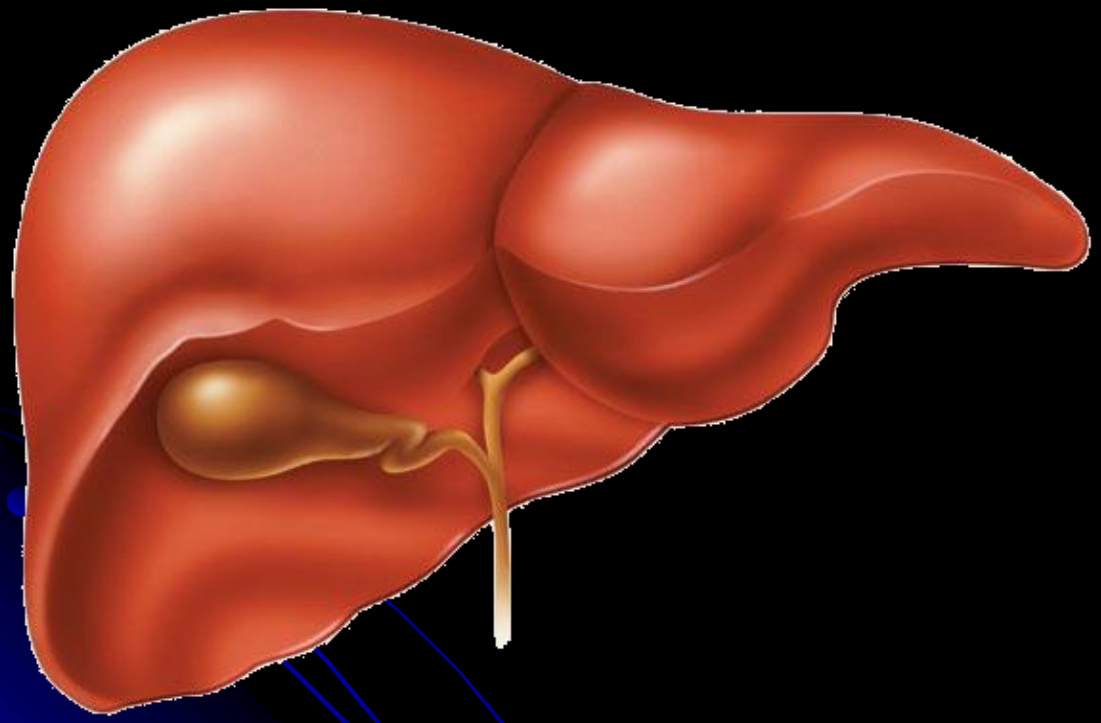
Phase One Metabolism

Oxidative Dealkylation



Liver Form and Function

Phase Two Metabolism:



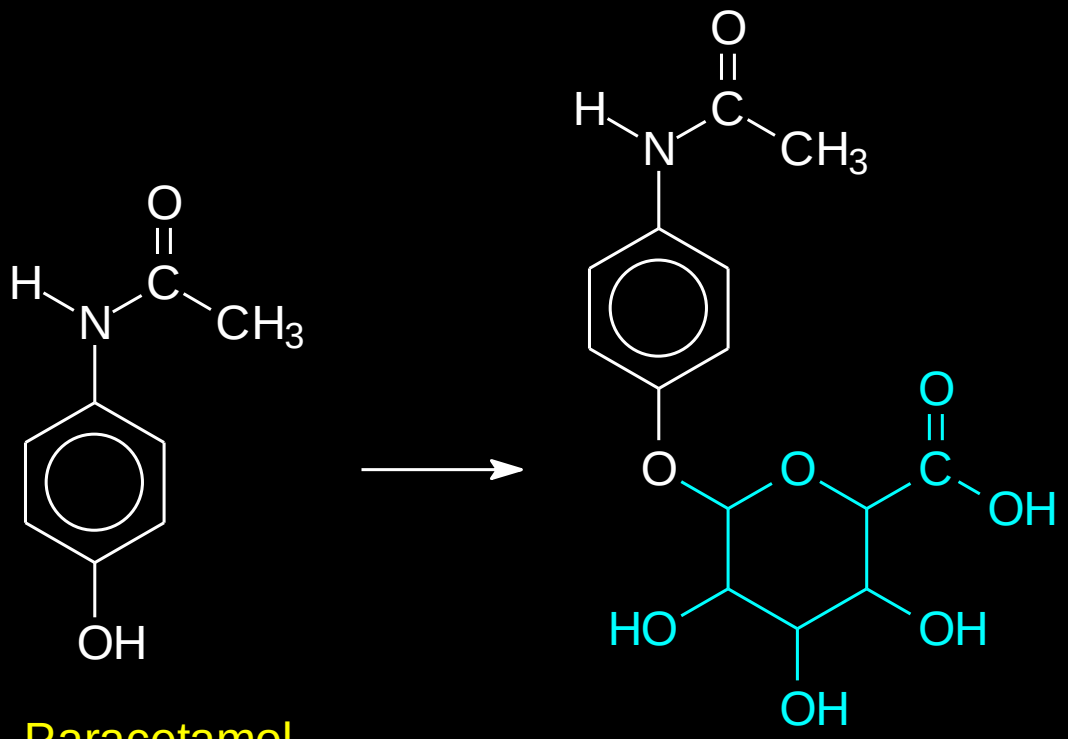
Phase two metabolism of a drug usually occurs in the liver and involves the drug (or its metabolic products from phase one metabolism) being *conjugated* to a *polar, water soluble molecule*. Metabolism of the analgesic *paracetamol* illustrates this.

STUDENT ADVISORY

ADVANCED CHEMISTRY

Paracetamol Toxicity

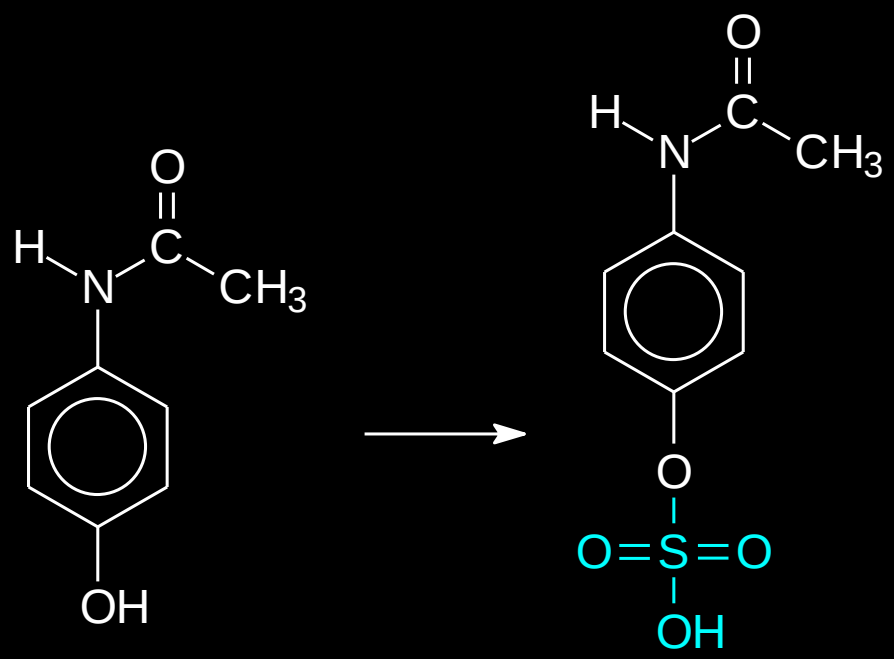
Phase Two Metabolism of Paracetamol



Paracetamol

Glucuronide Conjugate (excreted)

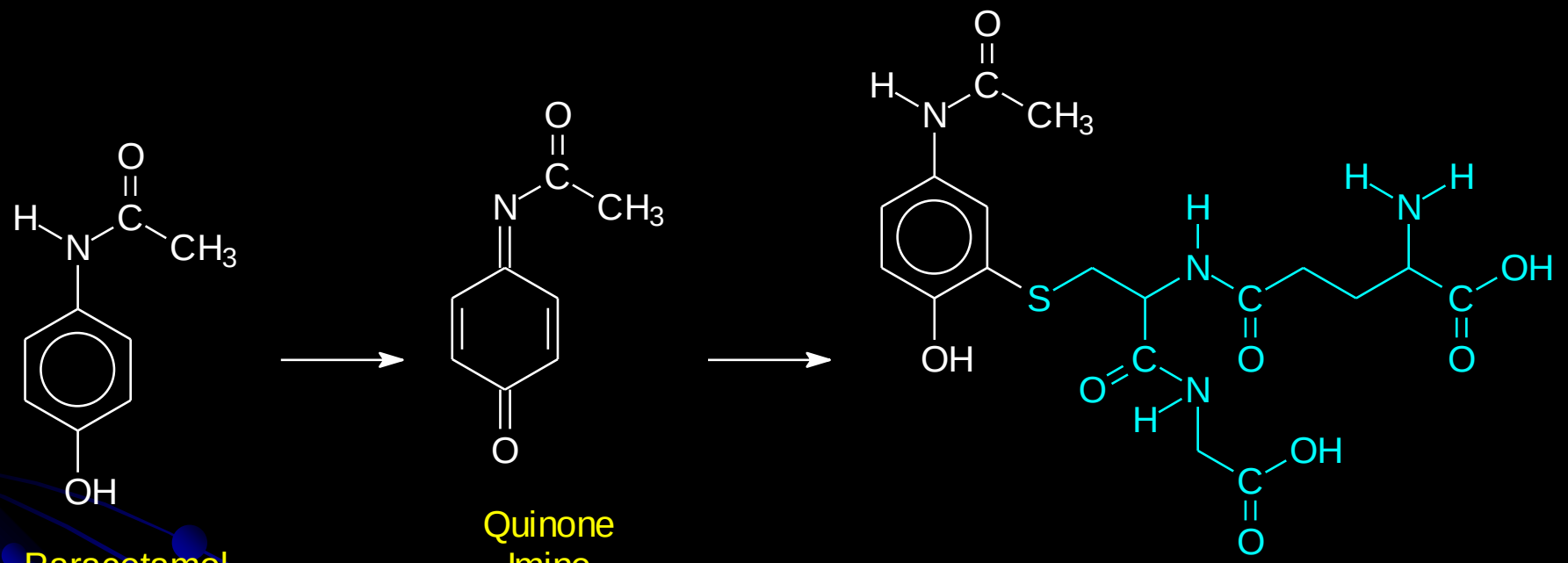
Phase Two Metabolism of Paracetamol



Paracetamol

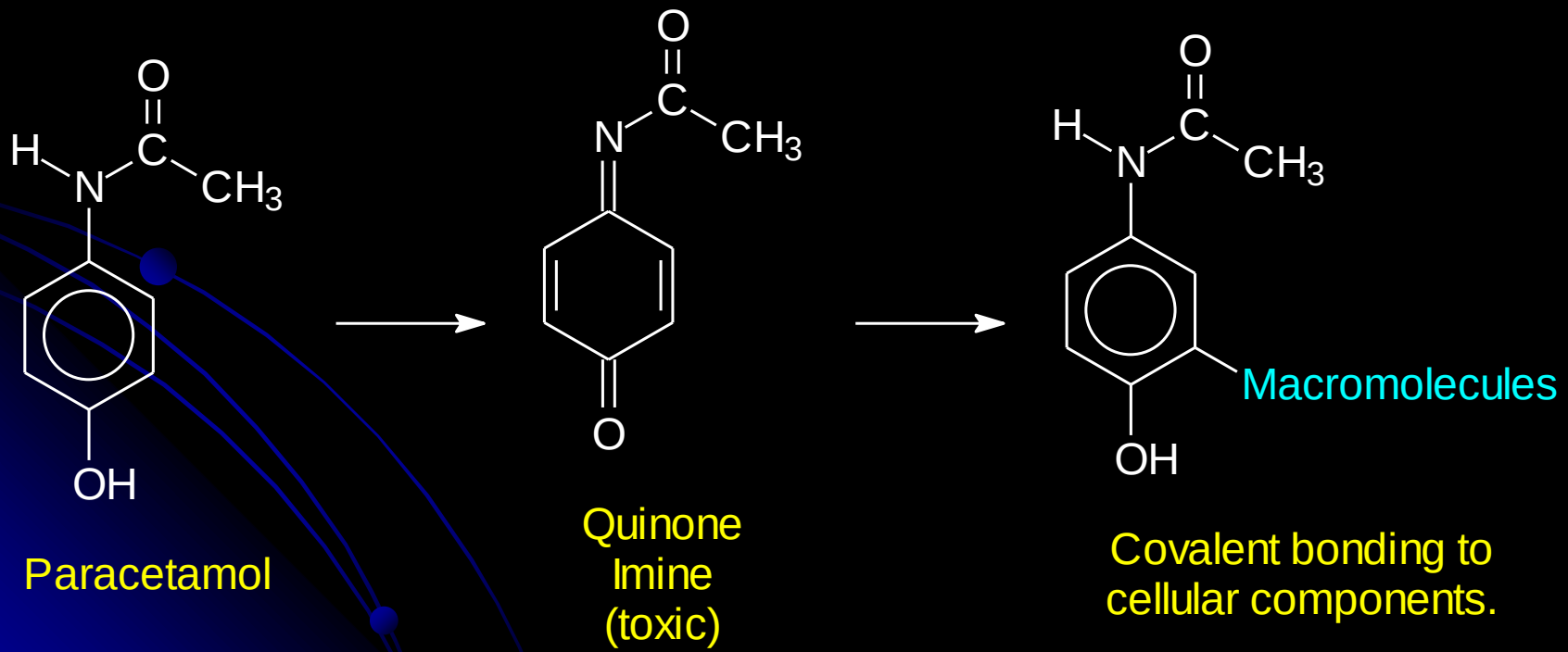
Sulphate Conjugate (excreted)

Phase Two Metabolism of Paracetamol



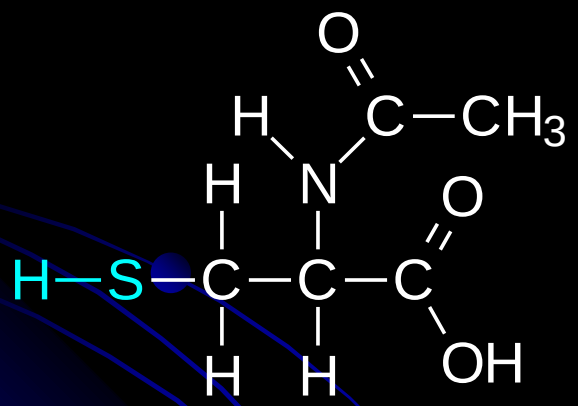
Phase Two Metabolism of Paracetamol

In the absence of sufficient *glutathione*, the *quinone imine* bonds to DNA, RNA and proteins within the cell. This leads to irreversible cellular damage, which may ultimately lead to liver failure and death:

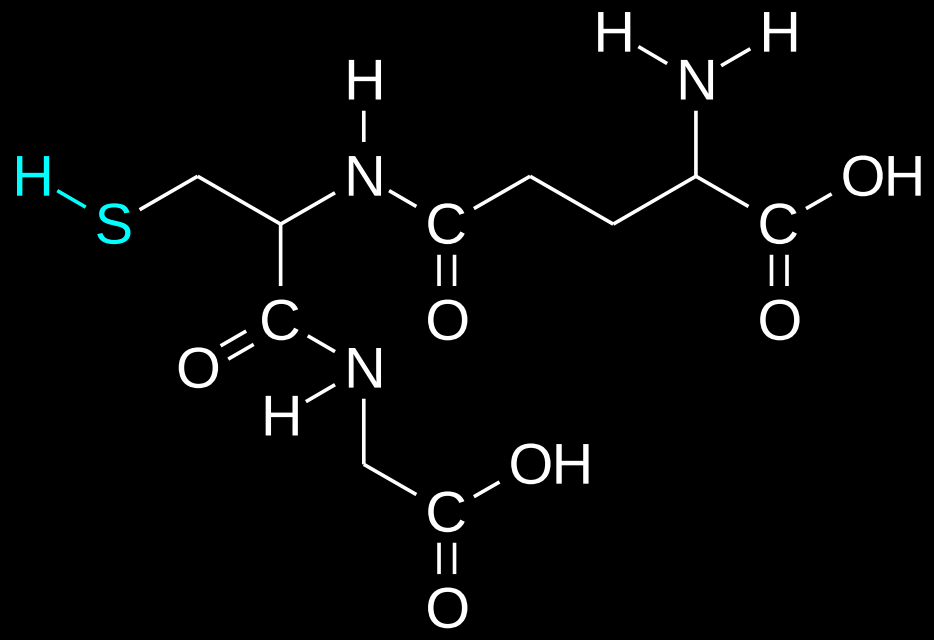


Phase Two Metabolism of Paracetamol

N-acetylcysteine acts as an antidote to paracetamol poisoning because it can substitute for *glutathione*:



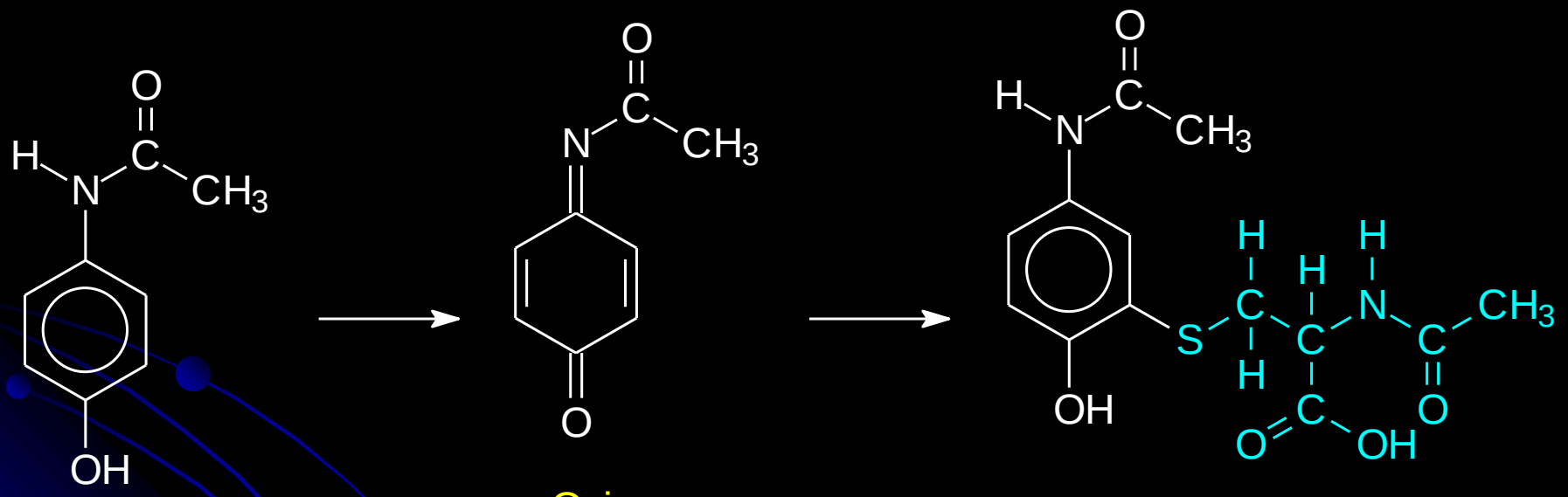
N-Acetylcysteine



Glutathione

Phase Two Metabolism of Paracetamol

N-acetylcysteine acts as an antidote to paracetamol poisoning because it can substitute for *glutathione*:

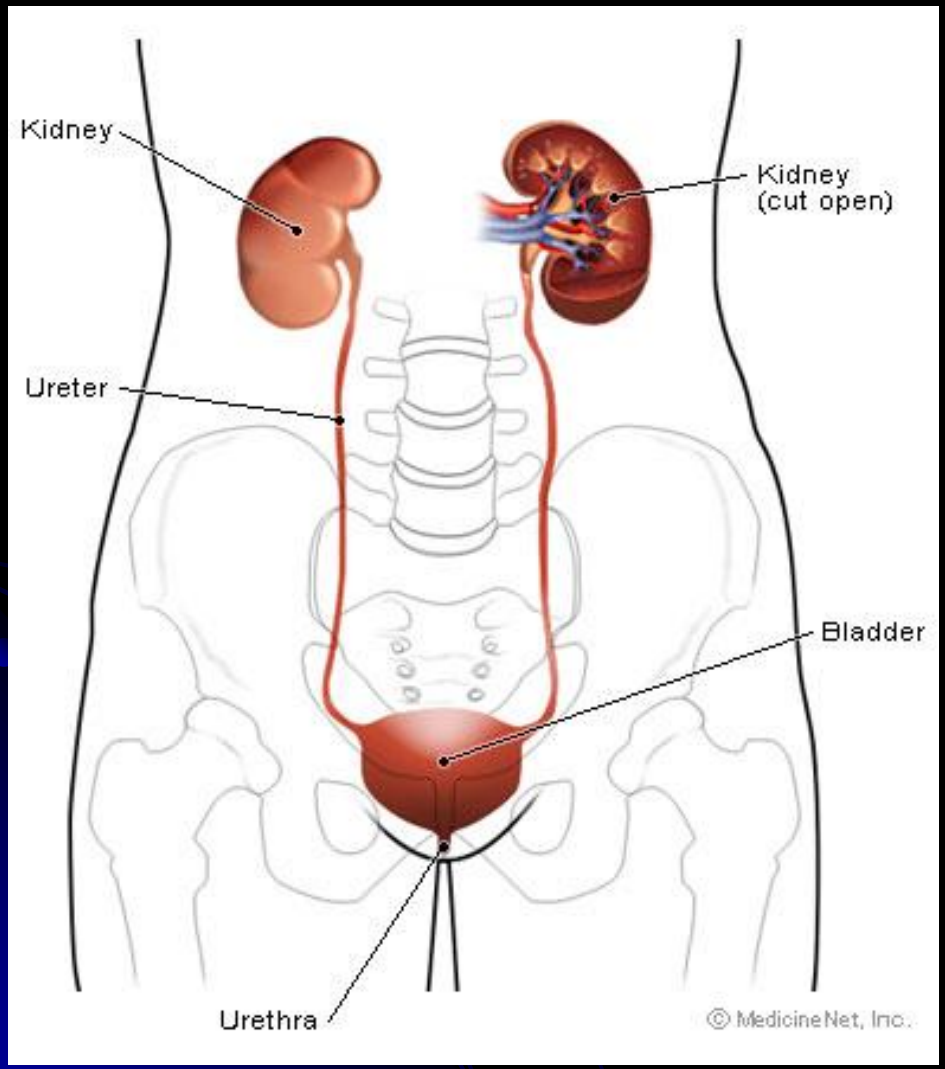


Paracetamol

Quinone Imine (toxic)

N-Acetylcysteine Conjugate (excreted)

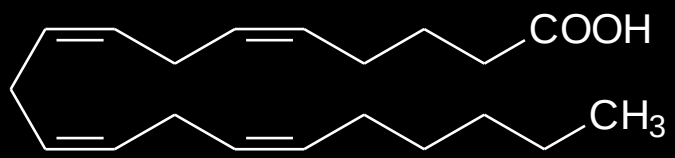
Excretion



Once the drug has been metabolised by the liver to increase its polarity and hence its solubility in water, it is excreted in the urine and consequently removed from the body.

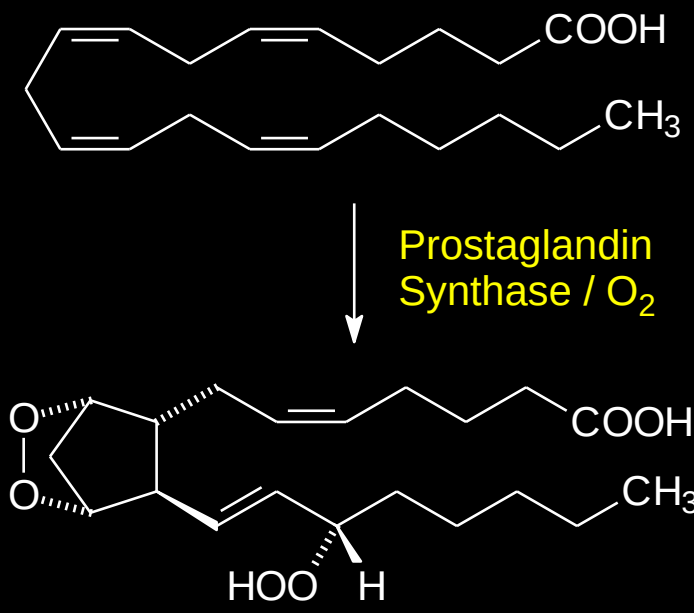
The Pharmacology of Aspirin

Prostaglandin Biosynthesis



Arachidonic Acid

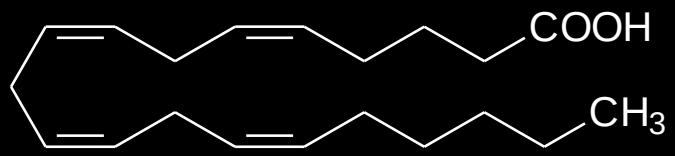
Prostaglandin Biosynthesis



Arachidonic Acid

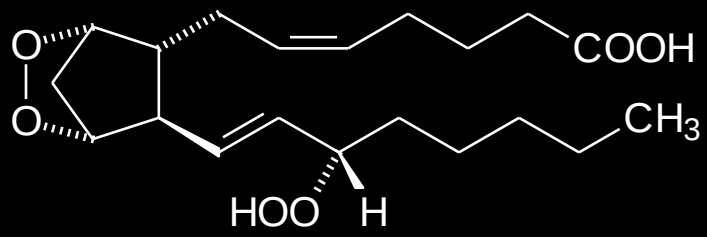
Prostaglandin G_2

Prostaglandin Biosynthesis



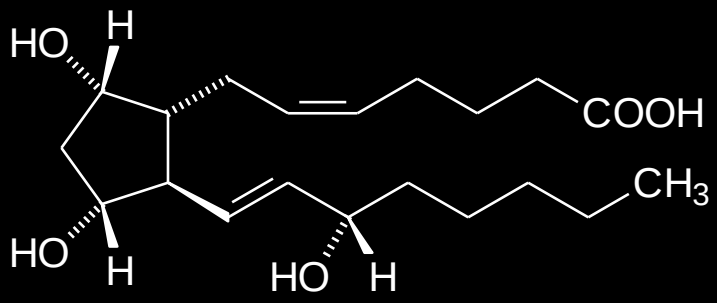
Arachidonic Acid

Prostaglandin Synthase / O_2



Prostaglandin G_2

Additional Biochemistry

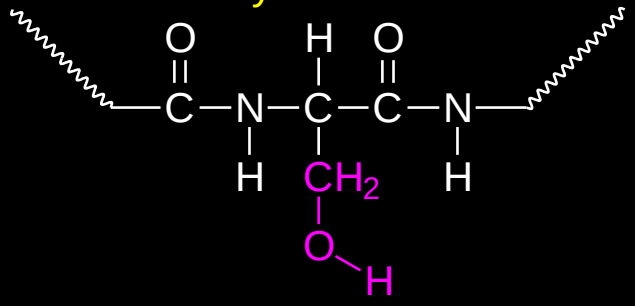


Prostaglandin $F_{2\alpha}$

Inflammation, fever, platelet aggregation, gastric secretions.

Aspirin Inhibits Prostaglandin Synthase

Active site of prostaglandin synthase.



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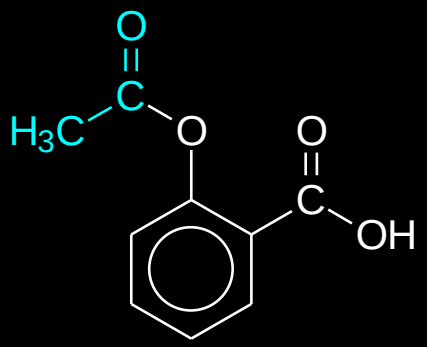
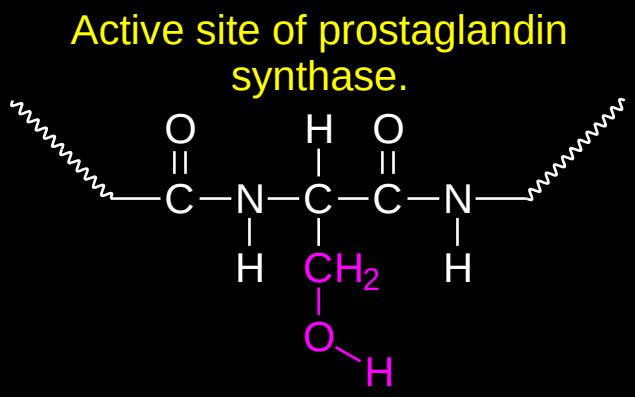
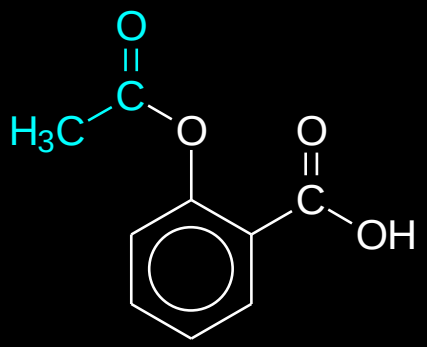
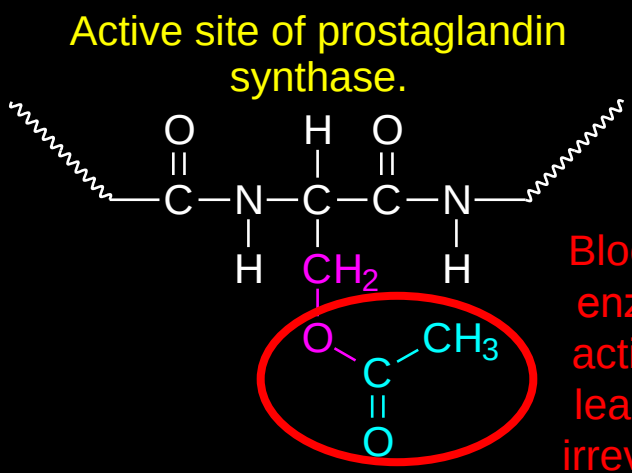


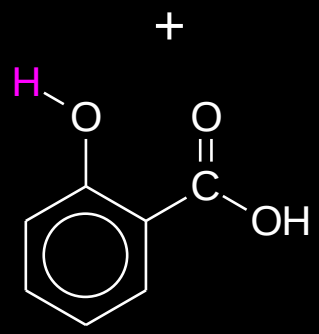
Aspirin

Aspirin Inhibits Prostaglandin Synthase

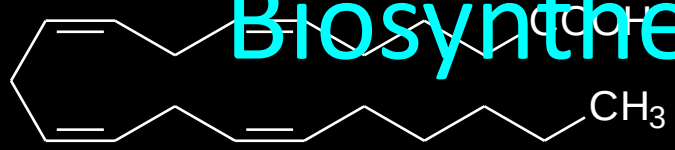






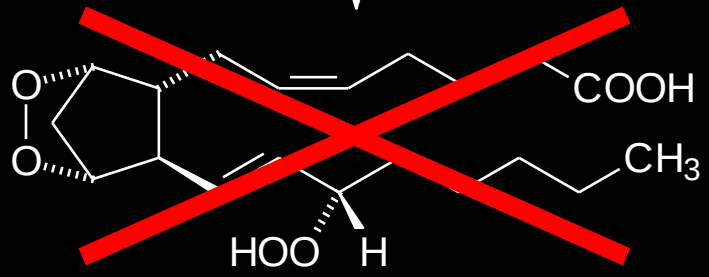


Inhibition of Prostaglandin Biosynthesis



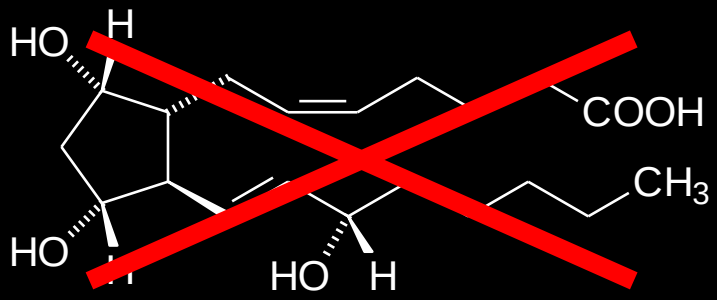
Arachidonic Acid

Prostaglandin Synthase / O_2



Prostaglandin G_2

Additional Biochemistry



Prostaglandin $F_{2\alpha}$

Inflammation, fever, platelet aggregation, gastric secretions.

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