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

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.

a) Internal receptors
b) Cell surface receptors
c) G proteins-coupled receptor.
d) Enzyme linked receptors.
e) Ion channel receptors

Effect trough Secondary messenger system

There are 3 major classes of second messengers:

i. cyclic nucleotides (e.g., cAMP and cGMP)
ii. inositol trisphosphate (IP3) and diacylglycerol (DAG)
iii. calcium ions (Ca2+) Cyclic AMP (cAMP)

Some of the hormones that achieve their effects through cAMP as a second messenger:

- adrenaline
- glucagon
- luteinizing hormone (LH)

Cyclic AMP is synthesized from ATP by the action of the enzyme adenylyl cyclase.

Binding of the hormone to its receptor activates a G protein which, in turn, activates adenylyl cyclase.

The resulting rise in cAMP turns on the appropriate response in the cell by either (or both): changing the molecular activities in the cytosol, often using Protein Kinase A (PKA) — a cAMP-dependent protein kinase that phosphorylates target proteins turning on a new pattern of gene transcription

Cyclic GMP (cGMP)

Cyclic GMP is synthesized from the nucleotide GTP using the enzyme guanylyl cyclase. Cyclic GMP serves as the second messenger for atrial natriuretic peptide (ANP) nitric oxide (NO) the response of the rods of the retina to light Some of the effects of cGMP are mediated through Protein Kinase G (PKG) — a cGMP-dependent protein kinase that phosphorylates target proteins in the cell.

Inositol trisphosphate (IP3) and diacylglycerol

(DAG) Peptide and protein hormones like vasopressin, thyroid-stimulating hormone (TSH), and angiotensin and neurotransmitters like GABA bind to G protein-coupled receptors (GPCRs) that activate the intracellular enzyme phospholipase C (PLC).

As its name suggests, it hydrolyzes phospholipids — specifically phosphatidylinositol-4,5-bisphosphate (PIP2) which is found in the inner layer of the plasma membrane. Hydrolysis of PIP2 yields two products:

diacylglycerol (DAG):

DAG remains in the inner layer of the plasma membrane. It recruits Protein Kinase C (PKC) — a calcium-dependent kinase that phosphorylates many other proteins that bring about the changes in the cell. As its name suggests, activation of PKC requires calcium ions. These are made available by the action of the other second messenger — IP3.

inositol-1,4,5-trisphosphate (IP3): This soluble molecule diffuses through the cytosol and binds to receptors on the endoplasmic reticulum causing the release of calcium ions (Ca^{2+}) into the cytosol. The rise in intracellular calcium triggers the response.

Calcium ions (Ca^{2+})

As the functions of IP3 and DAG indicate, calcium ions are also important intracellular messengers. In fact, calcium ions are probably the most widely used intracellular messengers.

In response to many different signals, a rise in the concentration of Ca^{2+} in the cytosol triggers many types of events such as muscle contraction exocytosis, e.g. release of

neurotransmitters at synapses (and essential for the long-term synaptic changes that produce Long-Term Potentiation (LTP) and Long-Term Depression (LTD);

secretion of hormones like insulin activation of T cells and B cells when they bind antigen with their antigen receptors (TCRs and BCRs respectively) adhesion of cells to the extracellular matrix (ECM) apoptosis a variety of biochemical changes mediated by Protein Kinase C (PKC).

Normally, the level of calcium in the cell is very low (~100 nM). There are two main depots of Ca2+ for the cell:

The extracellular fluid (ECF — made from blood), where the concentration is ~ 2 mM or 20,000 times higher than in the cytosol;

the endoplasmic reticulum ("sarcoplasmic" reticulum in skeletal muscle).

However, its level in the cell can rise dramatically when channels in the plasma membrane open to allow it in from the extracellular fluid or from depots within the cell such as the endoplasmic reticulum and mitochondria.

Q2. Define drug interactions, enumerate its various types, and explain pharmacokinetic drug interactions and its factors with examples.

ANS :

Drug Interaction

DEFINITION : A drug interaction is a reaction between two (or more) drugs or between a drug and a food, beverage, or supplement. Taking a drug while having certain medical conditions can also cause a drug interaction. For example, taking a nasal decongestant if you have high blood pressure may cause an unwanted reaction.

Drug interactions can be categorised into 3 groups: Interactions of drugs with other drugs

(Drug-drug interactions)

Drugs with food interactions)

(Drug with disease condition)

Pharmacokinetic 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 behaviour of each drug when taken individually.

QNO3. Differentiate between general and local anesthesia, explain stages of anaesthesia in detail.

ANS :

Anaesthesia

Anaesthesia means "loss of sensation". Medications that cause anaesthesia are called anaesthetics.

Anaesthetics are used during tests and surgical operations to numb sensation in certain areas of the body or induce sleep.

This prevents pain and discomfort, and enables a wide range of medical procedures to be carried out.

Local anaesthetics and general anaesthetics are two commonly used types of anaesthetics:

local anaesthetic is where a small area of the body is numbed and you remain fully conscious – often used during minor procedures

general anaesthetic is where you're totally unconscious and unaware of the procedure – often used for more serious operations

There are four stages of general anesthesia, namely: analgesia - stage 1, delirium - stage 2, surgical anesthesia - stage 3 and respiratory arrest - stage 4. As the patient is increasingly affected by the anaesthetics his anesthesia is said to become 'deeper'.

Stage 1 - Analgesia or Disorientation:

This stage can be initiated in a preoperative anaesthesiology holding area, where the patient is given medication and may begin to feel its effects but has not yet become unconscious. This stage is usually described as the "induction stage." Patients are sedated but conversational. Breathing is slow and regular. At this stage, the patient progresses from analgesia free of amnesia to analgesia with concurrent amnesia.[3] This stage comes to an end with the loss of consciousness.

Stage 2 - Excitement or Delirium:

This stage is marked by features such as disinhibition, delirium, uncontrolled movements, loss of eyelash reflex, hypertension, and tachycardia. Airway reflexes remain intact during this phase and are often hypersensitive to stimulation. Airway manipulation during this stage of anesthesia should be avoided, including both the placement and removal of endotracheal tubes and deep suctioning manoeuvres. There is a higher risk of laryngospasm (involuntary tonic closure of vocal cords) at this stage, which may be aggravated by any airway manipulation. Consequently, the combination of spastic movements, vomiting, and rapid, irregular respirations can compromise the patient's airway. Fast-acting agents help to reduce the time spent in stage 2 as much as possible and to facilitate entry to stage 3.

Stage 3 – Surgical Anesthesia:

This is the targeted aesthetic level for procedures requiring general anesthesia. Ceased eye movements and respiratory depression are the hallmarks of this stage. Airway manipulation is safe at this level. There are four "planes" described for this stage. During plane 1, there is still regular spontaneous breathing, constricted pupils, and central gaze. However, eyelid, conjunctival, and swallow reflexes usually disappear in this plane. During plane 2, there are intermittent cessations of respiration along with the loss of corneal and laryngeal reflexes. Halted ocular movements and increased lacrimation may also occur. Plane 3 is marked by complete relaxation of the intercostal and abdominal muscles and loss of the pupillary light reflex. This plane is referred to as "true surgical anesthesia" because it is the ideal state for most surgeries. Finally, Plane 4 is marked by irregular respiration, paradoxical rib cage movement, and full diaphragm paralysis resulting in apnea.

Stage 4 - Overdose:

This stage occurs when too much aesthetic agent is given relative to the amount of surgical stimulation, which results in worsening of an already severe brain or medullary depression. This stage begins with respiratory cessation and ends with potential death. Skeletal muscles are flaccid, and pupils are fixed and dilated at this stage.[4][6] Blood pressure is typically significantly lower than normal, with weak and thready pulses due to the suppression of the cardiac pump and vasodilation in the peripheral bloodstream. Without cardiovascular and respiratory support, this stage is lethal. Hence, the goal of the anaesthetist is to transition the patient as soon as possible to stage 3 of anesthesia and keep them there for the duration of the operation.

QNO 4.(a). What does heart failure means, explain the pathophysiology of heart failure.

ANS :

Heart Failure :

Heart failure, sometimes known as congestive heart failure, occurs when your heart muscle doesn't pump blood as well as it should. Certain conditions, such as narrowed arteries in your heart (coronary artery disease) or high blood pressure, gradually leave your heart too weak or stiff to fill and pump efficiently.

Pathophysiology of Heart Failure brings together leading basic scientists and clinicians, presenting new approaches to this complex problem, involving cardiomyopathic processes and ischemia perfusion injury. ...

QNO 4(b). Classify the drug used for the treatment of heart failure, explain along with mechanism.

ANS :

Medicines for heart failure

Most people with heart failure are treated with medication. Often you'll need to take 2 or 3 different medicines.

Some of the main medicines for heart failure include:

ACE inhibitors angiotensin-2 receptor blockers (ARBs) beta blockers mineralocorticoid receptor antagonists diuretics ivabradine sacubitril valsartan hydralazine with nitrate digoxin.

You may need to try a few different medicines before you find a combination that controls your symptoms but doesn't cause unpleasant side effects.

ACE inhibitors:

Angiotensin-converting enzyme (ACE) inhibitors work by relaxing and opening up your blood vessels, which makes it easier for your heart to pump blood around the body.

Examples of ACE Inhibitors Include Ramipril, captopril, enalapril, lisinopril and perindopril.

The most common side effect of ACE inhibitors is a dry, irritating cough.

If you have a troublesome cough, an ACE inhibitor may be switched to an ARB.

ACE inhibitors can also cause your blood pressure to fall too low, and they may cause kidney problems. Your GP will monitor this.

Angiotensin-2 receptor blockers (ARBs)

Angiotensin-2 receptor blockers (ARBs) work in a similar way to ACE inhibitors by relaxing blood vessels and reducing blood pressure.

They tend to be used as an alternative to ACE inhibitors because they don't usually cause a cough, although they may not be quite as effective as ACE inhibitors.

Examples of ARBs include candesartan, losartan, telmisartan and valsartan.

Side effects of ARBs can include low blood pressure and high levels of potassium in your blood.

Your doctor will carry out regular blood tests to monitor your potassium level **etc....**

QNO 5 (a) Differentiate between broad spectrum and narrow spectrum antibiotics classify antibiotics drugs.

Description:

A broad-spectrum antibiotic is an antibiotic that acts on the two major bacterial groups, gram-positive and gram-negative, or any antibiotic that acts against a wide range of disease-causing bacteria. Wikipedia

Examples of narrow-spectrum antibiotics are the older penicillins (penG), the macrolides and vancomycin. Examples of broad-spectrum antibiotics are the aminoglycosides, the 2nd and 3rd generation cephalosporins, the quinolones and some synthetic penicillins.

QNO 5 (b) Explain briefly the mechanisms of action of antiviral agents.

ANS :

Unlike other antimicrobials, antiviral drugs do not deactivate or destroy the microbe (in this case, the virus) but act by inhibiting replication. In this way, they prevent the viral load from increasing to a point where it could cause pathogenesis, allowing the body's innate immune mechanisms to neutralize the virus.

THE END.....