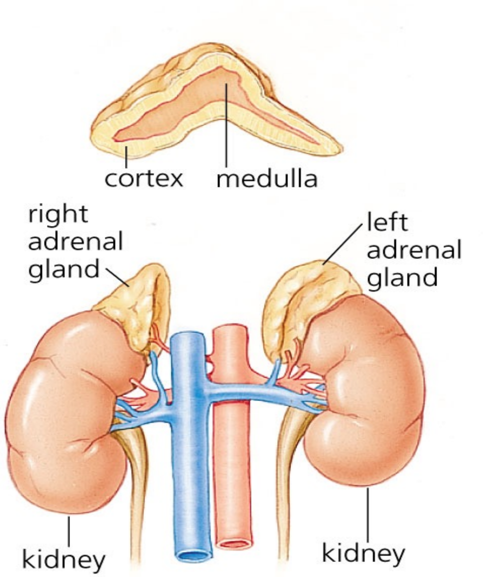
Hormones of adrenal cortex and adrenal medulla
&
Stress

Organization of the Adrenal Gland

- There is an adrenal cortex and adrenal medulla.
- The adrenal gland are paired orangs that cap the superior borders of the 2 kidney.

adrenal gland divided into two morphologically and distinct regions

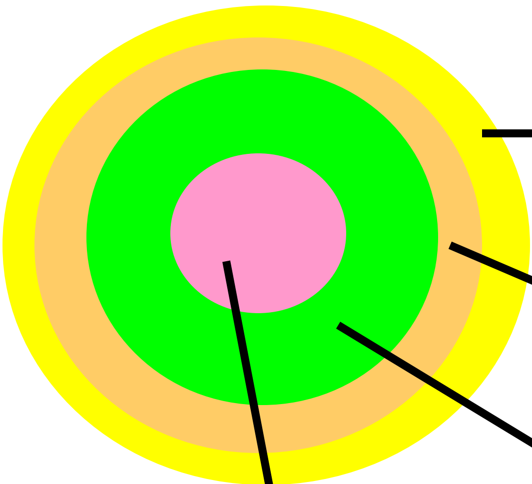
1. adrenal cortex (outer)
2. adrenal medulla (inner)



Adrenal glands

- weight 4-5 g
- Cortex - 80% : synthesis of steroid hormones Steroids are made in the 3 zones of the adrenal cortex:
  - zona glomerulosa - mineralocorticoids
  - zona fasciculata – glucocorticoids
  - zona reticularis – adrenal androgens
- Medulla - 20% : synthesis of noradrenaline and adrenaline
  - Functionally: a part of sympathetic nervous system

Adrenals



CORTEX

Zona Glomerulosa

Mineralocorticoids (Aldosterone)

Na+, K+ and water homeostasis

Zona Fasciculata

Glucocorticoids (Cortisol)

Glucose homeostasis and many others

Zona Reticularis

Sex steroids (androgens)

Medulla: "Catecholamines"

Epinephrine, Norepinephrine, dopamine

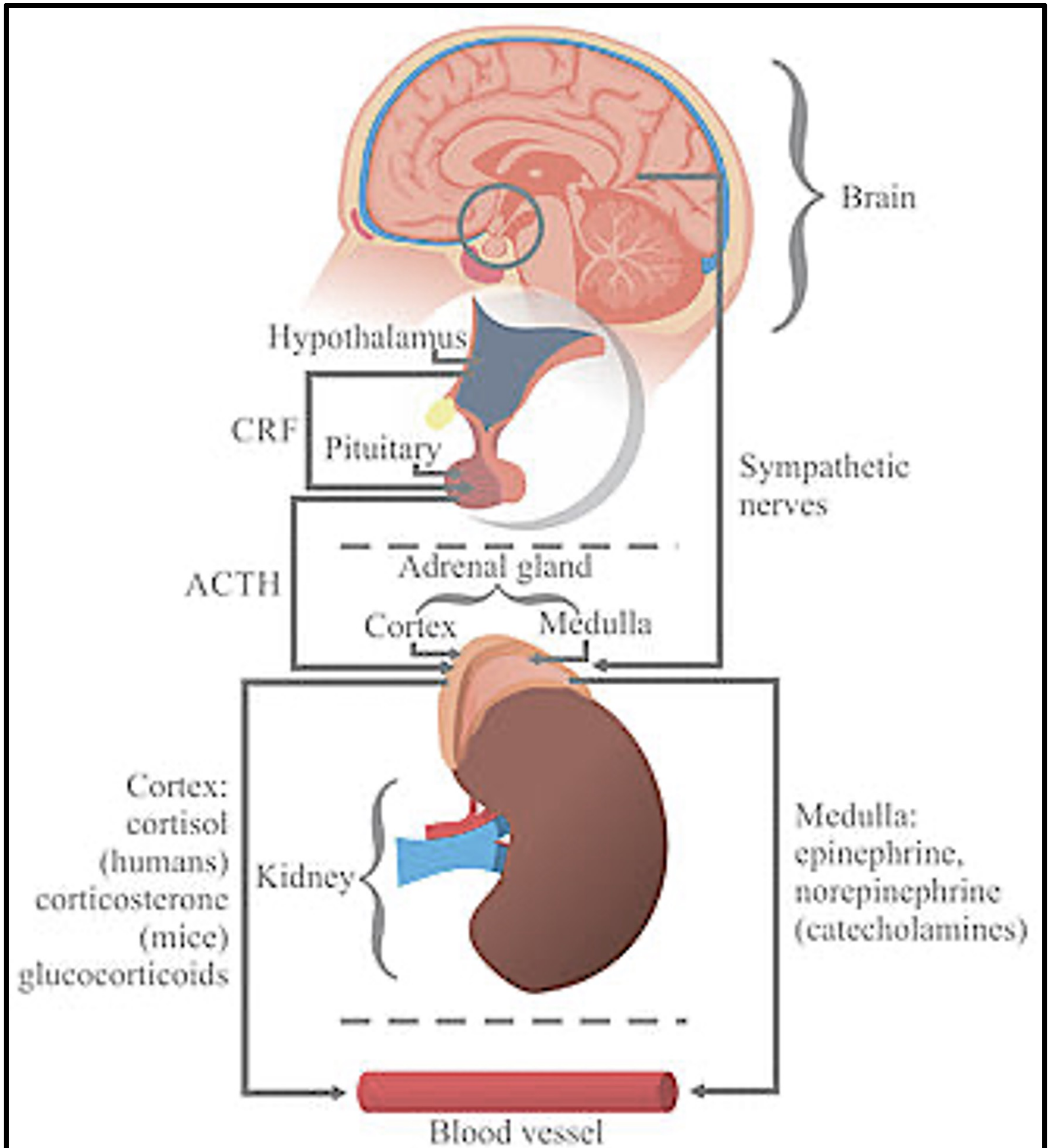
Hormones of the Adrenal Medulla

- adrenaline (epinephrine) 80%
- noradrenaline (norepinephrine) 20%

Hormones are secreted and stored in the adrenal medulla and released in response to appropriate stimuli

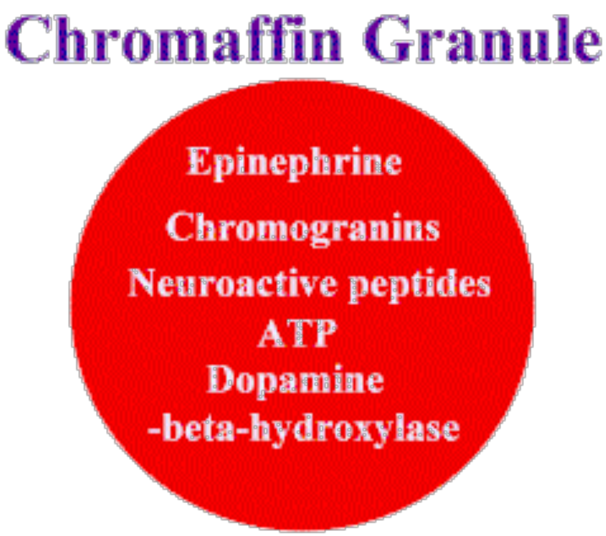
Catecholamines & the Sympathoadrenal System

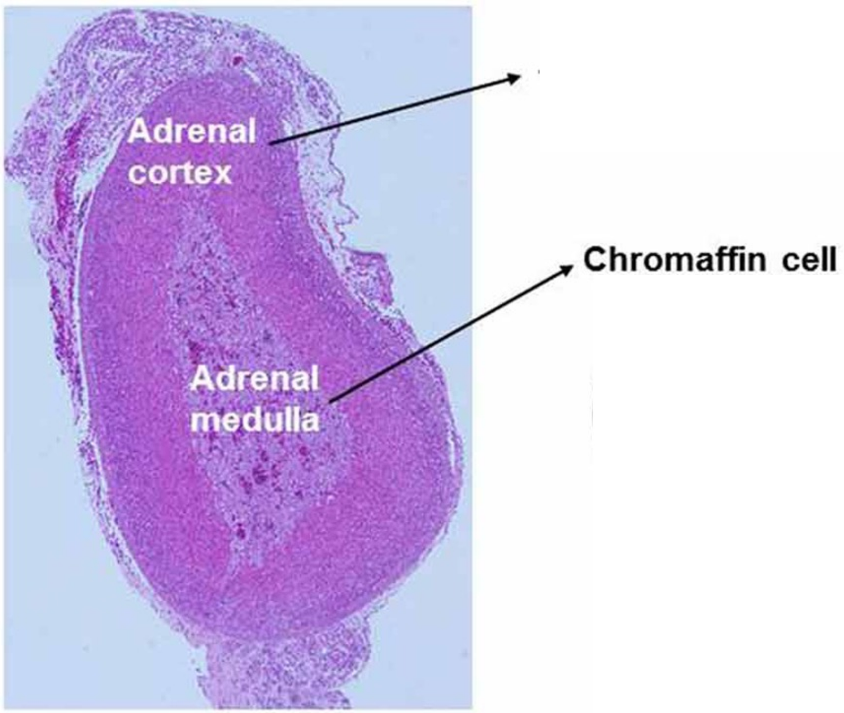
- Physiologically catecholamines are epinephrine (E), norepinephrine (NE) and dopamine (DA).
- Epinephrine (E) has been considered a classic example of a **hormone** and norepinephrine (NE) a **neurotransmitter** .
- **E** is produced primarily by the chromaffin tissue (adrenal medulla) and **NE** by the sympathetic neurons but they both have similar structures and biological actions.


Brain
Hypothalamus
CRF
Pituitary
Sympathetic nerves
ACTH
Adrenal gland
Cortex
Medulla
Cortex: cortisol (humans) corticosterone (mice) glucocorticoids
Kidney
Medulla: epinephrine, norepinephrine (catecholamines)
Blood vessel

Adrenal Chromaffin Tissue

- Chromaffin tissue is referred to as adrenal medulla.
- Adrenal medulla consists of two types of cells, **E storing and NE storing cells.**
- Chromaffin cells contain granules composed of catecholamines, ATP-Mg^{2+},Ca^{2+}, dopamine β-hydroxylase (DBH), proteins(chromogranin)and lipids.

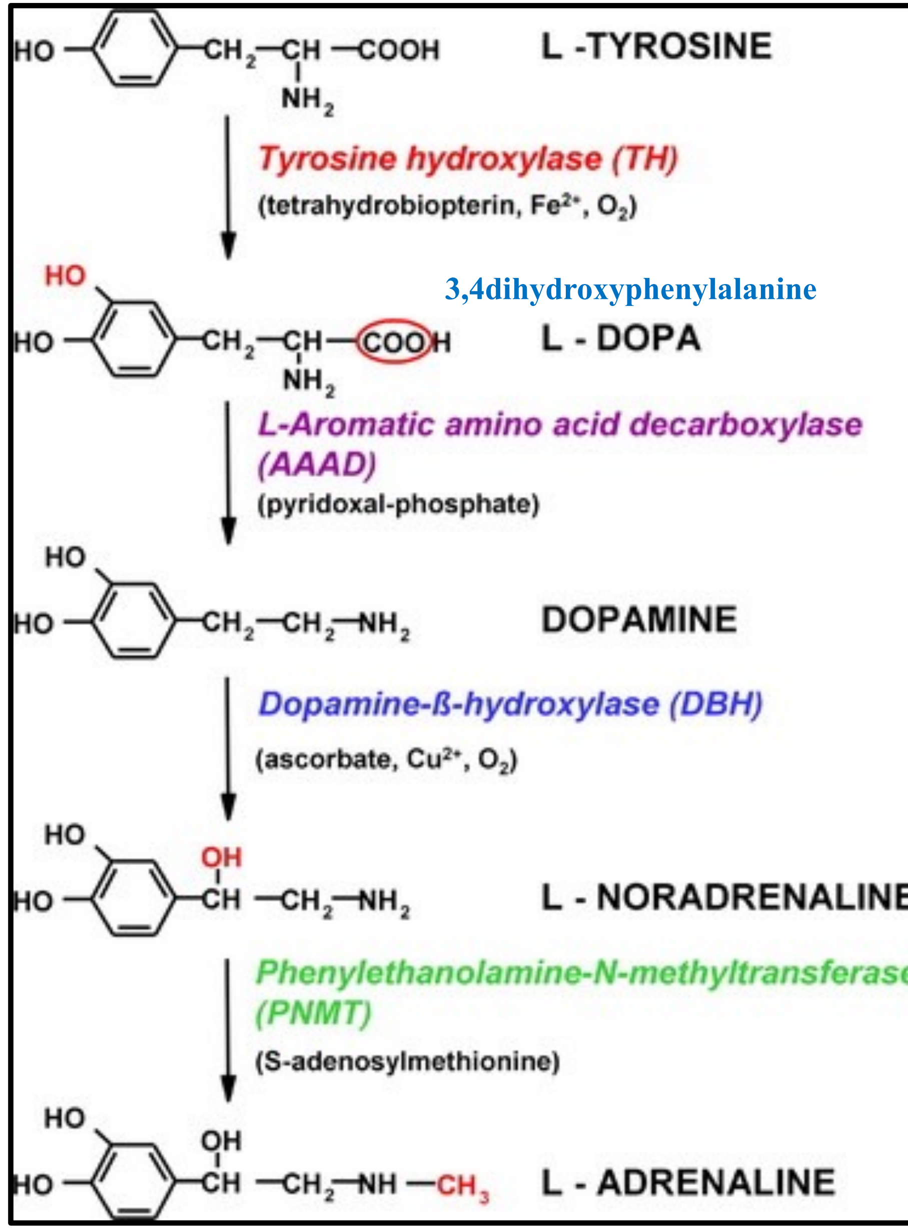




Synthesis of Catecholamines

- Pathways of catecholamine biosynthesis within the CNS, sympathetic neurons and chromaffin tissue appear to be identical.
- The number of steps in each pathway depends on the product, DA, NE, or E.
- Conversion of **tyrosine to E** involves four steps:

1) **hydroxylation** of the phenolic ring,
2) side chain **decarboxyaltion,**
3) side-chain hyrdoxylation,
4) N-**methylation**.



Synthesis of Catecholamines

- 1- **Tyrosine** is transported into the cell where it is converted to 3,4dihydroxyphenylalanine (DOPA) by tyrosine hydroxylase, which is found only in the tissues that synthesize catecholamines.
- Conversion of tyrosine to DOPA is the rate limiting step in catecholamine biosynthesis.
- Tyrosine hydroxylase is oxidoreductase.
- Activity of this enzyme is controlled by end-product inhibition by cytoplasmic catecholamines.
- **α-methyl tyrosine** is a competitive inhibitor of tyrosine hydroxylase.

2- **3,4 dihydroxyphenylalanine** (DOPA) is then decarboxylated to dopamine (DA) by DOPA decarboxylase, a nonspecific decarboxyalse found in many tissues.

3- DA is then hydroxylated by dopamine β hydroxylase (DBH) to norepinephrine (NE).

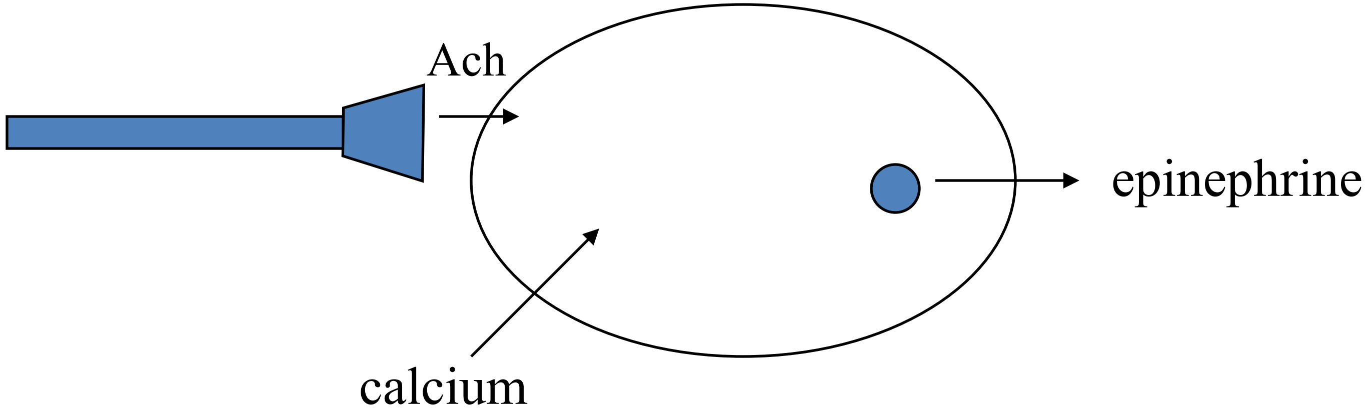
- In dopaminergic neurons DA is the final step
- in noradrenergic neurons and adrenal medulla DA is converted to NE within the chromaffin granule.

4-The NE produced is converted to E by phenylethanolamine-N-methyltransferase (PNMT) *outside* the granule (in the cytoplasm).

This enzyme is only found in cells that synthesize E (adrenal chromaffin tissue).

Regulation of Epinephrine Release

- Released in response to sympathetic stimulation that cause release of acetylcholine (A ch).
- A ch binds to receptors on chromaffin cells, causing increased calcium uptake.
- Calcium causes release of vesicles containing epinephrine (exocytosis).



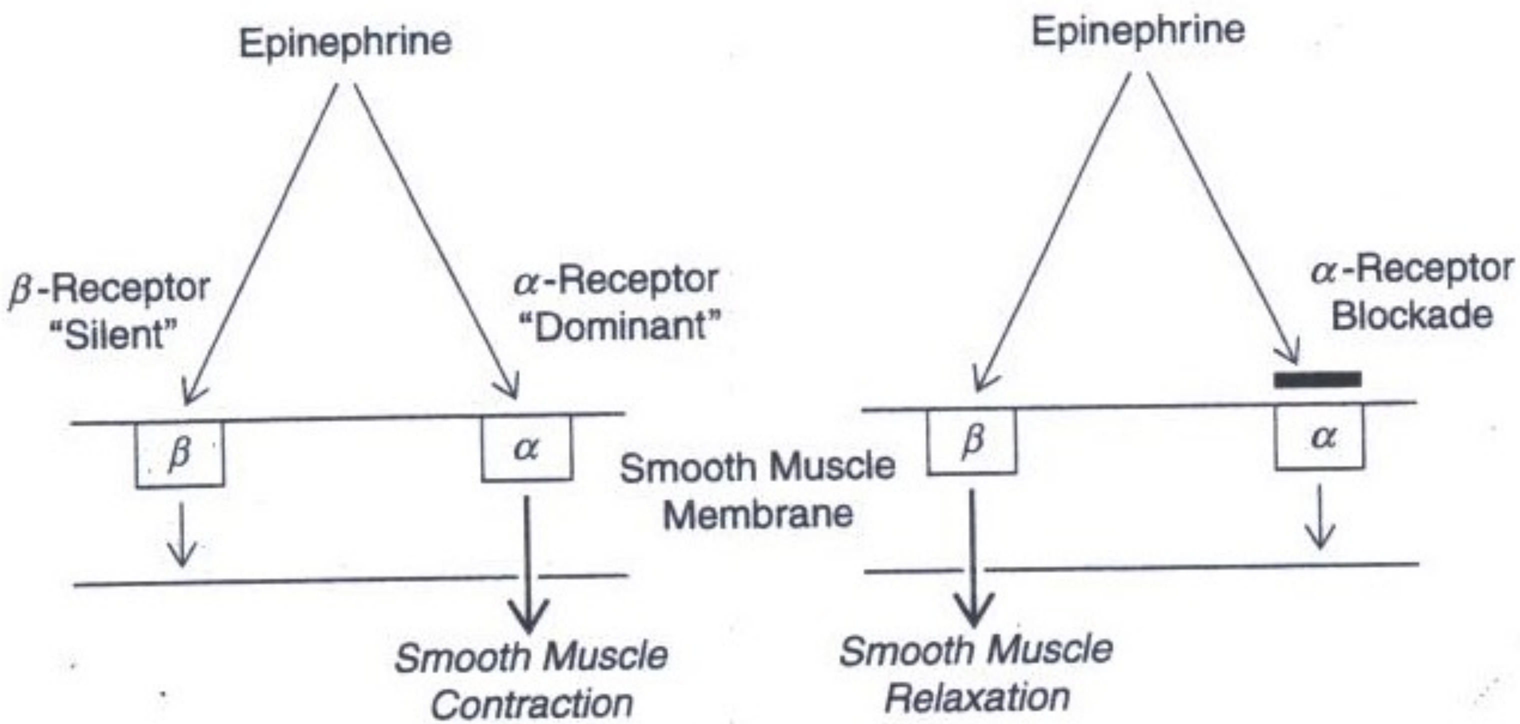
Storage and Release

- Catecholamines (E or NE) are contained in granules where they are complexed with ATP, and a specific protein, chromogranin A .
- NE is synthesized and stored in the granule but E is made outside the granule, then stored in the granules.
- Secretory vesicles are released through a stimulus- requiring Ca^{++}.
- All the contents of the granules are released during vesicular exocytosis.
- Once E is secreted into the bloodstream, it affects a receptors on hepatocytes to increase blood glucose and it interacts with a receptors on vascular smooth muscle cells to cause contraction and increase blood pressure.

Adrenergic Receptors

- Two different types of adrenergic receptors exist designated the α and β adrenergic receptor.

1. The α– receptors cause smooth muscle contraction
2. The β– receptors cause smooth muscle relaxation.



Adrenergic Receptors

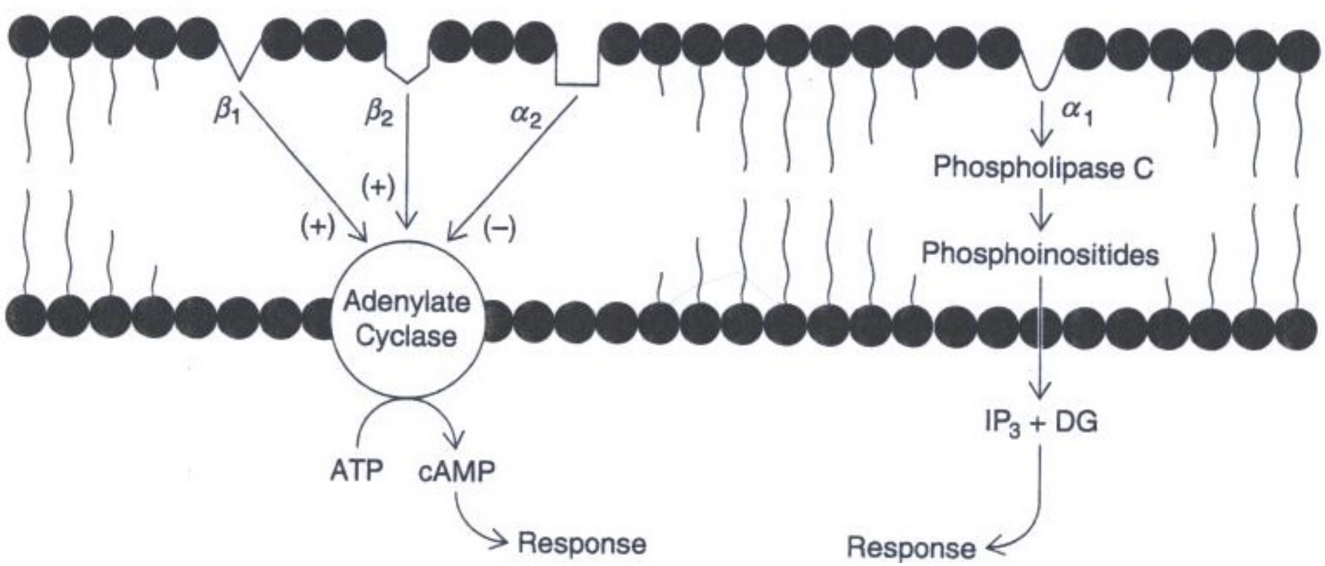
- Four subtypes of these catecholamine receptors have been identified, a_1, a_2, b_1, b_2 adrenoceptors.
- Chemical agents that selectively block or stimulate these receptors are used in clinical medicine.

α Adrenoceptors

- Activation of α1 AR by NE increases hydrolysis of PIP_2 by phospholipase C.
- The resulting Ins(1,4,5)P_3 and diacyl glycerol (DAG) into the intracellular space, mobilizes Ca^{++} stored in intracellular pools in endoplasmic and sarcoplasmic reticulum and activates PKC.
- while α_2 AR inhibits adenylate cyclase.

β -Adrenoceptors

- Evidence exists that b AR represent at least two different subgroups.
- The b_1 AR are involved with the lipolytic response of adipose tissue and contraction of cardiac muscle.
- The b_2 AR are involved in bronchodilation.
- β_1, β_2 AR stimulate adenylate cyclase and increase cAMP.



Thyroid Hormones

- Sympathoadrenal activity is enhanced under conditions of hyperthyroidism
- and **depressed** under conditions of **low levels of thyroid hormones.**

Sympathoadrenal Functions

- Any decrease in blood pressure (BP), or blood glucose (BG), leads to an acute increase of the sympathoadrenal activity resulting in elevated catecholamines.
- In addition, the sympathoadrenal system is activated in- STRESS

Effects of Epinephrine

1- Carbohydrate metabolism

- stimulates **glycogenolysis** in liver and skeletal muscle **can lead to hyperglycemia**

2- increased metabolic rate :O_2 consumption increases

3- Fat Metabolism

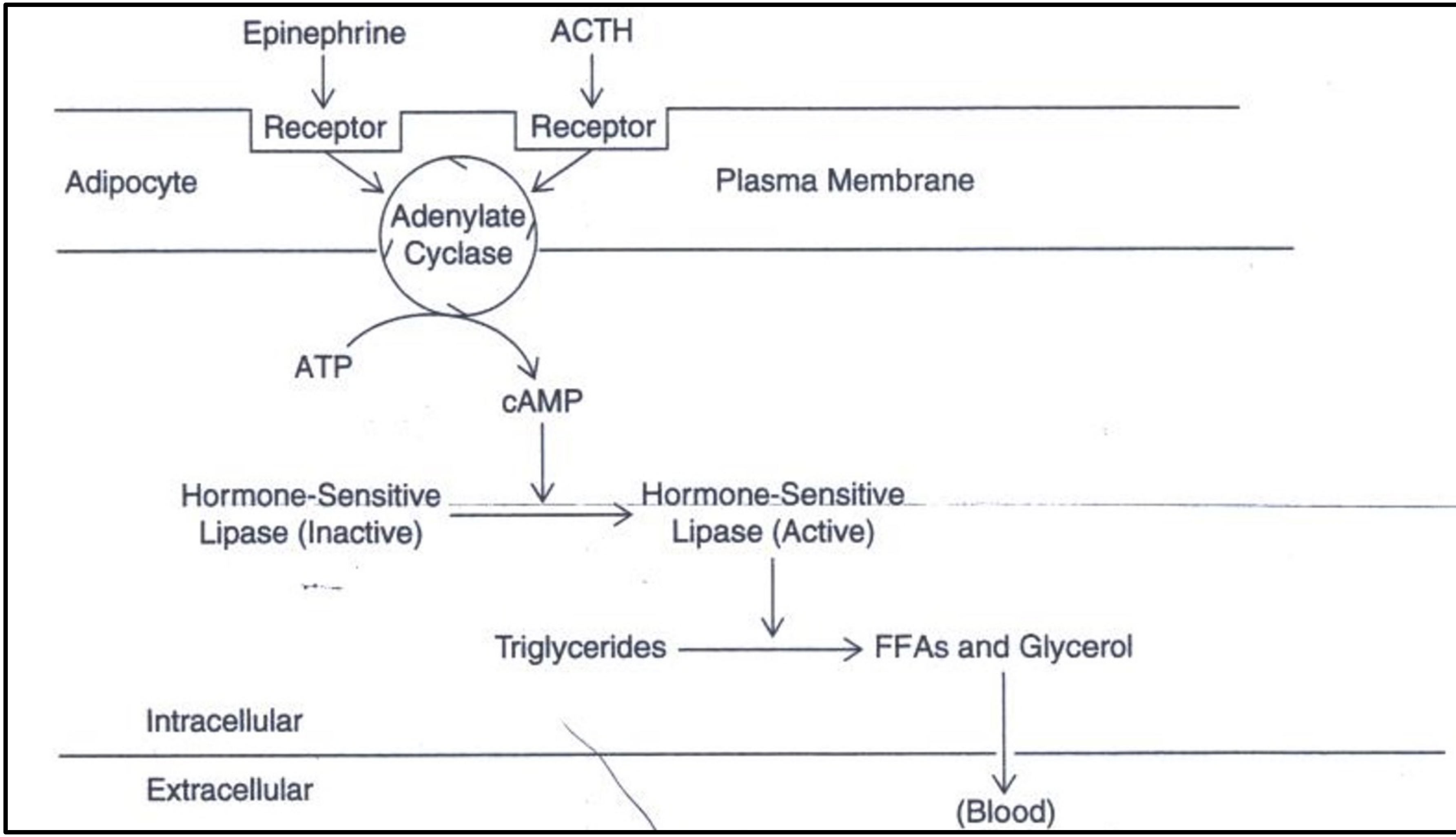
-stimulates mobilization of free fatty acids **(Lipolysis)**

- E induced cAMP production activates a hormone-sensitive lipase, triglyceride lipase, which metabolizes fats into FFA and glycerol.
- FFA released into the blood are then used directly by certain tissues as sources of energy.

4- Protein Metabolism

E decreases the release of amino acids from skeletal muscle

E and ACTH stimulate fat cell lipolysis through separate receptors but through a common adenylate cyclase(AC).



Actions of Epinephrine

- **Typical responses**

  - increased heart rate

  - bronchodilatation

  - intestinal relaxation

  - glycogenolysis

  - lipolysis

Pheochromocytoma

- Pheochromocytoma is a rare, benign tumor that develops in an adrenal gland.
- Pheochromocytomas are catecholamine-producing tumors presenting with various clinical symptoms, but mostly with headache, sweating, palpitations and hypertension.
- produces excess catecholamines, causing a sustained elevation of Blood Pressure