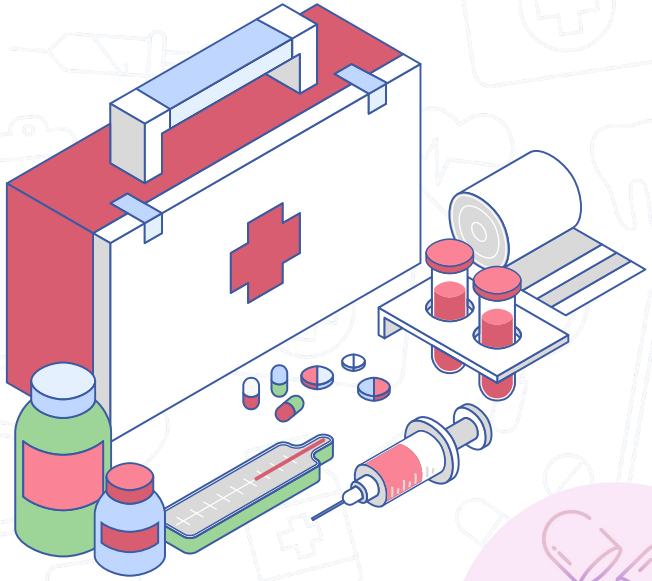
AUTOCIDS PARACRINE MEDIATORS PART 2 442



EDITING FILE

Pharmacology
Team 442

Important
Main text
Male slide
Female slide
Extra info
Doctor notes

Angointensin

Angiotensinogen : circulating protein in the blood that comes from the liver

Thanks to med39

Biosynthesis

1-Renin-circulating protein that comes from the kidney- released from the kidney

2-Renin will convert Angiotensinogen to Angiotensin I (inactive)

ACE will convert Angiotensin I to Angiotensin II (Active)

Angiotensin II affection

1. Vasoconstriction will increase blood pressure
2. Increases aldosterone secretion and this will support blood pressure

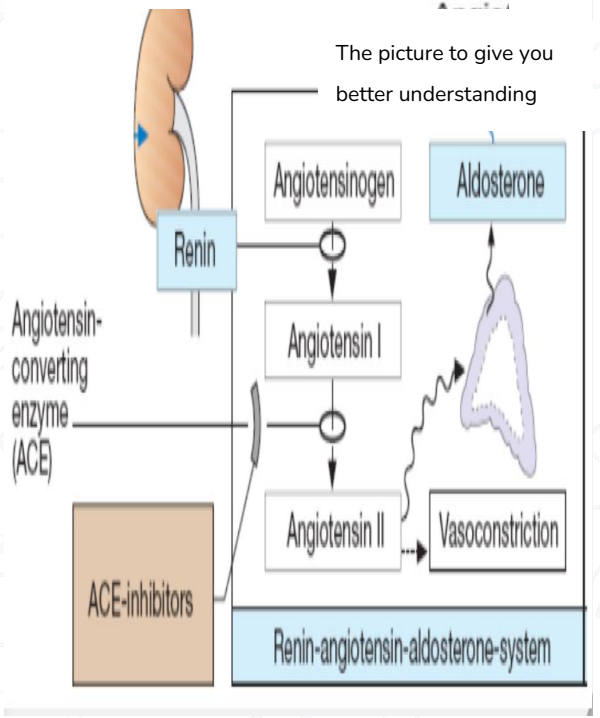
Renin ACE*

Angiotensinogen → Angiotensin I (Ag I) → Angiotensin II (Ag II)

(from the liver) (inactive form)

when this whole system is activated ?
When there is a change in blood pressure

The picture to give you better understanding

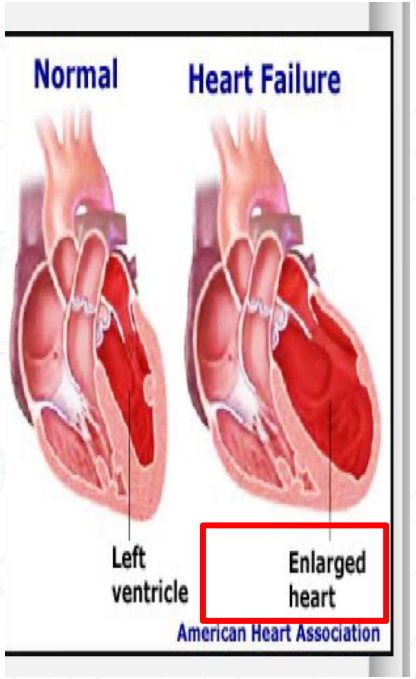


Med441: ال ACE هو الي يحول Angiotensin I الى Angiotensin II الي
يرفع ضغط الدم ف المرضى مع ضغط الدم
العالي نعطيهم ACE inhibitors الي يثبط ال ACE ف يمنع تكوين angiotensin II الي يرفع ضغط الدم

Actions of angiotensin II

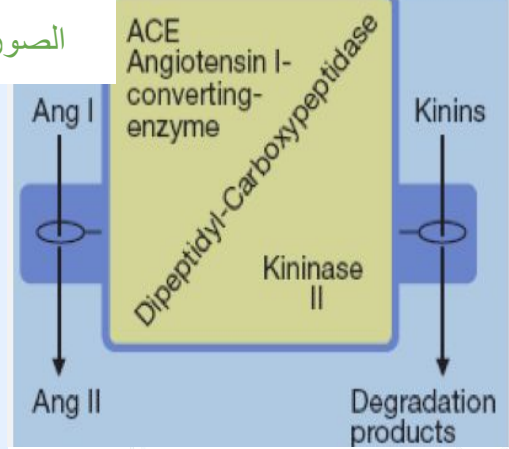
- Promotes vasoconstriction directly or indirectly by releasing NA & AD
- Increases force of contraction of the heart by promoting Ca2+ influx
- Increases aldosterone release → sodium & water retention
- **Causes**

-hypertrophy of vascular & cardiac cells
-increases synthesis & deposition of collagen by cardiac fibroblasts (remodeling).



ANGIOTENSIN(ACE) INHIBITORS

الصورة للتوضيح فقط



Definition: Cause a fall in blood pressure in hypertensive patients especially those with **high renin levels**

CLINICAL USES: 1-Hypertension 2- Cardiac failure 3 - myocardial infarction

Eg. Captopril , enalap

Memorise drug name

ANGIOTENSIN RECEPTOR BLOCKERS(ARBs)

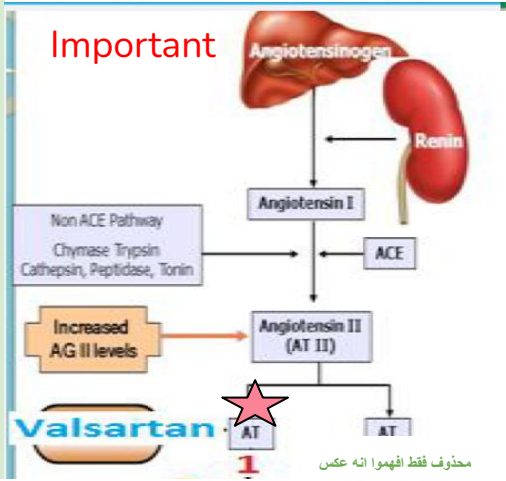
AT 1 receptor act has opposite effect to AT2 receptor

AT 1 receptors predominate in vascular smooth muscle, mediate most of the known actions of Ang, coupled to G proteins & DAG

E.g. losartan,valsartan

The therapeutic uses of the ACE inhibitors and receptors are similar

Important



-Vasoconstriction
-Renal sodium reabsorption
-Cell growth proliferation

•Vasodilation
• Natriuresis
•Antiproliferation

441 notes:
kinogen with kallikrein will produce Bradykinin

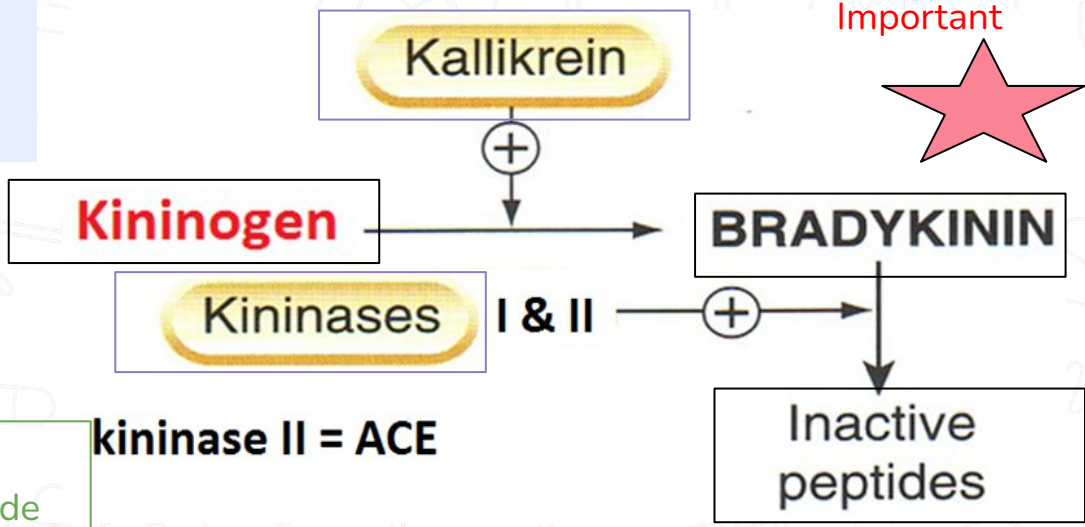
Bradykinin is inactivated by kininase 1&2 (kinase II is another name of ACE)

kinins

- Bradykinin (Mainly)
- kallidin

Bradykinin is formed by proteolytic cleavage of circulating proteins (kininogens)

Important



Black the pathway
Purple the enzyme that will affect pathway

1-Kallikrein convert kininogen to bradykinin
2-kinases metabolise bradykinin to inactive peptide

Actions of bradykinin

1. Potent Vasodilator, reduces blood pressure (10 times stronger than histamine)

2. If injected locally it dilates arterioles [generation of PGI release of NO] and increases permeability of post capillary venules
(it's a vasodilator that produces other vasodilators)

3. Causes pain, this effect is potentiated by prostaglandins(PG).
Has a role in inflammation

4. Constricts most non-vascular smooth muscles , intestine , uterus, bronchiole, contraction is slow and last long

5. Stimulation of epithelial ion transport & fluid secretion in airways & GIT

Receptors & clinical uses

1	Receptors B1 & B2 (both are G protein-coupled receptors)
2	B1 inducible under condition of inflammation
3	B1 receptor has low affinity to bradykinin plays a significant role in inflammation & hyperalgesia (hyperalgesia = pain sensation)
4	B2 constitutive High affinity to bradykinin & mediates the majority of its effects.

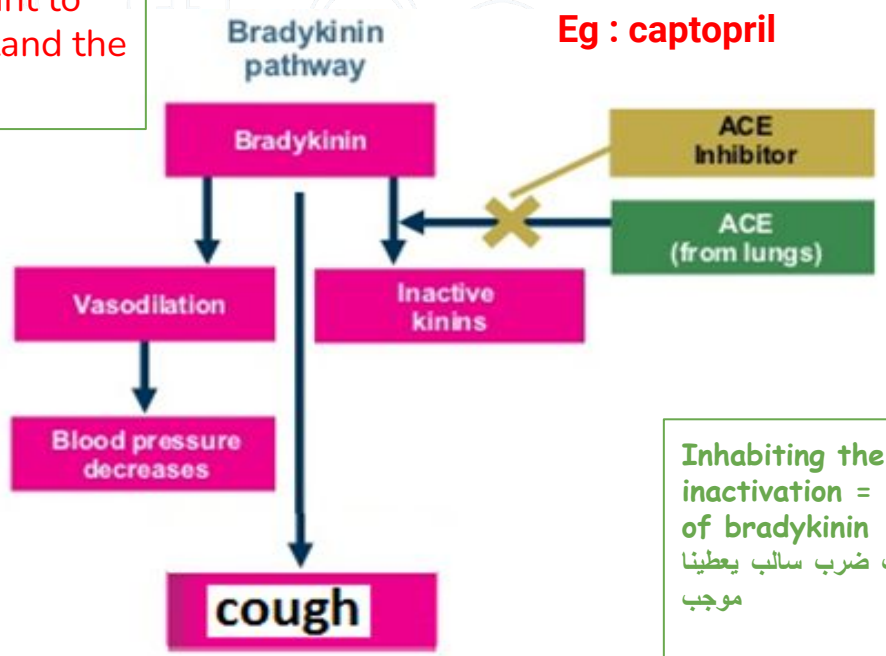
441 note: which receptor has a higher efficacy? B2 receptor
B1 is only used in cases of inflammation and foreign objects

Therapeutic uses

No current therapeutic use of bradykinin (because it has severe hypotensive action but it helps the ACE inhibitors)

Increased bradykinin is implicated in the therapeutic efficacy & cough and angioedema produced by ACE inhibitors.

Important to understand the graph



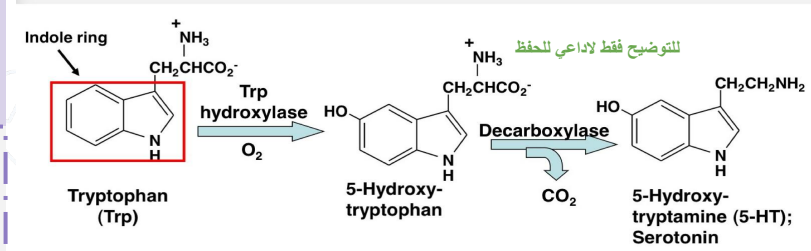
The ACE inhibitor used for treatment of hypertension (such as captopril) works by inhibiting the inactivation of Bradykinin so the bradykinin increases which is good for hypertension treatment , however it causes cough because the bradykinin causes smooth muscle constriction in bronchioles

Inhabiting the inactivation = increase of bradykinin

مثل: سالب ضرب سالب يعطينا موجب

Serotonin (5-HT)

Definition : Serotonin is synthesized from the amino acid L-tryptophan



Action :

- **Platelets**:- causes aggregation, aggregated platelets release 5-HT
- **Neuronal terminals**: 5-HT stimulates nociceptive neuron endings → pain
- **CNS**;- stimulates some neurons & inhibits others, inhibits release of other neurotransmitters.
- **GIT**: 5-HT

1-increases motility
2-Contracts uterus, bronchiole, other smooth muscles

- **Blood vessels**:-

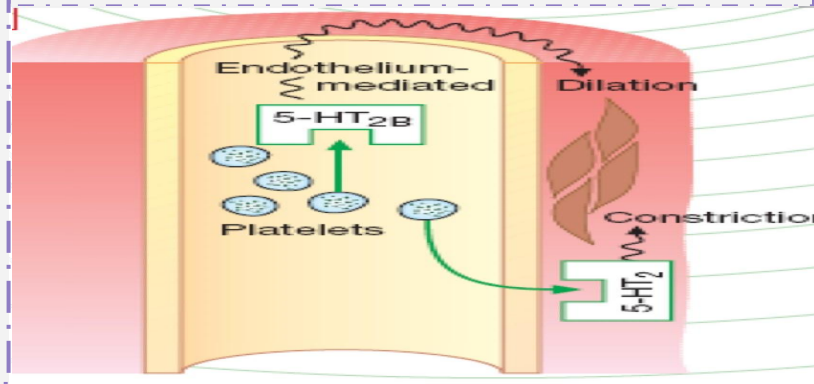
1-Contracts large vessels by a direct action & relaxes other vessels by releasing NO
2-Increases capillary pressure & permeability.

DISTRIBUTION :

1] Intestinal wall: in chromaffin cells, in neuronal cells in the myenteric plexus

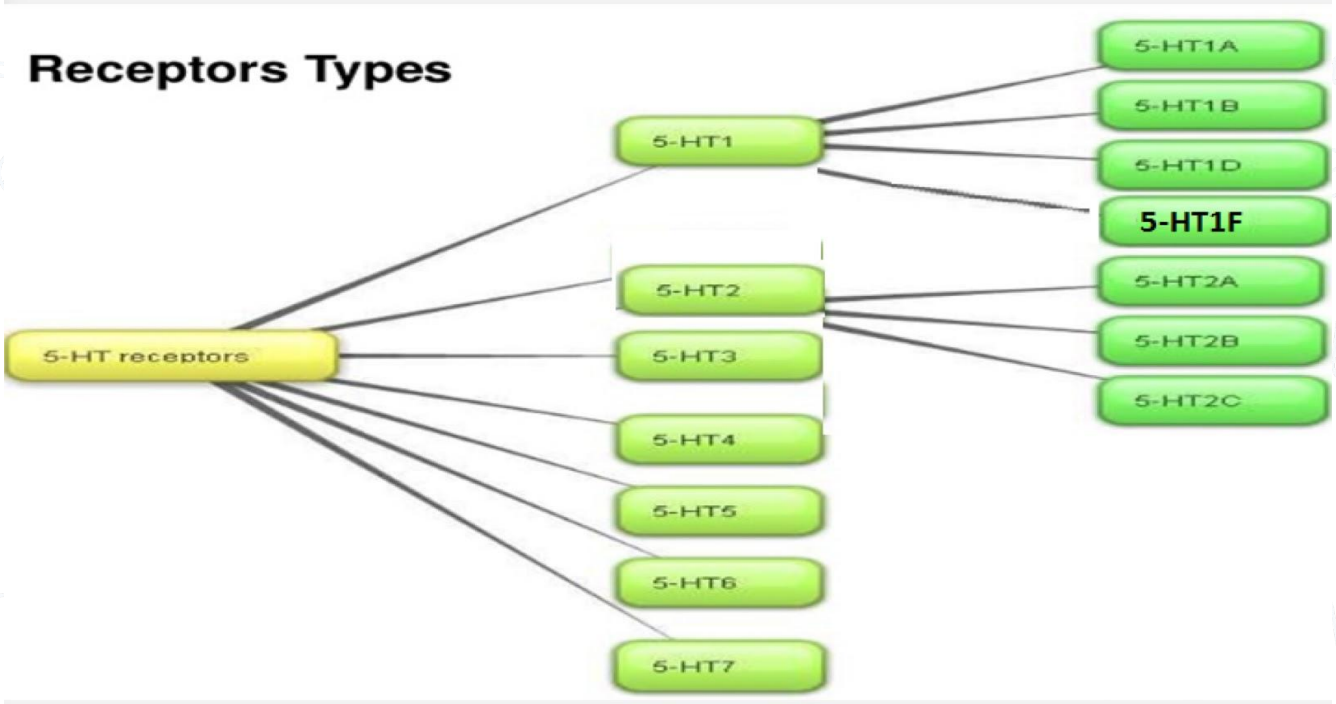
2] Blood, in platelets, released when aggregated, in sites of tissue damage

3] CNS: a neurotransmitter, in midbrain



Serotonin (5-HT) Receptor

Focus on what will discuss next slides

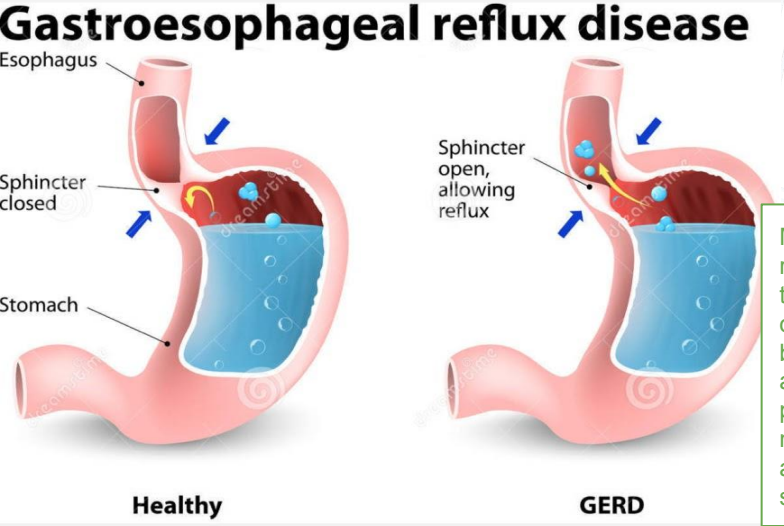


5 -HT RECEPTOR AGONISTS

Important slide
You must know each one
-drug
-receptor
-treat
-agonist/antagonist

Buspirone:- 5-HT1A agonist, effective anxiolytic

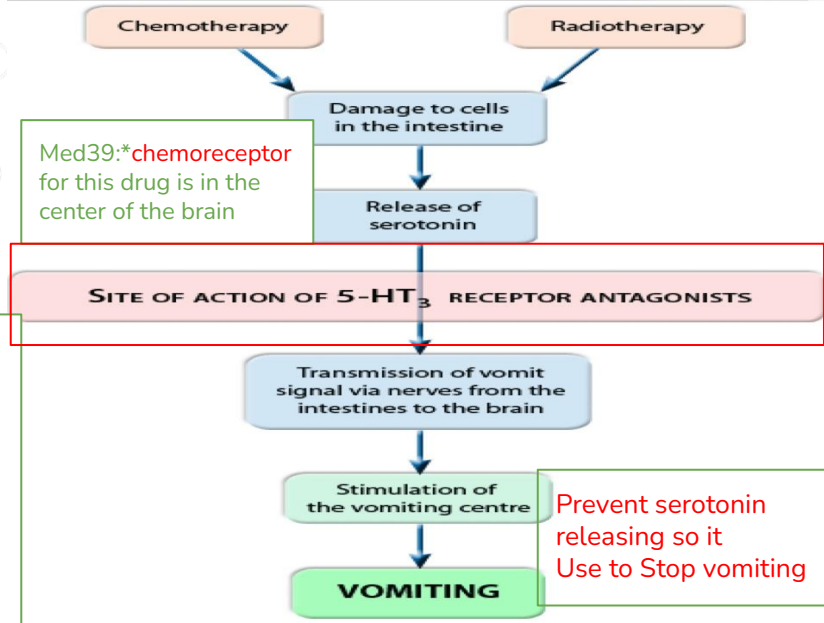
Cisapride:-
5 -HT4 -receptor agonist, used in gastroesophageal reflux & motility disorders.(تسرع في عملية افراغ المعدة)



Med39:In gastroesophageal reflux, the gastric acid enters the esophagus through an open sphincter causing burning sensation→ patients are given antacids or prokinetic drugs (increases motility, decreasing the amount of contents in the stomach)

5 -HT RECEPTOR ANTAGONISTS

Selective 5-HT3 antagonist, Ondansetron, antiemetic action, for cancer chemotherapy



Med39:*chemoreceptor for this drug is in the center of the brain

Prevent serotonin releasing so it
Use to Stop vomiting

CLINICAL CONDITIONS IN WHICH 5-HT IS IMPLICATED

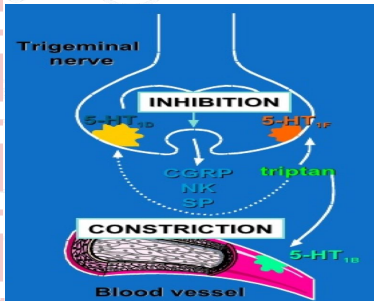
الصور للتوضيح فقط

1-SUMATRIPTAN

5-HT 1B, 1D & 1F-receptor **agonists**, effective in **acute migraine attack** (binds with 3 types of 5-HT)

Mechanism of action:

It binds to 5HT1B, in cranial blood vessels causing vasoconstriction & 1D & 1F in presynaptic trigeminal nerve causing **inhibition** of pro- inflammatory neuropeptide release.

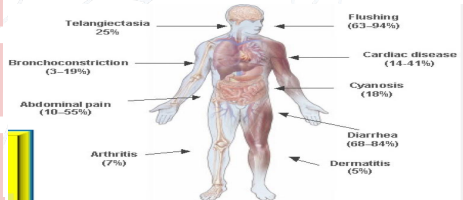


2 - CARCINOID SYNDROME

A malignant tumor of intestinal chromaffin cells

The tumor releases(all mediators)5-HT, SP, PGs, kinins & histamine **causing** :
flushing, diarrhea, bronchoconstriction & hypotension

Serotonin antagonists (cyproheptadine, 5HT2 antagonist) could be administered to control diarrhea, flushing & malabsorption.



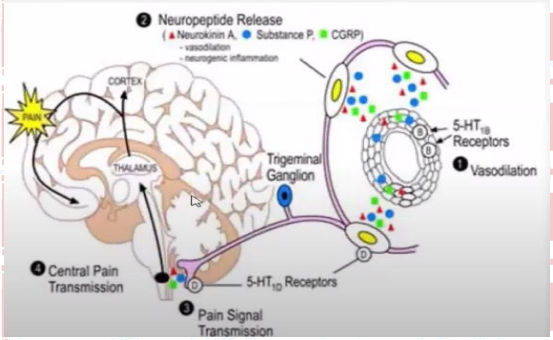
Med39:They don't treat malignancy just control the symptoms

3-Migraine

Activation of trigeminal system leads to vasodilator peptide release promoting an inflammatory reaction

This increase flow of sensory traffic through the brain stem, the thalamus, the cortex

Med39:Neuropeptides release causing vasodilation and neurogenic inflammation→ Migraine, causing vasodilation only→ pain



MCQ

Q-1 serotonin is distributed in?

a-liver. b- blood c-skin.

Q-2 Ondansetron is a selective antagonist for 5-HT receptor

A) 5-HT4. B) 5-HT1A. C) 5-HT3. D) 5HT2

Q-3 Which of the following receptors have High affinity to bradykinin

A) B1. B) B2. C) AT I. D)AT II

Q4 Serotonin is synthesized from the amino acid:

A) 5-hydroxytryptophan B) L-Tryptophan. C) 5-hydroxytryptamine. D) cyproheptadine

1-B

2-C

3-B

4-B

SAQ

Q-1 Give examples of the two types of drugs that work on 5-HT receptors?

Q-2 list 3 CLINICAL CONDITIONS IN WHICH 5-HT IS IMPLICATED?

Answers

1- agonists: Buspirone and Cisapride , antagonist: Ondansetron

2- slide 12

DONE BY THE AMAZING TEAM

You GOT THIS!

Shahed Bukhari
Kadi aldossari
Hend Almogary
Razan Almohanna
razan almanjomi
Noura bin hammad
Lina alyahya
Tharaa Alhowaish
Reema Aljubreen
Reema Alhussien
*OUR AMAZING Q BANK
Renad Alayidh

Mohammed Alrashod
Mohammed aloraini
Musaed almutairi
Mohammed al-zeer
Ibrahim alharbi
Hamad Alotaibi
Ahmed Abdualaziz
Mohammed AlShehri

Leader	Khalid Al Rasheed	Reema Alquraini

Contact us:Pharmacology442@gmail.com