
بسم الله الرحمن الرحيم

Nervous System

PNS *CNS*

Autonomic Nervous System

Introduction and Neurotransmitters

By

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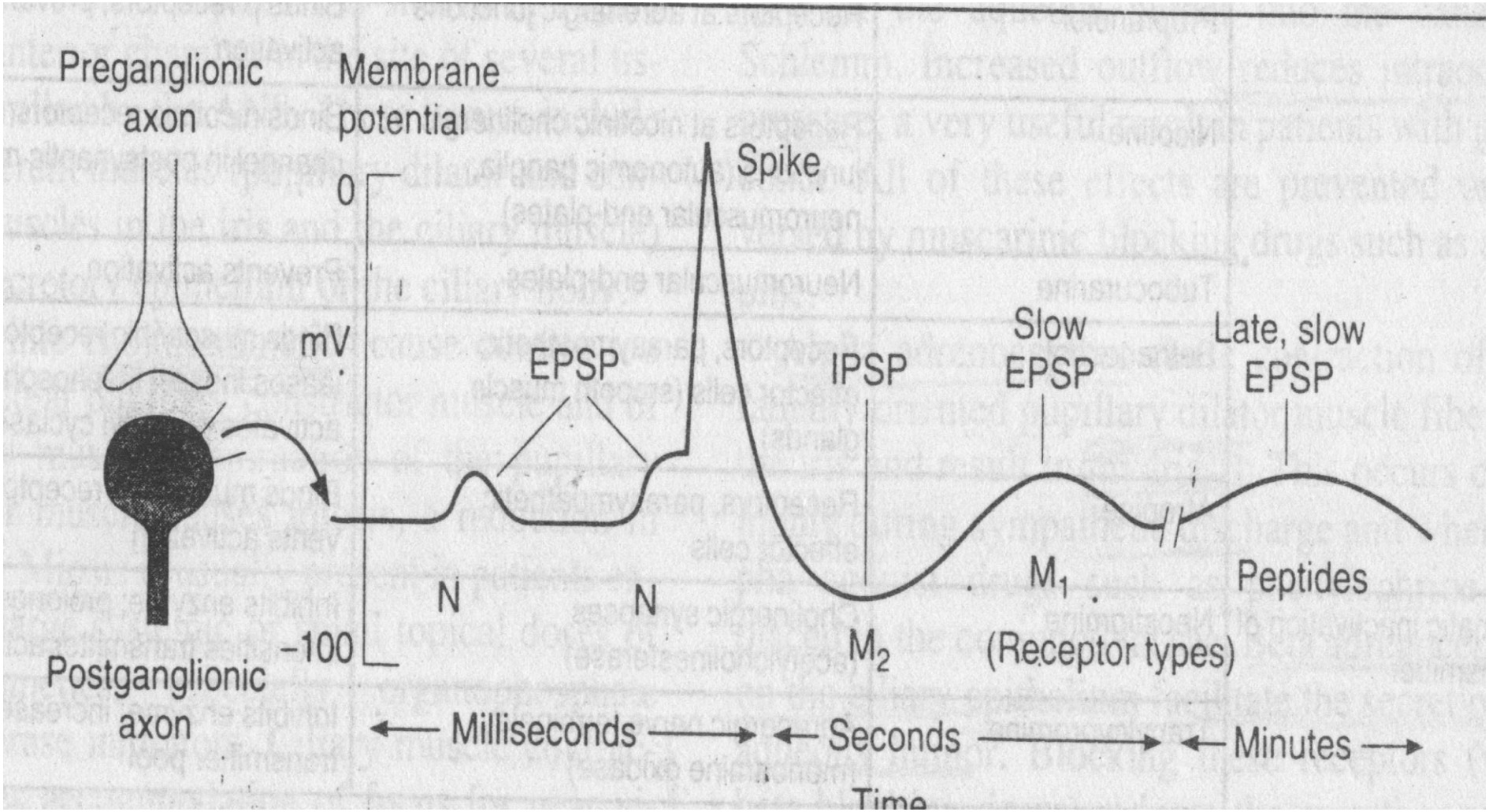
➢ Combination with Post junctional Receptors.

- **Neurotransmitters released in the synaptic cleft diffuse through the cleft and combine their specific postsynaptic receptors ----- activating or inhibiting them, thus producing EPSP or IPSP.**

➢ Postjunctional potentials; **EPSP or IPSP.**



➢ *Initiation of Post junctional Activity;*

- If an **EPSP** exceeds a certain threshold value, it initiates
  - **Propagation** of Action Potential in a **postsynaptic neuron,**
  - **Contraction of Muscle,**
  - **Secretion in gland cells**.
  - **In smooth muscle a localized contractile response.**
- **IPSP –**
  - **IPSP** does not occur in skeletal muscles.
  - ***Hyperpolarization*** of the membrane.
  - **Stabilizes** the postjunctional membrane and resists depolarizing stimuli.
  - Opposes EPSP initiated by other neuronal sources at the same time and site.
- Algebraic sum of EPSP and IPSP will determine the response.

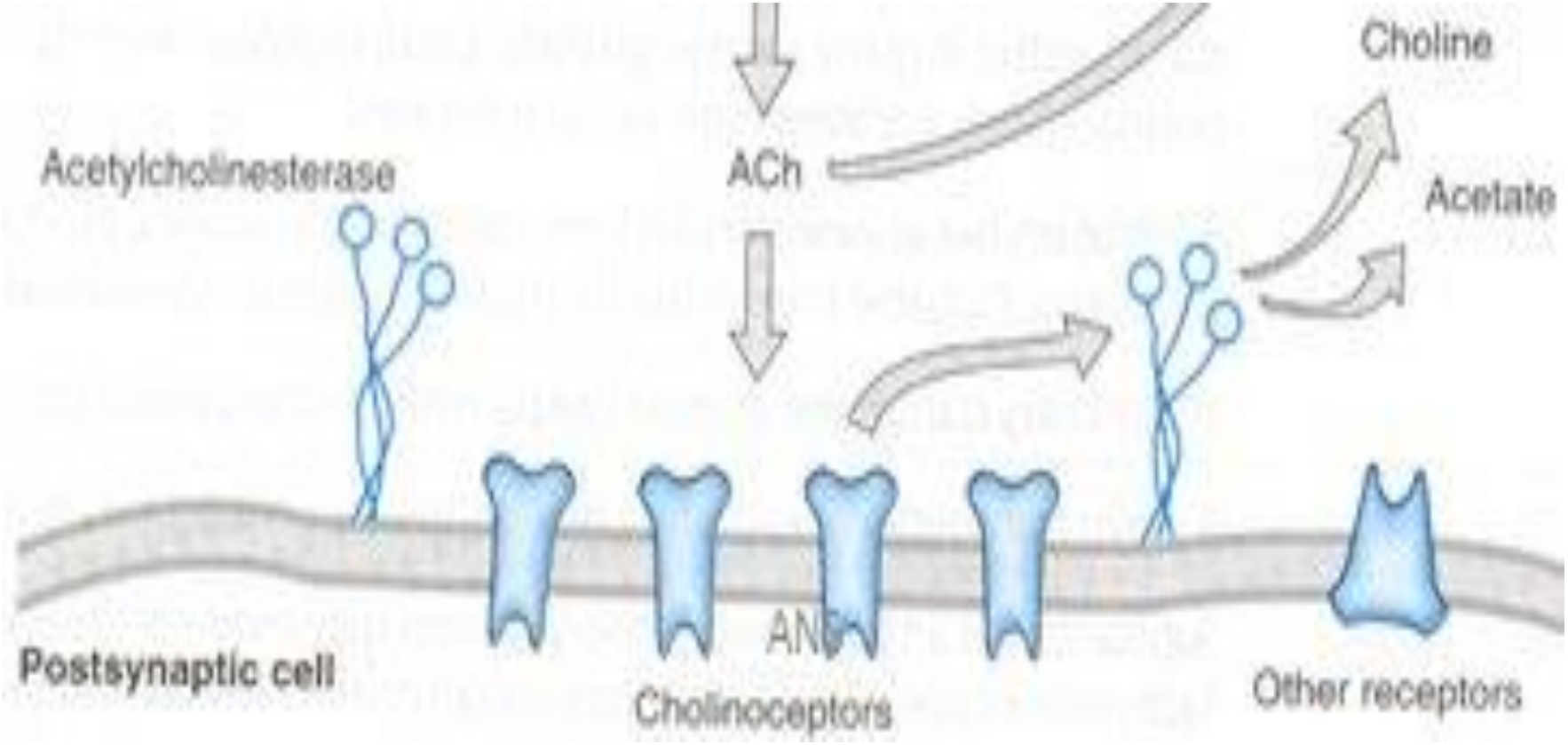
➢ Presynaptic regulation;

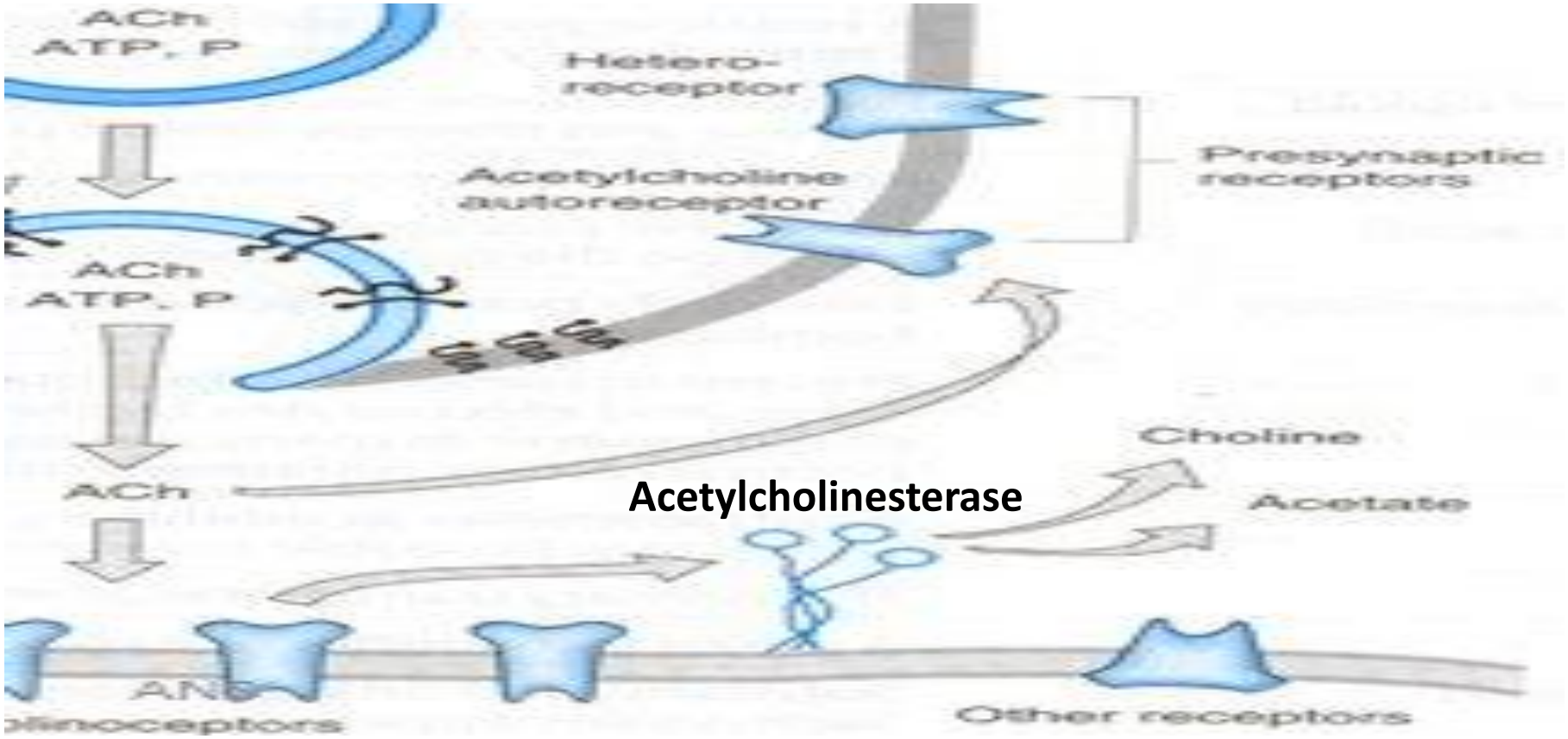
- **Autoreceptors;**
  - **Presynaptic receptors** that respond to the primary transmitter --- **Usually inhibitory.**
    - **α_2 receptors on adrenergic nerve terminals.**
      - Activated by **Norepinephrine.**
      - Activation ↓ further release of NE.
- **Heteroreceptors;**
  - **Regulatory receptors** that respond to substances other than the primary neurotransmitters **(cotransmitters).**

➢ Termination of action;

acetylcholinestrase

- **Ach ---------- acetate + choline**
- **Acetate and choline are not excreted but are recycled.**



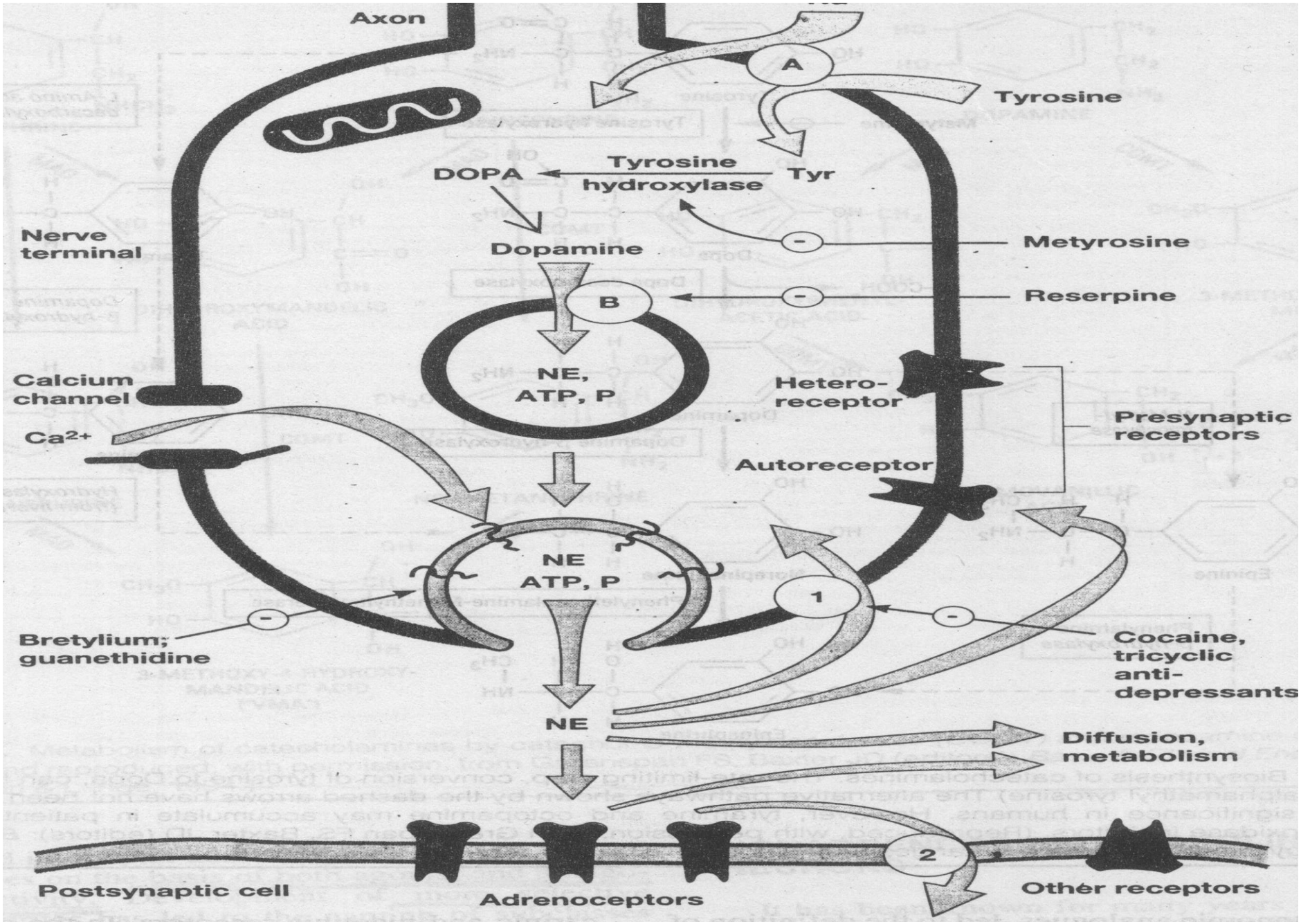


Drugs that block Ach.

- **Synthesis of Ach;** Hemicholinium
- **Storage;** Vesamicol
- **Release;** Botulinum toxin
- **Not useful** because the effects are not selective.
- **Botulinum toxin** can be used by injection for local effects.

Termination of action; Adrenergic neuron:

- ***Reuptake; Uptake I ---*** *into* ***same nerve terminal.*** **Uptake 2 ---** Active transport system located on glia and smooth muscle cells.
- **Metabolized by COMT in the synaptic cleft. Metabolism by MAO in the nerve terminals.**
- ***Diffusion;*** Simple diffusion of NE away from the receptor site, with eventual metabolism in plasma or liver.


Axon
A
Tyrosine
Tyrosine hydroxylase
DOPA
Tyr
Nerve terminal
Dopamine
Metyrosine
B
Reserpine
NE, ATP, P
Calcium channel
Hetero-receptor
Presynaptic receptors
Ca2+
Autoreceptor
NE ATP, P
1
Bretylium; guanethidine
Cocaine, tricyclic anti-depressants
NE
Diffusion, metabolism
2
Postsynaptic cell
Adrenoceptors
Other receptors

Drugs affecting adrenergic transmission;

- **Metyrosine;**
  - Metyrosine (α methyltyrosine) – **competitive inhibitor of tyrosine hydroxylase.**
  - Interfere with the synthesis of dopamine, NE, & E.
  - used in inoperable or metastatic **pheochromocytoma**
- **Reserpine** alkaloid;
  - Inhibit the VMAT (vesicular monoamine transporter)
  - Reserpine **causes depletion of transmitter stores.**

- **Guanethidine and bretylium;**
  - Block the release of NE.
- **Cocaine and TCA;**
  - inhibit the NET (NE transporter).
  - Uptake 1 is inhibited.
  - **An ↑ of transmitter activity in the synaptic cleft.**
- **MAO inhibitors** may ↑ the store of these transmitters & amines in the nerve endings -- Therapeutic and toxic potential.


Thank You