Name Ali mehran

Id:13724

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Q1:Define drug receptors, enumerate different receptor families and explain the receptor that shows its effect through second messenger system

Ans: **Drug receptors**

Receptor is a macromolecule in the membrane or inside the cell that specifically (chemically) bind a ligand (drug). The binding of a drug to receptor depends on types of chemical bounds that can be established between drug and receptor. The strength of this chemical bonds (covalent, ionic, hydrogen, hydrophobic) determine the degree of affinity of ligand to receptor. Ligands (drugs) that attracted the receptors may be classified as agonists or antagonists. Agonists produce the biological response as a results of receptor –ligand interactions therefore agonists posses efficacy. On the contrary antagonists did not provoke any biological activity after binding to its receptor.

There are different types of receptors (1):

1. Transmembrane ion-channels receptors
2. Transmembrane G-protein-coupled receptors
3. Transmembrane receptors with cytosolic domain
4. Intracellular (cytoplasm or nucleus) receptors

- ## Receptor families

- **Channel-linked receptors** (also called ligand-gated ion channels) have the receptor and transducing functions as part of the same protein molecule. Interaction of the chemical signal with the binding site of the receptor causes the opening or closing of an ion channel pore in another part of the same molecule. The resulting ion flux changes the membrane potential of the target cell and, in some cases, can also lead to entry of Ca^{2+} ions that serve as a second messenger signal within the cell. Good examples of such receptors are the neurotransmitter receptors .

- **Enzyme-linked receptors** also have an extracellular binding site for chemical signals. The intracellular domain of such receptors is an enzyme whose catalytic activity is regulated by the binding of an extracellular signal. The great majority of these receptors are **protein kinases,** often tyrosine kinases**,** that phosphorylate intracellular target proteins, thereby changing the physiological function of the target

cells. Noteworthy members of this group of receptors include the Trk family of neurotrophin receptors and other receptors for growth factors.

- G-protein-coupled receptors regulate intracellular reactions by an indirect mechanism involving an intermediate transducing molecule, called the **GTP-binding proteins** (or G-proteins). Because these receptors all share the structural feature of crossing the plasma membrane seven times, they are also referred to as 7-transmembrane receptors (or metabotropic receptors; see . Hundreds of different G-protein-linked receptors have been identified. Well-known examples include the β-adrenergic receptor, the muscarininc type of acetylcholine receptor, metabotropic glutamate receptors, receptors for odorants in the olfactory system, and many types of receptors for peptide hormones. Rhodopsin, a light-sensitive 7-transmembrane protein in retinal photoreceptors, is another form of G-protein-linked receptor (see Chapter 11).

- **Intracellular receptors** are activated by cell-permeant or lipophilic signaling molecules). Many of these receptors lead to the activation of signaling cascades that produce new mRNA and protein within the target cell. Often such receptors comprise a receptor protein bound to an inhibitory protein complex. When the signaling molecule binds to the receptor, the inhibitory complex dissociates to expose a DNA-binding domain on the receptor. This activated form of the receptor can then move into the nucleus and directly interact with nuclear DNA, resulting in altered transcription. Some intracellular receptors are located primarily in the cytoplasm, while others are in the nucleus. In either case, once these receptors are activated they can affect gene expression by altering DNA transcription.

Effect through Second messengers :

- are intracellular signaling molecules released by the cell in response to exposure to extracellular signaling molecules—the **first messengers**. (Intracellular signals, a non-local form or cell signaling, encompassing both first messengers and second messengers, are classified as juxtacrine, paracrine, and endocrine depending on the range of the signal.) Second messengers trigger physiological changes at cellular level such as proliferation, differentiation, migration, survival, apoptosis and depolarization.
- They are one of the triggers of intracellular signal transduction cascades.[1]
- Examples of second messenger molecules include cyclic AMP, cyclic GMP, inositol trisphosphate, diacylglycerol, and calcium.[2] First messengers are extracellular factors, often hormones or neurotransmitters, such as epinephrine, growth hormone, and serotonin. Because peptide hormones and neurotransmitters typically are biochemically hydrophilic molecules, these first messengers may not physically cross the phospholipid bilayer to initiate changes within the cell directly—unlike steroid hormones, which usually do. This functional limitation requires the cell to have signal transduction mechanisms to transduce first messenger into second messengers, so that the extracellular signal may be propagated intracellularly. An important feature of the second messenger

signaling system is that second messengers may be coupled downstream to multi-cyclic kinase cascades to greatly amplify the strength of the original first messenger signal[3][4]. For example, RasGTP signals link with the Mitogen Activated Protein Kinase (MAPK) cascade to amplify the allosteric activation of proliferative transcription factors such as Myc and CREB.

- Earl Wilbur Sutherland, Jr., discovered second messengers, for which he won the 1971 Nobel Prize in Physiology or Medicine. Sutherland saw that epinephrine would stimulate the liver to convert glycogen to glucose (sugar) in liver cells, but epinephrine alone would not convert glycogen to glucose. He found that epinephrine had to trigger a second messenger, cyclic AMP, for the liver to convert glycogen to glucose.[5] The mechanisms were worked out in detail by Martin Rodbell and Alfred G. Gilman, who won the 1994 Nobel Prize[6][7].
- Secondary messenger systems can be synthesized and activated by enzymes, for example, the cyclases that synthesize cyclic nucleotides, or by opening of ion channels to allow influx of metal ions, for example Ca^{2+} signaling. These small molecules bind and activate protein kinases, ion channels, and other proteins, thus continuing the signaling cascade.

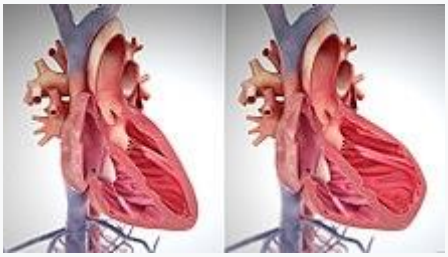
Q4:What does heart failure means, explain the pathophysiology of heart failure .

Ans: Heart failure is a chronic, progressive condition in which the heart muscle is unable to pump enough blood to meet the body's needs for blood and oxygen. Basically, the heart can't keep up with its workload.

Pathophysiology of heart failure:

The main **pathophysiology of heart failure** is a reduction in the efficiency of the heart muscle, through damage or overloading. As such, it can be caused by a wide number of conditions, including myocardial infarction (in which the heart muscle is starved of oxygen and dies), hypertension (which increases the force of contraction needed to pump blood) and amyloidosis (in which misfolded proteins are deposited in the heart muscle, causing it to stiffen). Over time these increases in workload will produce changes to the heart itself:

Pathophysiology of heart failure



A comparison of healthy heart with contracted muscle (left) and a weakened heart with over-stretched muscle (right).

Biological system	Cardiovascular system
Health	Harmful

The heart of a person with heart failure may have a reduced force of contraction due to overloading of the ventricle. In a healthy heart, increased filling of the ventricle results in increased contraction force (by the Frank–Starling law of the heart) and thus a rise in cardiac output. In heart failure, this mechanism fails, as the ventricle is loaded with blood to the point where heart muscle contraction becomes less efficient. This is due to reduced ability to cross-link actin and myosin filaments in over-stretched heart muscle.[1]

A reduced stroke volume may occur as a result of a failure of systole, diastole or both. Increased end systolic volume is usually caused by reduced contractility.

Decreased end diastolic volume results from impaired ventricular filling; this occurs when the compliance of the ventricle falls (i.e. when the walls stiffen). As the heart works harder to meet normal metabolic demands, the amount cardiac output can increase in times of increased oxygen demand (e.g., exercise) is reduced. This contributes to the exercise intolerance commonly seen in heart failure. This translates to the loss of one's cardiac reserve, or the ability of the heart to work harder during strenuous physical activity. Since the heart has to work harder to meet the normal metabolic demands, it is incapable of meeting the metabolic demands of the body during exercise.

A common finding in those with heart failure is an increased heart rate, stimulated by increased sympathetic activity[2] in order to maintain an adequate cardiac output. Initially, this helps compensate for heart failure by maintaining blood pressure and perfusion, but places further strain on the myocardium, increasing coronary perfusion requirements, which can lead to worsening of ischemic heart disease. Sympathetic activity may also cause potentially fatal abnormal heart rhythms. An increase in the physical size of the heart's muscular layer may occur. This is caused by the terminally differentiated heart muscle fibers increasing in size in an attempt to improve contractility. This may contribute to the increased stiffness and thus decrease the ability to relax during diastole. Enlargement of the ventricles can also occur and contributes to the enlargement and spherical shape of the failing heart. The increase

in ventricular volume also causes a reduction in stroke volume due to mechanical and inefficient contraction of the heart.[3]

The general effect is one of reduced cardiac output and increased strain on the heart. This increases the risk of cardiac arrest (specifically due to abnormal ventricular heart rhythms) and reduces blood supply to the rest of the body. In chronic disease the reduced cardiac output causes a number of changes in the rest of the body, some of which are physiological compensations, some of which are part of the disease process

B)Classify the used for the treatment of heart failure, explain along with mechanism.

Ans: Treatment of heart failure:

Angiotensin-Converting Enzyme (ACE) Inhibitors

Commonly prescribed include:

1. Captopril (Capoten)
2. Enalapril (Vasotec)
3. Fosinopril (Monopril)
4. Lisinopril (Prinivil, Zestril)
5. Perindopril (Aceon)
6. Quinapril (Accupril)
7. Ramipril (Altace)
8. Trandolapril (Mavik)

Angiotensin II Receptor Blockers (or Inhibitors)

(Also known as ARBs or Angiotensin-2 Receptor Antagonists)

Commonly prescribed include:

1. Candesartan (Atacand)
2. Losartan (Cozaar)
3. Valsartan (Diovan)

Angiotensin-Receptor Neprilysin Inhibitors (ARNIs)

ARNIs are a new drug combination of a neprilysin inhibitor and an ARB.

1. Sacubitril/valsartan

I_f Channel Blocker (or inhibitor)

This drug class reduces the heart rate, similar to another class of drugs called beta blockers.

1. Ivabradine (Corlanor)

Beta Blockers (Also known as Beta-Adrenergic Blocking Agents)

Commonly prescribed include:

1. Bisoprolol (Zebeta)
2. Metoprolol succinate (Toprol XL)
3. Carvedilol (Coreg)
4. Carvedilol CR (Coreg CR)Toprol XL

Aldosterone Antagonists

Commonly prescribed include:

1. Spironolactone (Aldactone)
2. Eplerenone (Inspra)

Hydralazine and isosorbide dinitrate (specifically benefits African-Americans with heart failure)

Commonly prescribed:

1. Hydralazine and isosorbide dinitrate (combination drug) - (Bidil)

Diuretics (Also known as water pills)

Commonly prescribed include:

1. Furosemide (Lasix)
2. Bumetanide (Bumex)
3. Torsemide (Demadex)
4. Chlorothiazide (Diuril)
5. Amiloride (Midamor Chlorthalidone (Hygroton)
6. Hydrochlorothiazide or HCTZ (Esidrix, Hydrodiuril)
7. Indapamide (Lozol)
8. Metolazone (Zaroxolyn)
9. Triamterene (Dyrenium)
10.
11. Anticoagulants (*blood thinners) These drugs may be prescribed if you are a heart failure patient with atrial fibrillation or have another problem with your heart. Anticoagulants are not used to treat heart failure without the presence of atrial fibrillation.
12. Cholesterol-lowering drugs (statins) Your doctor may prescribe this class of medication if you have high cholesterol or have had a heart attack. This class of drugs is not used to treat heart failure, but other conditions as indicated.
13. Digoxin Some heart failure patients might be prescribed this drug if the doctor feels it's warranted.

Q3 Differentiate between general and local anesthesia, explain stages of anesthesia in detail?

Ans:Local anesthetics are chemicals designed to be injected around nerves. Once injected they block inward sodium ion channels. This renders any nerve touched by these chemicals unable to depolarize and to send any signals to the spinal cord and brain. This block is reversible over time as the body breaks down the chemical. Unless an overdose is given, there is no effect on your mental status. (The first local anesthetic invented was Cocaine FYI.)

General anesthesia is produced by a group of drugs, either IV or inhaled, that work (we think) by acting at areas along the length of a nerve that greatly decrease its firing. These inhibitors of nerve firing use the GABA system to affect chloride ion channels. The most sensitive area in your brain to this effect is a group of neurons that govern sleep called the Reticular Activating System (RAS). This is why the first effect of an anesthetic is loss of consciousness. Increasing the amount in your bloodstream causes other systems to decrease their firing and become less sensitive to incoming signals. This is desirable because even when you are asleep pain can raise your heart rate and even asleep a person will withdraw to pain. The level of General anesthesia is increased until people are 1) unconscious 2) motionless 3) reasonable heart rate and blood pressure during surgery. This state continued until the anesthetic gas is exhaled or the IV drug is metabolized. When the blood level falls below a certain point the patient wakes up.

TLDR—Local blocks pain at the site of injection and general anesthesia doesn't block pain at all. It just renders you unable to notice pain or be aware.

Stages of anesthesia:

Stage 1

Stage 1, also known as *induction*, is the period between the administration of induction agents and loss of consciousness. During this stage, the patient progresses from analgesia without amnesia to analgesia with amnesia. Patients can carry on a conversation at this time.

Stage 2

Stage 2, also known as the *excitement stage*, is the period following loss of consciousness and marked by excited and delirious activity. During this stage, the patient's respiration and heart rate may become irregular. In addition, there may be uncontrolled movements, vomiting, suspension of breathing, and pupillary dilation. Because the combination of spastic movements, vomiting, and irregular respiration may compromise the patient's airway, rapidly acting drugs are used to minimize time in this stage and reach Stage 3 as fast as possible.

Stage 3

In Stage 3, also known as *surgical anaesthesia*, the skeletal muscles relax, vomiting stops, respiratory depression occurs, and eye movements slow and then stop. The patient is unconscious and ready for surgery. This stage is divided into four planes:

1. The eyes roll, then become fixed;
2. Corneal and laryngeal reflexes are lost;

3. The pupils dilate and light reflex is lost;
4. Intercostal paralysis and shallow abdominal respiration occur.

Stage 4

Stage 4, also known as *overdose*, occurs when too much anaesthetic medication is given relative to the amount of surgical stimulation and the patient has severe brainstem or medullary depression, resulting in a cessation of respiration and potential cardiovascular collapse. This stage is lethal without cardiovascular and respiratory support.

Q4:Define drug interactions, enumerate its various types, and explain pharmacokinetic drug interactions and its factors with examples.

Ans:Drug interaction:

In medicine, a **side effect** is an effect, whether therapeutic or adverse, that is secondary to the one intended; although the term is predominantly employed to describe adverse effects, it can also apply to beneficial, but unintended, consequences of the use of a drug. Developing drugs is a complicated process, because no two people are exactly the same, so even drugs that have virtually no side effects, might be difficult for some people. Also, it is difficult to make a drug that targets one part of the body but that does not affect other parts,[1] the fact that increases the risk of side effects in the untargeted parts.
Occasionally, drugs are prescribed or procedures performed specifically for their side effects; in that case, said side effect ceases to be a side effect and is now an intended effect. For instance, X-rays were historically (and are currently) used as an imaging technique; the discovery of their oncolytic capability led to their employ in radiotherapy (ablation of malignant tumours).

Drug interaction types

1. Fluoxetine and Phenelzine. ...
2. Digoxin and Quinidine. ...
3. Sildenafil and Isosorbide Mononitrate. ...
4. Potassium Chloride and Spironolactone. ...
5. Clonidine and Propranolol. ...
6. **Warfarin** and Diflunisal. ...
7. Theophylline and Ciprofloxacin

Pharmakonytic drug interactions

Modifications in the effect of a drug are caused by differences in the absorption, transport, distribution, metabolism or excretion of one or both of the drugs compared with the expected behavior of each drug when taken individually. These changes are basically modifications in the concentration of the drugs. In this respect, two drugs can be homergic if

they have the same effect in the organism and heterergic if their effects are different.. Some drugs, such as the prokinetic agents increase the speed with which a substance passes through the intestines. If a drug is present in the digestive tract's absorption zone for less time its blood concentration will decrease. The opposite will occur with drugs that decrease intestinal motility.

5. pH: Drugs can be present in either ionised or non-ionised form, depending on their pKa (pH at which the drug reaches equilibrium between its ionised and non-ionised form).[10] The non-ionized forms of drugs are usually easier to absorb, because they will not be repelled by the lipidic bylayer of the cell, most of them can be absorbed by passive diffusion, unless they are too big or too polarized (like glucose or vancomycin), in which case they may have or not have specific and non specific transporters distributed on the entire intestine internal surface, that carries drugs inside the body. Obviously increasing the absorption of a drug will increase its bioavailability, so, changing the drug's state between ionized or not, can be useful or not for certain drugs.

Certain drugs require an acid stomach pH for absorption. Others require the basic pH of the intestines. Any modification in the pH could change this absorption. In the case of the antacids, an increase in pH can inhibit the absorption of other drugs such as zalcitabine (absorption can be decreased by 25%), tipranavir (25%) and amprenavir (up to 35%). However, this occurs less often than an increase in pH causes an increase in absorption. Such as occurs when cimetidine is taken with didanosine. In this case a gap of two to four hours between taking the two drugs is usually sufficient to avoid the interaction.[11]

- Drug solubility: The absorption of some drugs can be drastically reduced if they are administered together with food with a high fat content. This is the case for oral anticoagulants and avocado.
- Formation of non-absorbable complexes:
    - Chelation: The presence of di- or trivalent cations can cause the chelation of certain drugs, making them harder to absorb. This interaction frequently occurs between drugs such as tetracycline or the fluoroquinolones and dairy products (due to the presence of Ca^{++}).
    - Binding with proteins. Some drugs such as sucralfate binds to proteins, especially if they have a high bioavailability. For this reason its administration is contraindicated in enteral feeding.[12]
    - Finally, another possibility is that the drug is retained in the intestinal lumen forming large complexes that impede its absorption. This can occur with cholestyramine if it is associated with sulfamethoxazol, thyroxine, warfarin or digoxin.
- Acting on the P-glycoprotein of the enterocytes: This appears to be one of the mechanisms promoted by the consumption of grapefruit juice in increasing the bioavailability of various drugs, regardless of its demonstrated inhibitory activity on first pass metabolism.

Example

Pharmacokinetic interactions occur at the levels of absorption (e.g., levothyroxine and neutralizing antacids), elimination (e.g., digoxin and macrolides), and metabolism, as in the competition for cytochrome P450 enzymes (e.g., SSRIs and certain beta-blockers).

Q5: Differentiate between broad spectrum and narrow spectrum antibiotics, classify antibiotic drugs?

Ans:broad spectrum:

A **broad-spectrum antibiotic** is an antibiotic that acts on the two major bacterial groups, gram-positive and gram-negative,[1] or any antibiotic that acts against a wide range of disease-causing bacteria.[2] These medications are used when a bacterial infection is suspected but the group of bacteria is unknown (also called empiric therapy) or when infection with multiple groups of bacteria is suspected. This is in contrast to a narrow-spectrum antibiotic, which is effective against only a specific group of bacteria.[3] Although powerful, broad-spectrum antibiotics pose specific risks, particularly the disruption of native, normal bacteria and the development of antimicrobial resistance. An example of a commonly used broad-spectrum antibiotic is ampicillin

B narrow spectrum :

A **narrow-spectrum antibiotic** is an antibiotic that is only able to kill or inhibit limited species of bacteria.

Examples of narrow-spectrum antibiotics

include vancomycin, fidaxomicin and sarecycline

Classification of Antiboitics

Classification

Antiboitics can be classified into different types based on different classification modes.

The first classification is according to the spectrum: The spectrum means the number of the organisms affected by the same drug.

Broad Spectrum Antibiotics: The Broad spectrum antibiotics affect several types of bacteria and fungi and it is usually used where the specific type of the microorganism is unknown.

Narrow spectrum antibiotics: Narrow spectrum antibiotics are used only when we know the specific type of the microorganism. These are more effective on specific microorganisms but less effective on others.

The second classification is according to the type of the action of antibiotics. Antibiotics can be divided into two classes based on their mechanism of action.

Bactericidal antibodies: They kill bacteria by inhibiting cell wall synthesis.

Examples include:

Beta-lactam antibiotics (penicillin derivatives (penams),

cephalosporins (cephems), monobactams,

and carbapenems) and vancomycin.

Also bactericidal are daptomycin, fluoroquinolones, metronidazole, nitrofurantoin, co-trimoxazole, telithromycin.

Bacteriostatic antibiotics: They limit the growth of bacteria by interfering with bacterial protein production, DNA replication, or other aspects of bacterial cellular metabolism. They must work together with the immune system to remove the microorganisms from the body. However, there is not always a precise distinction between them and bactericidal antibiotics. High concentrations of some bacteriostatic agents are also bactericidal, whereas low concentrations of some bacteriocidal agents are bacteriostatic.

This group includes:

tetracyclines , sulfonamides, spectinomycin, trimethoprim, chloramphenicol,macrolides and lincosamides.

Another classification is according to the chemical structure:

Penicillins such as penicillin and amoxicillin

Cephalosporins such as cephalexin (Keflex)

Macrolides such as erythromycin (E-Mycin), clarithromycin (Biaxin), and azithromycin (Zithromax)

Fluoroquinolones such as ofloxacin (Cipro), levofloxacin (Levaquin), and ofloxacin (Floxin)

Sulfonamides such as co-trimoxazole (Bactrim) and trimethoprim (Proloprim)

Tetracyclines such as tetracycline (Sumycin, Panmycin) and doxycycline (Vibramycin)

Aminoglycosides such as gentamicin (Garamycin) and tobramycin (Tobrex)

B)Explain briefly the mechanism of action of antiviral agents

Ans: **Antiviral drugs** are a class of medication used for treating viral infections.[1] Most antivirals target specific viruses, while a broad-spectrum antiviral is effective against a wide range of viruses.[2] Unlike most antibiotics, antiviral drugs do not destroy their target pathogen; instead they inhibit its development.

Antiviral drugs are one class of antimicrobials, a larger group which also includes antibiotic (also termed antibacterial), antifungal and antiparasitic drugs,[3] or antiviral drugs based on monoclonal antibodies.[4] Most antivirals are considered relatively harmless to the host, and therefore can be used to treat infections. They should be distinguished from viricides, which are not medication but deactivate or destroy virus particles, either inside or outside the body. Natural viricides are produced by some plants such as eucalyptus and Australian tea trees