Introduction to Pharmacology (W1)

Pharmacology (L1)

Overview of Pharmacology

- **Pharmacodynamics** (PD): How drugs work in the body
- **Pharmacokinetics** (PK): How the body works on drugs (ADME)
- **Medicinal chemistry**: design, development, and synthesis of new drugs
- **Pharmaceutics**: turning drugs into medications
- **Analytical chemistry**: assurance of quality, safety and efficacy
- **Clinical trials**: reduction of unwanted effects
- **Therapeutic Goods Administration** (TGA): regulatory approval
- **Therapeutic interaction**: refers to the relationship between a drug and its molecular or cellular target in the body to achieve a desired therapeutic effect

Definitions

- **Pharmacology**: the branch of science that studies the **effects of drugs** upon the functions of living systems = **human** for our purposes
  - Derived from Pharmakon (drug) + Logos (word/study)
- **Drug**: a **chemical substance** that has a **physiological effect** when introduced into the body - usually exogenous rather than endogenous, e.g. exogenous insulin for diabetes
- **Medicine**: a **chemical preparation** that usually but not necessarily contains **one or more drugs** that is used to **treat a disease**, i.e. a remedy

History of Pharmacology

- **Herbal beginnings**: early drugs were extracted from plants and animals
- **Ancient Pharmacopoeias**: Egypt, China, India
- **Hippocrates** (~400BC): “Father of medicine” used locally available herbs such as garlic and olives
- **Medicines** (1738): Edinburgh University med students learned properties of 250 plants, 60 minerals, gums, resins and extracts from snails, worms and vipers
- **21st century**: over 10,000 named generic and combination drugs

Where do drugs come from?

- **Herbs** - many still in use, e.g. digoxin
- **Fungi** - penicillin
- **Animals** - insulin, exenatide, cone shell toxin
- Early analytical chemists isolated active medicinal components, e.g. opium poppy —> morphine
- Era of parhamcology:
  - 20 century —> **synthetic** medicinal chemistry begins
  - Post-WWII —> screening of **micro-organisms** etc. for antibiotics, antimalarials, immunosuppressants, statins and anti-cancer drugs
  - 1980s —> **biologics** and high throughput screening (HTS)

Drug development process

- Stages of drug development
  - Preclinical testing —> safety in animals
  - Phase I-III trials -> safety and efficacy in humans
  - Regulatory approval and post-market surveillance
- Stage 1: drug discovery, 10,000 compounds
- Stage 2: pre-clinical development, 100s of compounds
- Stage 3: clinical development: <10 compounds
- Stage 4: regulatory approval: 1 compound
- Final drug

Timeline

1. **Preclinical Testing** (2-4) years
   - Laboratory and **animal** studies to assess **safety**

   - Example: testing new compounds in cell cultures and animal models
2. **Phase I clinical trials** (1-2 years)
   - **20-100** healthy volunteers
   - Focus: **safety** and **dosage**
   - Example: first-in-human trials of COVID-19 vaccines
3. **Phase II clinical trials** (2 years)
   - **100-500** patient volunteers
   - Focus: **efficacy** and **side effects**
   - Example: testing new diabetes medications in diabetic patients
4. **Phase III clinical trials** (3-4 years)
   - **1,000-5,000** patient volunteers
   - Focus: confirm **effectiveness**, monitor **side effects**
   - Example: large-scale testing of new cancer treatments
5. **FDA review and approval** (6 months-2 years)
   - Review of all data and approval decision
6. **Post-market safety monitoring**
   - Continuous monitoring of **safety** and **effectiveness**
   - Example: tracking **long-term effects** and **rare side effects**

<u>Emerging trends in pharmacology</u>
- **Personalised medicine**:
  - **Pharmacogenomics**: tailoring drugs to genetic profiles
  - **Novel therapies**: mRNA vaccines and gene editing (e.g. CRISPR)
- **Biologics** and **precision drugs**:
  - **Monoclonal antibodies** (e.g. Trastuzumab): taret specific molecules for conditions like cancer and autoimmune diseases
  - **Targeted small molecules** (e.g. Imatinib): inhibit specific pathways involved in diseases like cancer
- **Emerging technologies**
  - **High-throughput screening** (**HTS**) and **artificial intelligence** (**AI**) in drug discovery for faster, cost-effective development of therapies

<u>Key Terms: Pharmacogenomics, CRISPR, and Biologics</u>
- **Pharmacogenomics**: the study of **how genes affect a person's response to drugs**
  - Real-world example: genetic testing to determine optimal dosage of warfarin (blood thinner)
- **CRISPR**: A precise **genome-editing** technology
  - Real-world example: editing T-cells to fight cancer more effectively
- **Biologics**: **Medications** derived from **living organisms**
  - Real world-example: mRNA vaccines for COVID-19

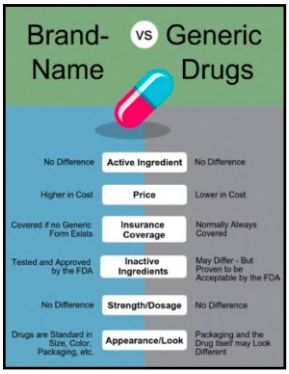
<u>The Scale of Pharmacology</u>
- Number of drugs: exploded in the second half of the 20th century
- Size of drugs: expanded significantly
  - Early drugs: small molecules (<1kDa)
  - Biologics: therapeutic proteins, eg. Antibodies (100>kDa)

<u>Small molecules vs biologic drugs</u>
- **Small Molecule** Drugs:
  - Widely used in clinical medicine
  - Made by synthetic chemists —> simple/cheap
  - Easy to store —> **room temperature** (usually)
  - Membrane permeable
  - Often **orally administered**
  - Hit **multiple receptors - side effects**
  - **Subject to drug-drug interactions** (DDIs)
  - Cause problems with toxicity
  - Often undergo extensive metabolism (liver)
- **Biologic Drugs**:

- Insulin, cytokines, antibodies etc.
  domain of biotechnology —> **expensive**
- **Heat sensitive** —> fridge or freezer storage
- Acid (stomach) + membrane impermeable
- Need **injection or even infusion**
- Specific for **one receptor —> few side effects**
  - Can cause **immunogenic/allergic effects**
- **Rarely subject to DDIs**
- Undergo minimal metabolism

Drug names = Tower of Babel
- No international body —> no uniformity
  - Same drug with different names (e.g. paracetamol (Aust/UK) = acetominophen (US))
- Chemical name: describes chemical structure —> complex and unwieldy
  - Example: 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulphonamide
- **Generic name**: simplified, often with roots and endings that imply origins —> **preferred** in pharmacology
  - Example: **celecoxib** (**COX-2 selective NSAID**)
- Brand/trade name: invented by marketing —> "catchy"
  - Example: Celebrex, Celebra (Pfizer)

Understanding drug names
- Navigating drug nomenclature - why its important
  - Ensures clarity in communication and prescriptions
- Examples:
  - **Chemical**: acetylsalicylic acid
  - **Generic**: Aspirin
  - **Brand**: Bayer Aspirin
- Tips: Always prioritise using generic names in clinical settings



Common stems in drug names - help categorise medications based on their therapeutic classes
- "**-cillin**":
  - Drug class: **antibiotics**; examples: amoxycillin, penicillin
- "**-azole**"
  - Drug class: **antifungals**; examples: ketoconazole, miconazole
- "**-olol/alol**"
  - Drug class: **beta blockers**; examples: propranolol, metoprolol
- "**-pril**"
  - Drug class: **ACE inhibitors**; examples: captopril, enalapril
- "**-oxib**"
  - Drug class: **Selective COX inhibitors**; examples: Celecoxib
- "**-ib**"
  - Drug class: **Small molecule inhibitor**; examples: Imatinib, Crizotinib
- "**-ab**"
  - Drug class: **therapeutic antibody**; examples: trastuzumab, nivolumab

Stem	Drug Class	Examples
-cillin	Antibiotics	Amoxycillin, Penicillin
-azole	Antifungals	Ketoconazole, Miconazole
-olol/alol	Beta blockers	Propranolol, Metoprolol
-pril	ACE inhibitors	Captopril, Enalapril
-oxib	Selective COX inhibitors	Celecoxib
-ib	*Small molecule inhibitor*	*Imatinib, Crizotinib*
-ab	*Therapeutic antibody*	*Trastuzumab, Nivolumab*

Common drugs name suffixes - help categorise medications based on their therapeutic classes
- **ACE inhibitors**:
  - Suffix: -**pril**
  - Examples: Captopril, Lisinopril, Ramipril - ACE inhibitors for hypertension and heart failure
  - Meaning: These medications reduce blood pressure by **dilating blood vessels**
- **Beta blockers**:
  - Suffix: -**olol**
  - Examples: Atenolol, metoprolol, propranolol - beta-blockers for hypertension, arrhythmias, and migraines
  - Meaning: these drugs are used to manage hypertension and heart conditions by **blocking beta-adrenergic receptors**

- **Statins**:
  - Suffix: -**statin**
  - Examples: Atorvastatin, Simvastatin, Rosuvastatin - Statins for cholesterol management
  - Meaning: statins are used to lower cholesterol levels by **inhibiting HMG-CoA reductase**
- **Antibiotics**:
  - Suffix: -**mycin** (for **macrolid** antibiotics)
  - Examples: Azithromycin, Erythromycin, Clarithromycin - antibiotics for **bacterial infections**
  - Meaning: these medications are used to treat bacterial infections by **inhibiting protein synthesis**

Drug targets and receptors

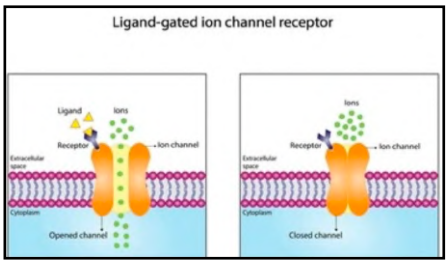
- **Drug targets**: mostly proteins (DNA can also be a target)
- **Receptor**: used to denote target molecules like Na+ channels or enzymes, but 'drug target' is a better description in some cases
- Four main type of drug target proteins
  1. Receptors
  2. Ion channels
  3. Enzymes
  4. Transporters/carrier molecules

Receptors (1)

- Definition: **cell sensors that normally respond to endogenous mediators** such as hormones and transmitters
- **Drug action**: bind many clinically useful drugs that either activate (**agonist**) or block (**antagonist**) the receptor
- **Nicotinic ACh** receptor (important)
  - **Agonist**: acetylcholine, nicotine
  - **Antagonist**: tubocurarine
- **Beta-adrenoceptor** (important)
  - **Agonist**: noradrenaline
  - **Antagonist**: Propranolol
- **μ-opioid** receptor (important)
  - **Agonist**: morphine
  - **Antagonist**: naloxone

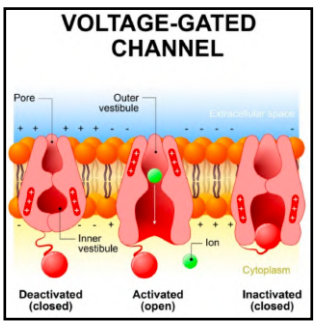
Receptor	Agonist	Antagonist
Nicotinic ACh receptor	Acetylcholine, nicotine	Tubocurarine
β-adrenoceptor	Noradrenaline	Propranolol
μ-opioid receptor	Morphine	Naloxone

- Clinical Uses
  - Acetylcholine & Nicotine: Support nerve and muscle signaling; nicotine also impacts addiction pathways.
  - Tubocurarine: Muscle relaxant during surgeries (no longer widely used).
  - Noradrenaline: Increases heart rate and is used in critical care (e.g., shock treatment).
  - Propranolol: Lowers blood pressure, controls arrhythmias, and reduces anxiety.
  - Morphine: Relieves severe pain (e.g., post-surgical or cancer-related pain).
  - Naloxone: Reverses opioid overdoses and prevents respiratory depression.



Ion channels (2)

- Function: **gateways** that selectivity allow **ions** to pass through membranes
- Types:
  - **Ligand-gated** -> **bind agonists** (also considered receptors)
    - Open in response to a **chemical signal (ligand)**
    - Example: **nicotinic acetylcholine receptor**
  - **Voltage-gated** -> open when the cell membrane is **depolarised**
    - Open in response to **changes in membrane potential**
    - Example: **voltage-gated sodium channels** in neurons
    - **Blockers**: local anaesthetics; **modulators**: veratridine
- **Drug actions**:

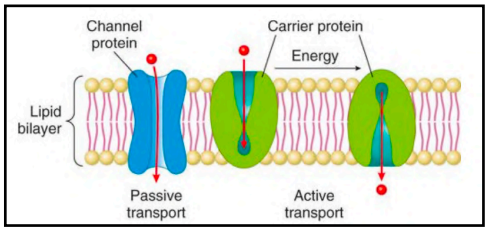


  - **Blockers**: bind to and block the channel
  - **Modulators**: bind to accessory (allosteric) sites to alter channel gating
- ATP-sensitive K+ channels
  - **Blockers**: ATP
  - **Modulators**: sulphonylureas
- Tip:
  - Local Anesthetics (e.g., Lidocaine): Block pain signals by inhibiting sodium channels.
  - Veratridine: Used in research to understand sodium channel dynamics.
  - Sulphonylureas (e.g., Glibenclamide): Increase insulin release for managing type 2 diabetes

Enzymes (3)
- Many drugs have been developed to **inhibit enzymes**
  - As a **substrate** analogue that as Glipalamide a **Competitive Inhibitor** (substrate analogue): E.g. captopril
  - As an **irreversible**, **non-competitive inhibitor**: e.g. aspirin (allosteric inhibition)
  - As a **False Substrate** where the product subverts normal pathway, e.g. 5-FU
- Enzyme: **Angiotensin converting enzyme (ACE)**
  - Inhibitor: **captopril**
- Enzyme: **cyclo-oxygenase (COX)**
  - Inhibitor: **aspirin**
- Enzyme: **DNA polymerase**
  - Inhibitor: **5-Fluorouracil**

Enzyme	Inhibitor
Angiotensin converting enzyme	Captopril
Cyclo-oxygenase	Aspirin
DNA polymerase	5-Fluorouracil

Transport proteins (4)
- Definition: **proteins that move ions** and small organic molecules **across membranes** due to their polarity/lack of lipid solubility
  - Ions and small organic molecules need channels or transport proteins to **move across membranes** due to their **polarity/ lack of lipid solubility**
  - Pharmacologically significant transporters move **Na+ and Ca2+ out of cells** or target renal tubules, intestinal epithelium, blood brain barrier synapses
- Transport protein: **noradrenaline transporter**
  - **Inhibitor**: tricyclic antidepressants, cocaine
- Transport protein: **Na+/K+/2Cl- co-transporter**
  - **Inhibitor**: Loop diuretics
- Transport protein: **Na+/glucose co-transporter 2**
  - **Inhibitor**: SGLT2 inhibitors



The basic concepts underpinning the discipline of Pharmacology (L2)

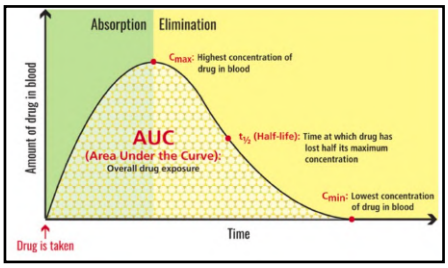
Foundations for understanding pharmacology
- Key systems to know:
  - **Cardiovascular**: blood regulation
  - **Nervous system**: neurotransmitter function
  - **GI**: absorption and metabolism of drugs
- Why it matters: understanding how physiological changes impact drug efficacy and safety

Pharmacodynamics (PD)
- Definition: “how drugs work in the body”
- Key points
  - Drugs work by **binding to molecular targets**
  - Most common drug targets are receptors
  - Drug-receptor interactions: binding and activation (**agonists and antagonists**)
  - **Dose-response** effects and drug potency
  - Downstream signalling —> mechanism of action
  - Adverse effects

- Receptor binding:
  - **Agonist**: **activates** the receptor to produce a response
  - **Antagonist**: **blocks** the receptor and prevents a response
- Dose-response relationship
  - Describes how the response changes with **drug concentration**
  - Key terms: **potency** (drug strength) and **efficacy** (maximum effect)

Pharmacokinetics (PK)
- Definition: “what the body does to a drug.”
- ADME process
  1. **Absorption**: how will the drug get in?
  2. **Distribution**: Where will it go?
  3. **Metabolism**: how is it broken down?
  4. **Excretion**: how does it leave?

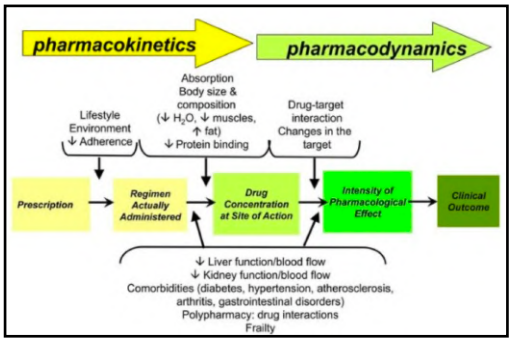
Pharmacokinetics



- **Absorption**
  - Process: drug enters the **bloodstream** (e.g. oral medications)
- **Distribution**
  - Process: drug is **transported to tissues and organs** (e.g. IV medications)
- **Metabolism**:
  - Process: drug is **broken down**, primarily in the **liver**
- **Excretion**:
  - Process: drug is **eliminated** from the body (e.g. via **kidneys**)

Drug administration routes comparison
- **IV administration**
  - **Immediate** drug availability
  - **100% bioavailability**
  - Used in **emergency** situations
- **Oral administration**
  - **Delayed** onset of action
  - **First-pass metabolism**
  - More **convenient** for patients

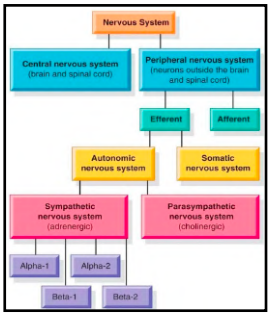
Simplifying PK/PD
- Pharmacokinetics (PK)
  - “what the body does to the drug”
  - Example: how ibuprofen is absorbed, distributed, metabolised and excreted
- Pharmacodynamics (PD)
  - “What the drug does to the body”
  - Example: how ibuprofen reduces inflammation



Ethics and Safety
- Pharmacology and patient safety
- Ethical principles
  - **Informed consent** in clinical trials
  - Transparency about **risks and benefits** of treatment
- Monitoring for safety
  - Importance of **reporting adverse drug reactions** (ADRs)
  - Role of **pharmacovigilance** in clinical practise
- Real life example:
  - Phase 4 trials gather long-term safety data

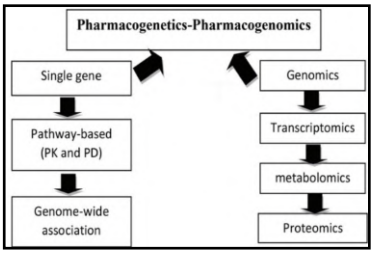
Pharmacovigilance
- Definition: is the **science of detecting, assessing and preventing adverse effects** or any drug-related problems
- Key roles:
  - Ensure **patient safety**: identifies and minimises risks associated with medications
  - **Monitor** advance drug reactions (ADRs): **tracks side effects to improve drug safety**
  - Improve **drug dosage**: provides data to optimise prescribing practises
  - **Regulatory support**: helps update guidelines and approve safer medications
- Example: reporting an unexpected side effect of a medication (e.g. severe rash after an antibiotic) to regulator authorities (e.g. TGA) for further investigation

Treatment and healing - workshop
- Key points
  - A response to drug therapy is not just about the drug
  - **Placebo and nocebo effects** play important roles
  - **Therapeutic adherence** is essential for an effective response
  - Evidence-based medicine and approaches to alternative medicines



ANS
- Peripheral nervous system, especially the autonomic nervous system (ANS), was central to early physiology and pharmacology research
- ANS regulates heart, blood vessels, bronchial tree, GIT, skin, eye, etc
- Early studies led to understanding chemical transmission and mechanisms of action for many major drug groups

Pharmacogenetics/genomics
- **Genetic differences** (polymorphisms) underlie **variable drug responses**
- Polymorphisms and associated ADRs may have arisen due to regional disease prevalence
- Many such polymorphisms were silent until the era of drug development
- Most pharmacologically relevant **polymorphisms affect pharmacokinetics**
- Personalised approaches to drug therapy are needed based on genomic/genetic variations



Pharmacogenetics: Clinical Impact
- **Warfarin** dosing example
  - **CYP2C9**: drug-metabolising enzyme
  - Genetic variants affect enzyme activity
  - **Poor metabolisers need lower doses**
  - Clinical impact: reduce bleeding risk, more stable anticoagulation, better patient outcomes

Precision medicine
- Pharmacogenetics in practise
- Why genetics matter
  - **Polymorphisms affect drug metabolism** (e.g. CYP enzymes)
- Practical example:
  - Adjusting warfarin doses based on genetic testing
- Future impact:
  - **Reduced ADRs** and **optimised therapy** for individual patients
- Differences between personalised, precision and individualised medicine
- **Personalised medicine**:
  - Focuses on **tailoring medical treatment to an individual's unique characteristics**, such as **genetic profile, lifestyle, and environment**
  - Example: using pharmacogenomics to **adjust drug dosages**
- **Precision medicine**:

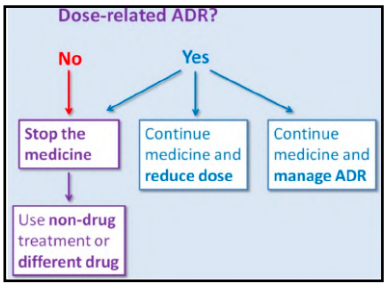
- Emphasises classifying patients into **subgroups based on shared biological or genetic traits** to deliver targeted therapies
- Example: targeted cancer treatments like HER2 inhibitors for **specific breast cancer subtypes**

- **Individualised medicine**
  - A broader, **patient centred** approach that customises care based on an **individual's specific preferences**, needs and circumstances
  - Example: adjusting **treatment for a diabetic patient** based on their preferences and **comorbidities**

Managing ADRs

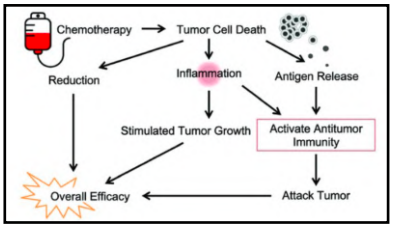
- Types of ADRs
  - **Mild**: rash, itching, hives
  - **Severe**: anaphylaxis (life-threatening)
- **Risk factors**:
  - Age, genetics, and polypharmacy
- **Prevention** tips:
  - Start low, go slow with doses
  - Regular monitoring and patient education
  - Grapefruit juice can block the action of intestinal CYP3A4

Unwanted effects of drugs —> ADRs and toxicology



- Dose-response relationships in toxicity.
- Two main types of **ADRs**:
  - **Type A**: Augmented (e.g., bleeding with warfarin) (**exaggeration of a drug's normal pharmacological actions**).
  - **Type B**: **Bizarre** (e.g., anaphylaxis with penicillin) (**hypersensitivity**)
  - Symptoms: Difficulty breathing, swelling, drop in blood pressure.
- Contribution of ADRs to hospital admissions.
  - 5-10% of hospital admissions globally
- Preventing ADRs and making drugs safer.
  - Document allergies in medical records
  - Avoid known allergens
  - Carry epinephrine auto-injectors

Treating cancer



- Cancer pathogenesis
  - Cancer is a multi-step process
  - Cells contain intrinsic barriers to prevent cancer development
  - Common **mutations** allow cancer cells to **breach these barriers**
- Cancer Management:
  - Traditional/classical chemotherapies.
  - **Targeted Therapies**:
    - Example: **Trastuzumab for HER2-positive breast**
    - Blocks HER2 receptors to **inhibit cancer growth**.
  - **Immunotherapies**:
    - Example: **Anti-PD-1 therapy** (e.g., pembrolizumab).
    - **Boosts immune response** to target cancer cells to target various cancers, including melanoma and lung cancer.

Clinical Pharmacology

- **Haematology**: Haematinics
  - Focuses on **drugs** that **treat blood disorders**, such as anaemia (e.g., iron supplements, vitamin B12, folic acid).
- **Dermatology**: Skin preparations & management of **eczema**, **psoriasis**, and **acne**
  - Discusses **topical and systemic drugs for skin diseases** (e.g., corticosteroids, retinoids, and antibiotics for acne).
- **Cardiovascular**:

- Includes drugs for managing **heart and blood vessel diseases**, such as:
  - **Antihypertensives**: Reduce **blood pressure** (e.g., ACE inhibitors, beta blockers).
  - **Diuretics**: Treat **fluid retention** and hypertension.
  - **Lipid-lowering drugs**: Reduce **cholesterol** levels (e.g., statins).
  - **Anticoagulants**/Antiplatelets: Prevent **blood clots** (e.g., warfarin, aspirin).
  - **Thrombolytics**: **Break down clots** during heart attacks or strokes.
  - Drugs for **heart failure and coronary artery disease**: Improve cardiac function and reduce symptoms.

<u>Clinical Relevance of Pharmacology</u>
- Why does pharmacology matter - managing patients with the correct medications
- Impact on patient care
  - Managing hypertension with ACE inhibitors
  - Treating infections with antibiotics like Amoxicillin
- Role in multidisciplinary teams:
  - Collaboration with other healthcare professionals for optimal patient outcomes

<u>How pharmacology impacts patient care</u>
- Effective **Disease Management**:
  - Example: Using **ACE inhibitors** (e.g., enalapril) to control **hypertension** and prevent complications like **stroke or heart failure**.
  - Example: Treating **bacterial infections** with **antibiotics** like amoxicillin to prevent **sepsis**.
- **Precision in Therapy**:
  - **Adjusting medication** doses for patients with **impaired kidney function** to avoid **drug toxicity** (e.g., reducing gabapentin in renal failure).
- Improving **Quality of Life**:
  - Example: Alleviating **chronic pain** with opioids like morphine while managing potential side effects with **naloxone**.
  - Example: Managing **asthma** with **inhaled β2 agonists** (e.g., salbutamol) for quick relief of bronchospasm

<u>Why pharmacology matters for medical practise</u>
- Informed **Decision-Making**:
  - Understanding mechanisms of drug action aids in **selecting the most appropriate therapy**.
- Patient **Safety**:
  - Knowledge of **pharmacokinetics** helps in **adjusting drug dosages** to prevent adverse reactions.
- **Personalised Medicine**:
  - Incorporating pharmacogenomics ensures drugs are **tailored** to individual patient needs.
- **Holistic Care**:
  - Pharmacology bridges the gap between science and bedside care, ensuring **treatments are evidence-based and patient-centric**

<u>Case Example: Managing stress-induced arrhythmias</u>
- Patient Scenario:
  - A 50-year-old patient presents with **stress-induced palpitations and arrhythmias**.
  - History reveals frequent episodes of emotional stress and irregular heartbeats.
- Pharmacological Approach:
  - **Beta-blockers** (e.g., propranolol or metoprolol):
    - Mechanism: Block β-adrenergic receptors to reduce heart rate and myocardial oxygen demand.
    - Clinical Benefit: **Helps stabilize the heart rhythm** and reduce stress-related cardiovascular strain.
- Key Considerations:
  - **Monitor** for **adverse effects** like bradycardia or fatigue.
  - Assess for **contraindications**, such as **asthma or severe bradycardia**

Pharmacology: Questions to think about

- Case Study 1: **Managing Pain**
  - A 45-year-old patient with **chronic back pain** is prescribed **opioids**.
- Discussion Questions:
  - What are the **risks and benefits** of using opioids in this case?
  - How would you monitor this patient to **minimize the risk of addiction or adverse effects**?
- Case Study 2: **Treating Hypertension**
  - A 60-year-old patient with **high blood pressure** and a history of **diabetes** is prescribed an **ACE inhibitor**.
- Discussion Questions:
  - Why might an **ACE inhibitor be a good choice** for this patient?
  - What are potential **side effects**, and how would you address them?

Pharmacodynamics (W5)

Pharmacodynamics 1 (L1)

Overview

- This overview of 'how drugs work' will be given primarily within the context of:
  - How one particular drug called metoprolol can be used to treat a person experiencing chest pain
  - How the pharmacological properties of metoprolol compares to there drugs
- Metoprolol has been chosen because it possess many of the characteristics features of commonly used drugs

Chest pain is a serious clinical problem

- John
  - In his late 50s
  - Started to feel chest pains on exercising
    - Which stopped after he rested
  - Decided to go to his doctor
- John's doctor
  - Advised John to stop smoking
    - And to lose a few kilos
  - Conducted a series of diagnostic tests
  - Prescribed John a drug, 'metoprolol'
- Why is John suffering chest pains while exercising?

What is John's chest pain

- John's pain is called **angina**
- It is a symptom produced when the **heart receives insufficient oxygen**
- It is caused by **partial blockage of the coronary arteries** that provide O2 to the heart
- Exercise:
  - Adrenaline release
    - **Increased heart rate and contraction**
      - When coronary arteries are blocked: **O2 supply to heart is less than needed**
        - Heart in O2 debt
          - Angina pain

How can John's angina be treated

- Treatment of angina involves a combination of approaches
  1. **Lifestyle changes**
     - Stop **smoking**
     - **Weight** reduction
     - Healthier **diet**
  2. **Medications**
     - To **relieve the intensity** of angina e.g. nitroglycerin
     - To **decrease the frequency** of angina e.g. metoprolol
     - To **reduce chances of heart attack**
       - e.g. drugs that thin the blood and lower cholesterol
  3. **Surgery**
     - To **clear** the **blocked coronary artery**

When should the drug be taken?

- To **decrease the frequency** of **angina** episodes, **metoprolol** must be taken **regularly, every day** (**prophylactically**)
- Prophylactic administration is typical drugs used to **treat chronic diseases** such as heart disease (incl. angina), cancer, stroke, diabetes, asthma, arthritis, etc
- Some drugs are only **taken as needed** (not prophylactically) to **relieve or prevent symptoms**, e.g. nitroglycerin is taken:
  - **During** an **angina attack** to relieve pain or
  - **Before activities** that **usually cause angina**, to reduce pain