## Introduction to pharmacology

List the *two major branches of pharmacology* and define each branch.

1. *Pharmacodynamics* – the biological and physiological effects of the drug
2. *Pharmacokinetics* – the absorption, distribution, metabolism and excretion of the drug

Explain the various names that can be given to the same drug, and the advantages of the generic name.

- *Chemical Name* – a systematic name of the structure of the substance
- *Generic Name* – the name of the drug itself. It is useful in that names of drugs which belong to the same class have a common ending (allows you to classify drug & predict effects)
- *Trade Name* – the name given by the company producing the drug

Describe the places where drugs can act, and give an example of a drug which acts on each of these types of "target"

1. *Receptors for endogenous substances (hormones, neurotransmitters, growth factors*)
   Opioid analgesics, Beta blockers, Bronchodilators, Tamoxifen, Antihistamines

2. *Transport molecules*
   SSRIs, Proton pump inhibitors, Cocaine

3. *Ion channels*
   Benzodiazepines, Inhaled anaesthetics, Calcium channel blockers, Alcohol

4. *Enzymes*
   NSAIDs, Statins – cholesterol lowering agents, ACE inhibitors – lower BP

Define the following terms:

*Bioavailability*: how much of a drug you would expect to make it to the bloodstream

*therapeutic index*: a comparison of amount of a drug that cause therapeutic effect vs toxicity

*adverse effect*: undesired harmful effects of a medication

*therapeutic effect*: any result of medication that is desirable and/or beneficial

*contraindication*: a specific situation in which a drug should not be used as it may be harmful

Explain what *receptor agonists and antagonists* are, and be able to give an example of the use of each in a clinical setting.

*Receptor agonist*s produce the same response as a natural substance would e.g. Opioid analgesics to reduce pain

*Receptor antagonists* bind to a receptor, have no effect themselves and present the natural substance or an agonist from binding e.g. Beta blockers to reduce blood pressure

Explain what the *affinity of a drug* for its receptor means in practical terms.

The *affinity* of a drug means how 'keen' a drug is to bind to a receptor. If a drug has high affinity, it will bind readily to a receptor and may even kick substances with a lower affinity off a receptor.

## Explain what the *selectivity of a drug* for its receptor means in practical terms.

The *selectivity* of a drug relates to how many different types of a receptors a drug can bind to, and it's affinity for different receptors.

## Explain what the *efficacy and potency of a drug* mean in practical terms.

*Potency* is the measured by the amount of drug needed to produce a particular size of effect. The more potent a drug is, the less is needed. *Efficacy* is the ability to produce the desired result.

## List the *four main pharmacokinetic processes*, and describe the factors which can alter these processes.

| | Definition | Factors which can alter process |
|---|---|---|
| Absorption | The movement of the drug from its administration site into the bloodstream | Route of administration, physiological state of patient, formulation of drug, chemical properties (molecule size etc.) |
| Distribution | The degree to which a drug spreads throughout the body | Binding to plasma proteins in blood, being attracted to something e.g. iodine |
| Metabolism | How the body breaks down the drug (mostly in the liver) to convert into a water soluble form | How water or lipid soluble a drug is |
| Excretion | How the drug is removed from the body (mostly in the kidneys) | Rate of metabolism, rate of renal filtration |

## Explain why the pharmacokinetics of a drug are just as important as its pharmacodynamics in deciding how useful it will be.

The pharmacokinetics of a drug are just as important as the pharmacodynamics because if a drug is unable to be absorbed or distributed appropriately, it will not have the intended affect. Similarly, if a drug fails to be metabolised or excreted appropriately, it may cause harm to the patient.

## Describe the types of interactions that can occur between drugs when multiple drugs are taken, and explain some possible outcomes of these interactions.

Drugs can interact pharmacokinetically and/or pharmacodynamically.

Another drug (or food) in the stomach may increase or decrease the absorption rate of an orally administered drug (e.g. tetracyclines and calcium). The distribution of a drug that is highly protein bound is likely to be affected if given with another drug that is also highly protein bound (e.g. warfarin & paracetamol). Metabolism requires enzymes, so if two drugs which are metabolised by the same enzyme are given together, the metabolism of both will be slowed, raising the blood level of both (e.g. grapefruit juice & many drugs). If the rate at which drug metabolites are removed from the body changes, they can accumulate in the body. They may retain some pharmalogical activity and cause interaction (e.g. digoxin & verapamil).

Two drugs that have similar effects are likely to increase that effect when combined – e.g. diazepam and alcohol (both CNS depressants) can result in death due to respiratory arrest. Two drugs which have opposite will counteract each other when combined.

## Pharmacology of major drug classes

### Explain the principles of chemotherapy

The use of chemicals to destroy pathogens which have entered to body, or malignant cancer cells. The idea is to exploit a fundamental difference between cells that are trying to kill you and your own healthy cells, so that the drug kills only the invading or malignant cells and not you. This is not always achievable, especially in cancer chemotherapy.

### Outline the targets which are exploited by the following classes of drugs:

- *Antibacterial* – inhibition of cell wall, protein and DNA or RNA synthesis
- *Antifungal* – cell wall and ergosterol synthesis (cell membrane)
- *Antiviral* – blocking attachment of virus to cell, block uncoating process, reverse transcriptase inhibitors & polymerase inhibitors to stop copying of genetic material, protease inhibitors block assembly of new virons, neuraminidase inhibitors block cleaving off
- *Cytotoxic* – inhibitors of DNA synthesis and integrity

### Briefly describe how drug resistance comes about, by giving some examples of resistance mutations which occur.

Resistance is evolution/natural selection action. Bacteria can develop expression of drug efflux pump, enzymatic degradation of the drug, or alteration of the drug binding site.

### List the *major neurotransmitters* mentioned in the lecture and give the major *roles* of each & their *involvement in disease*.

| Neurotransmitter | Function | Problems caused by imbalances |
|---|---|---|
| Serotonin | Affects mood, hunger, sleep, and arousal | Undersupply linked to depression |
| Dopamine | Influences movement, learning, attention and memory | Oversupply linked to schizophrenia<br>Undersupply linked to tremors and decreased mobility in Parkinson's Disease, and ADHD |
| Acetylcholine (ACh) | Enables muscle action, learning and memory | Ach-producing neurons deteriorate as Alzheimer's Disease progresses |
| Norepinephrine | Helps control alertness and arousal | Undersupply can depress mood and cause ADHD-like attention problems |
| GABA | Inhibitory neurotransmitter | Undersupply linked to seizures, tremors and insomnia |
| Glutamate | Excitatory neurotransmitter involved in memory | Oversupply can overstimulate the brain, producing migraines or seizures |

### Describe how neurotransmitters are removed from the synaptic space after release, and the ways in which this removal can be manipulated using drugs.

Neurotransmitters are removed from the synaptic space in one of two ways - either through enzyme breakdown or reuptake into the neuron. Drugs can act on both these actions, by either increasing or decreasing the effect eg. SSRIs selectively inhibit the reuptake of serotonin, helping to elevate mood in people diagnosed with major depression.

Give an overview of how antidepressants work, and explain the main differences between the older and the newer antidepressant drug classes.

| Class of Antidepressant | Action |
|---|---|
| Monoamine oxidase inhibitors (MAOIs)<br>e.g. Moclobemide | Irreversibly inhibit monoamine oxidases A & B, increasing the synaptic concentrations of adrenaline, noradrenaline, dopamine & serotonin |
| Tricyclic antidepressants (TCAs)<br>e.g. Amitriptyline, Imipramine | Inhibit reuptake of noradrenaline and serotonin into presynaptic terminals (also block cholinergic, histaminergic, α1-adrenergic & serotonergic receptor) |
| Selective serotonin reuptake inhibitors (SSRIs)<br>e.g.Fluoxetine, Paroxetine, Sertraline | Selectively inhibit the presynaptic reuptake of serotonin |
| Noradrenaline- serotonin reuptake inhibitors (NSRIs)<br>e.g.Venlafaxine | Selectively inhibits the reuptake of noradrenaline and serotonin |
| Selective Noradrenaline reuptake inhibitors (SNRIs)<br>e.g. Reboxetine | Inhibits noradrenaline reuptake |
| Noradrenaline-dopamine reuptake inhibitors (NDRIs)<br>e.g. Bupropion | Inhibits noradrenaline & dopamine reuptake |

Know the *receptor sub-types for noradrenaline and acetylcholine*, and the autonomic and other functions that they are responsible for.

| | Type | Subtype | Location | Function |
|---|---|---|---|---|
| Acetylcholine Receptors (Cholinergic) | Nicotinic | N/A | Skeletal Muscle | Contraction |
| | Muscarinic | N/A | Brain, organs, glands | Parasympathetic Response |
| Noradrenaline Receptors (Adrenoceptors) | α (alpha) | $\alpha_1$ | Blood vessels | Constriction |
| | | $\alpha_2$ | Brain | Reduce release of Noradrenaline |
| | β (beta) | $\beta_1$ | Heart | Increase rate & strength of beat |
| | | $\beta_2$ | Bronchioles and blood vessels | Dilation |
| | | $\beta_3$ | Fat cells | Mobilisation of fat |

Describe the mechanism of actions of the two major classes of analgesic drugs.

- *Non-steroidal analgesics (NSAIDs)* – works at site of injury – inhibiting the enzyme cyclooxygenase, thus blocking the production of prostaglandins which are essential to pain, inflammation and fever responses (analgesic, anti-inflammatory and anti-pyretic)

- *Narcotic analgesics (opioids)* – works in brain, spinal cord, and at site of injury – agonists at our endogenous opioid receptors, 'damps down' sensation of pain & emotional component

Use your knowledge of the mechanism of action of the analgesic drugs to be able to predict the likely side effects of members of these drug classes.

- NSAIDs: indigestion, stomach ulcer, hypertension, persistent headache, dizziness

- Opioids: analgesia, respiratory depression, constriction of pupils, nausea & vomiting, constipation, sedation, cough suppression (codeine & pholcodine), sphincter of Oddi and ureter spasms (morphine), vasodilation

## Use your knowledge of the mechanism of action of the analgesic drugs to be able to recognise the signs of overdose of an opioid.

Pinpoint pupils, decreased respiratory rate, coma, hypotension, convulsions

## Briefly describe the phenomenon of tolerance and its relationship to dependence.

- Tolerance – after using the drug for long enough, the dose needs to be increased to have the same effect (2- 3 weeks or regular use)
    - Cross tolerance with other opioids means that switching to another kind will have no effect
    - Dosing yourself with opioids will increase opioid receptor stimulation. This will lead to a change in homeostatic level – reduce number of receptors.

- Physical Dependence – unable to stop taking the drug suddenly without physical withdrawal symptoms (psychological dependence is related, but different)