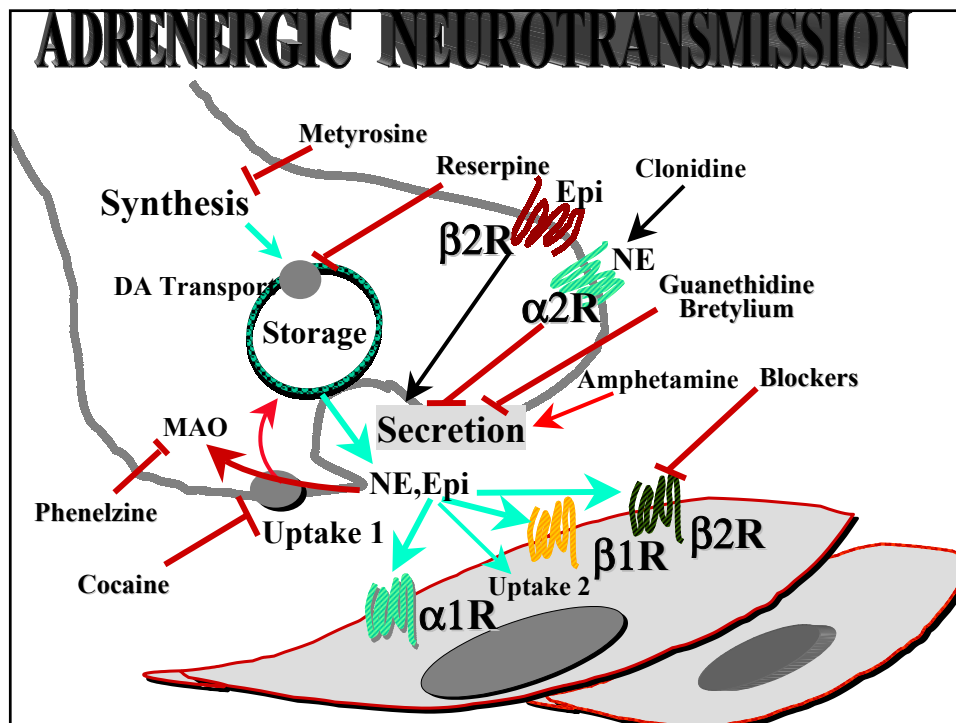


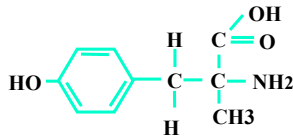
ADRENERGIC NEURON BLOCKING AGENTS

These agents affect adrenergic transmission at the adrenergic neuron by different mechanisms:

- 1) Interference with synthesis, i.e. α -methyl-tyrosine blocks tyrosine hydroxylase \rightarrow depletion of NE
- 2) Displacing NE from granules, i.e. α -methyldopa \rightarrow methyl-DA
- 3) Blockade of transport into storage, i.e. Reserpine \rightarrow NE destruction in cytoplasm by MAO
- 4) Blockade of transmitter release, i.e. Guanethidine/Bretylium
- 5) Inhibition of enzymatic breakdown, i.e. MAO inhibitors

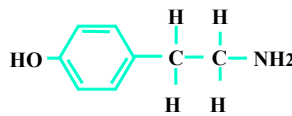


ADRENERGIC NEURON BLOCKERS



Metyrosine (Demser)
Blocks Tyr-Hydroxylase
Decreases catecholamines by 35-80%
in Pheochromocytomas
Use in association with α -blockers
in Pheochr.
Adverse effects: decr. baroreflex,
sedation, extrapyramidal signs.

ADRENERGIC NEURON BLOCKERS



Tyramine

- * Indirect-Acting monoamine**
- * Present in cheese and fermented foods**
- * Uses uptake 1 to enter neuron**
- *Induces release of NE into synapsis**
- *Is metabolized by MAO**
- *Does not work with tricyclics or Reserpine**
- *CAUTION with MAO inhibitors can cause hypertensive crisis**

ADRENERGIC NEURON BLOCKING AGENTS

α -methyl dopa :

1) Enters the synthesis pathway at the DOPA step

* Crosses membranes easily $\rightarrow \alpha$ -CH₃-DA $\rightarrow \alpha$ -CH₃-NE

* Conversion occurs only in neurons and CNS

* α -CH₃-NE:

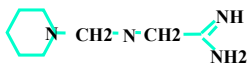
-Displaces NE from granules \rightarrow NE metabolized by MAO

-Higher affinity for presynaptic $\alpha_2R \rightarrow \downarrow$ NE release in vasomotor center $\rightarrow \downarrow$ TPR and \downarrow BP

-Is as potent as NE on peripheral receptors

* Does not affect: CO or blood flow to organs

ADRENERGIC NEURON BLOCKERS



Guanetidine (Ismelin)

* Enters the neuron using Uptake 1

* In the PNS:

-blocks NE release by uncoupling action potential and secretion

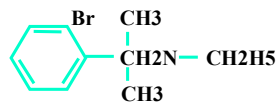
- competes with NE for uptake 1 and depletes NE from storage (does not cross BBB)

* Treatment of Hypertension (rare cases)

* Acute use can increase NE release \rightarrow increase BP

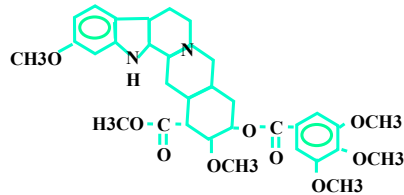
* Effects: veno- and arteriolar dilation, decrease CO,

Adverse effects: decr. baroreflex



Bretylium Blocks NE release

ADRENERGIC NEURON BLOCKERS



Reserpine

***Depletes monoamines by blocking transport into storage vesicles in CNS and PNS**

***NE, DA and 5HT leak into the cytoplasm->MAO metab.**

***After a few weeks: post-synaptic supersensitivity (receptor upregulation)**

Effects: decrease in CO and HR

Uses: Hypertension

Side Effects: CNS, GI,

ADRENERGIC NEURON BLOCKERS

Cocaine

***Cocaine, Imipramine and amitriptiline block uptake 1**

***NE acumulates in the synapsis**

***Drugs that block uptake 1 produce pre-synaptic supersensitivity**