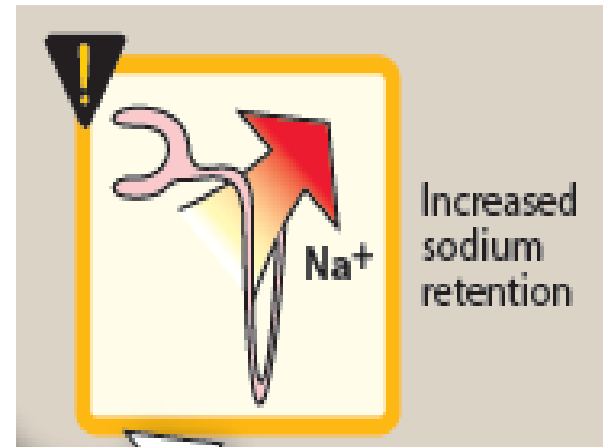
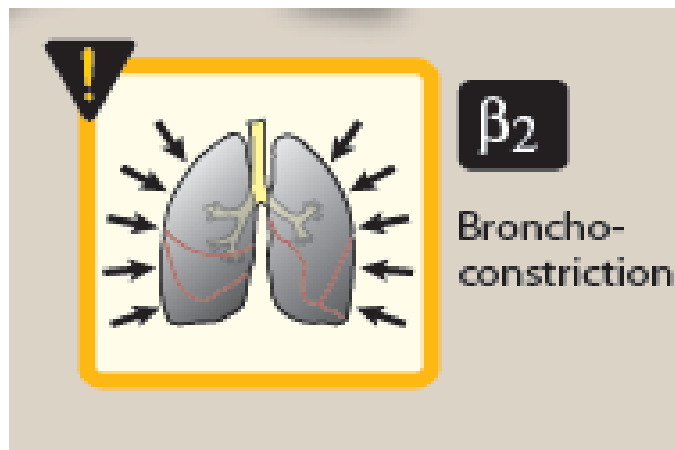
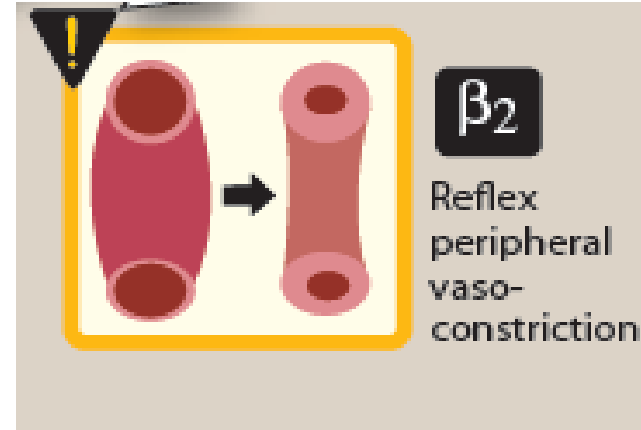
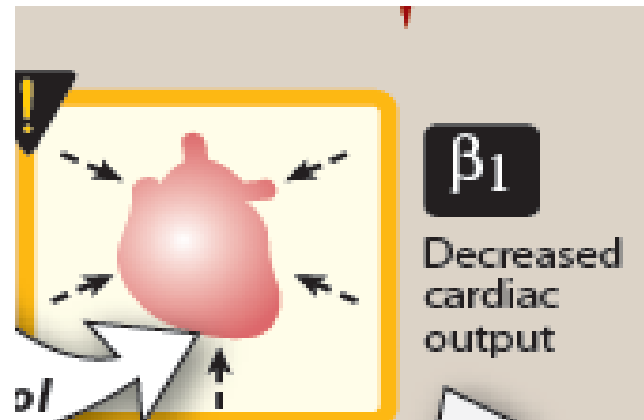


β -ADRENERGIC BLOCKING AGENTS

β -ADRENERGIC BLOCKING AGENTS



β -ADRENERGIC BLOCKING AGENTS

- Nonselective β - blockers act at both β_1 and β_2 receptors.
- whereas **cardio selective** β antagonists primarily block **β_1** receptors
- They **do not** induce postural hypotension
- Clinically important class with various therapeutic uses.

β -ADRENERGIC BLOCKING AGENTS

- I. HTN
- II. Angina
- III. MI
- IV. CHF
- V. Cardiac Arrhythmias
- VI. Glaucoma
- VII. Migraine prophylaxis

Propranolol

- **A nonselective β antagonist**
- The prototype β -adrenergic antagonist and blocks both β_1 and β_2 receptors with equal affinity
- SR allowed once daily dosing

Effects : of Propranolol

- **Cardiovascular :**

β_1 inhibition leads to :

1. Decrease in Cardiac output & Work

2. Decrease in O₂ consumption

****Decrease cardiac output (*negative chronotropic & inotropic effects*)**

- *Supress SA & AV node*

- *Bradycardia*

.

- In HTN the TPR returns to normal
- No Postural Hypotension

❖ **Bronchoconstriction**:**

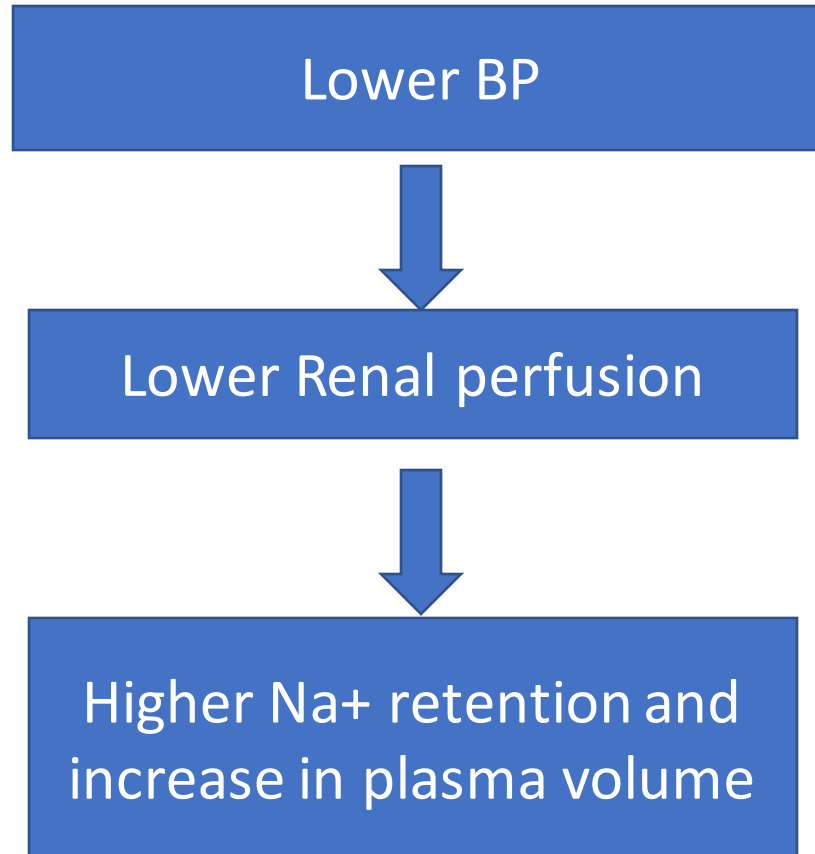
- Blocking β_2 receptors in the lungs of susceptible patients causes contraction of the bronchiolar smooth muscle.

Caution on COPD & Asthma patients.

- Instead use selective β_1 blockers.

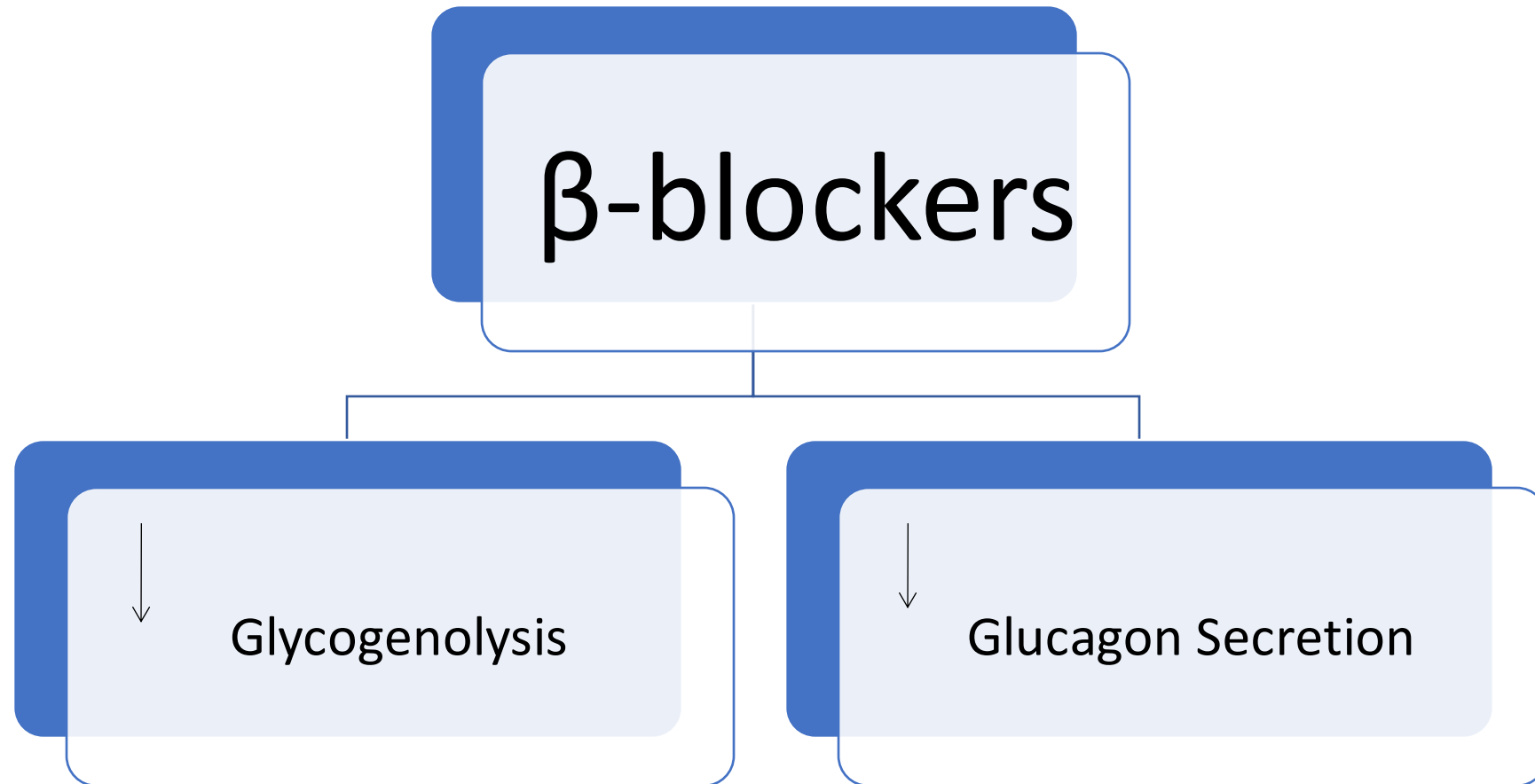
Other effects of Propranolol

❖ Increased Na⁺ retention:



Many Beta blockers are administered with diuretics to prevent Na⁺ retention

Disturbances in glucose metabolism associated with Propranolol



Pharmacokinetics

- ✓ Propranolol is completely absorbed orally
- ✓ 25% of the dose is BA (high 1st pass effect)
- ✓ Cross BBB , high V_d

Therapeutic effects

✓ HTN :

- via ↓ CO (mainly) & ↓ Renin production

✓ Migraine :

- ↓ Both incidence & Severity of attacks

✓ Angina pectoris and MI

✓ Hyperthyroidism

Adverse effects of Propranalol (Inderal)

- I. Bronchospasm
- II. Arrhythmias
- III. Sexual impairment
- IV. Metabolic disturbances
- V. Depression, dizziness, lethargy, fatigue, weakness, visual disturbances, hallucinations

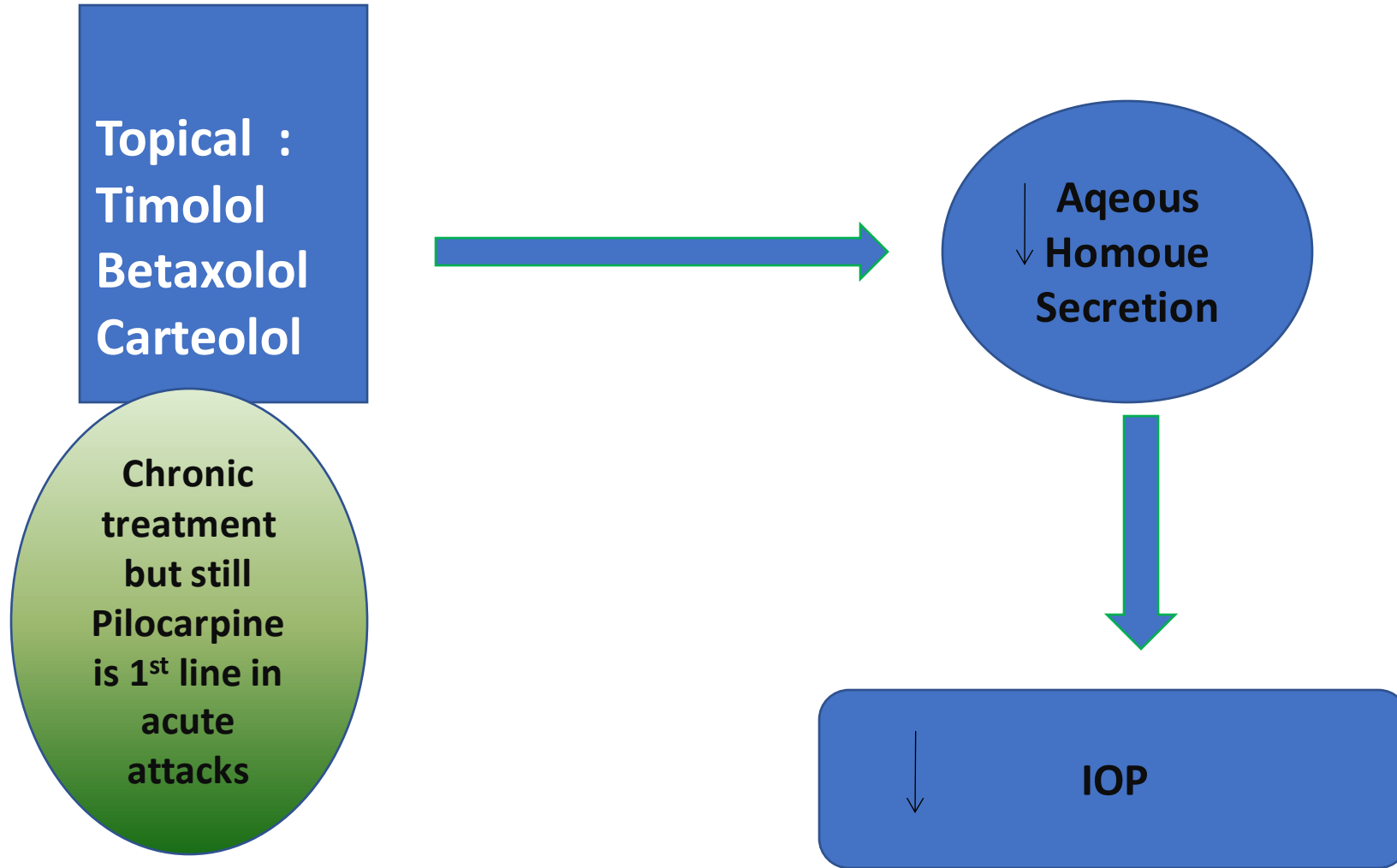
D-D/I

- ** Enzyme Inhibitors :cimetidine, fluoxetine, paroxetine,and ritonavir, may potentiate its antihypertensive effects*
- ** Enzyme Inducers :such as barbiturates, phenytoin, and rifampin, can decrease its effects.*

Timolol and nadolol

- Non-selective β -Antagonists
- Block β_1 - and β_2 - adrenoceptors and are more potent than *propranolol*
- *Nodalol has long half life*
- *Timolol used in open- angle glaucoma*

Treatment of glaucoma



Selective β_1 antagonists

- **Acebutolol**
- **Atenolol**
- **Metoprolol**
- **Bisoprolol**
- **Betaxolol**
- **Nebivolol,**
- **Esmolol**

- Drugs that preferentially block the β_1 receptors have been developed to eliminate the unwanted bronchoconstrictor effect (β_2 effect) of *propranolol* seen among asthma patients.
- Lower Dose is required 50-10 fold less than non-selective beta blockers

Selective β_1 antagonists

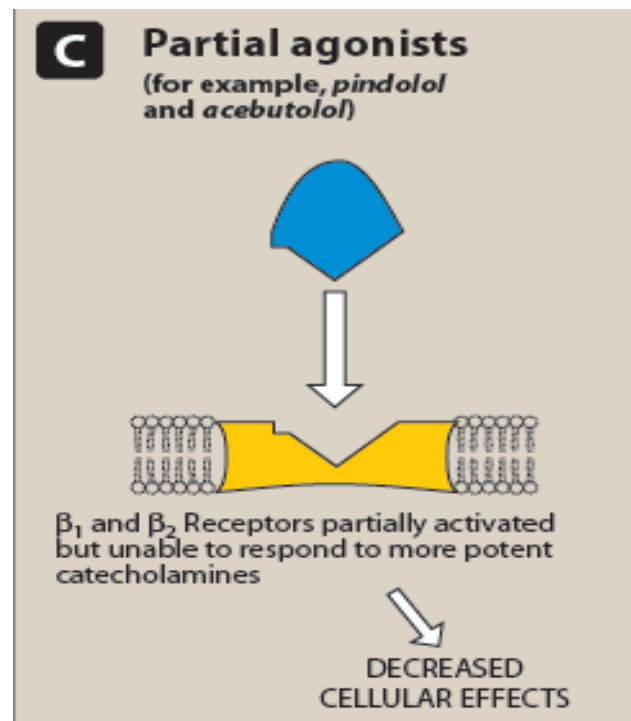
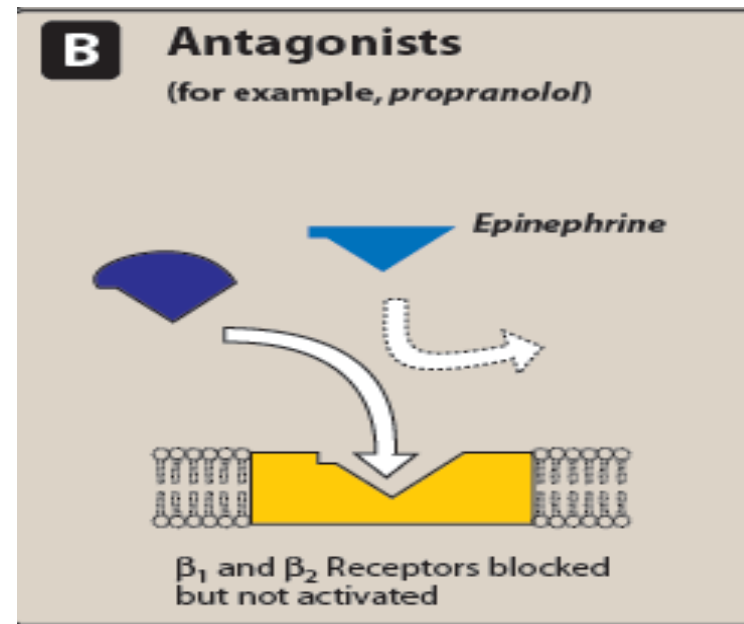
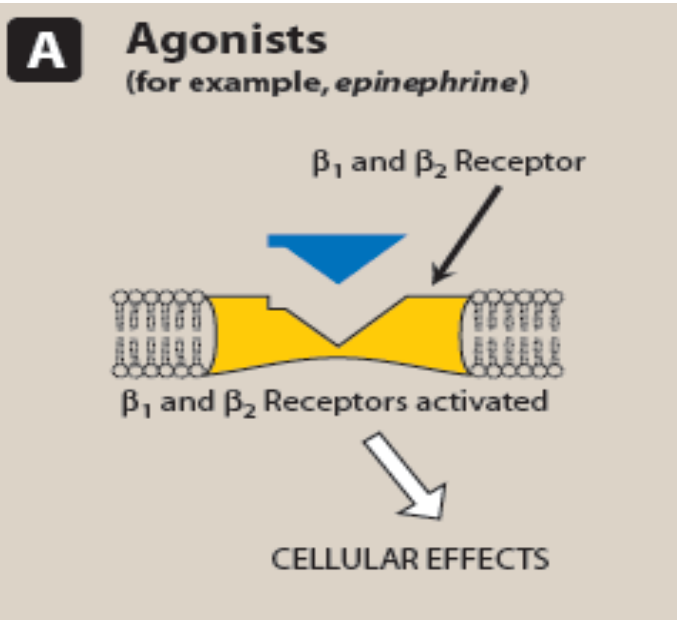
- Lower blood pressure in hypertension
- *Esmolol* has a very short lifetime IV
- Cardioselective β blockers are useful in diabetic hypertensive patients who are receiving *insulin or oral hypoglycemic* agents.
- Also safe in Asthma & COPD patients

Antagonists with partial agonist activity

Pindolol (Non selective β - Antagonist)

Acebutol (Selective β_1 - Antagonist)

- Not Pure Antagonists ,
- Also posses weak agonist activity ISA
- Prevent potent stimulants from acting
- Also less metabolic disturbances compared to full antagonists
- Effective in hypertensive patients with moderate bradycardia



Antagonists of both α and β adrenoceptors

➤ Labetalol and Carvedilol

- Non-selective β - blockers with concurrent α_1 -blocking actions that produce ***peripheral vasodilation****, thereby reducing blood pressure.

Therapeutic use in hypertension and heart failure

- **Labetalol** *is* useful for:
 - ✓ Elderly or black hypertensive patient
 - ✓ Alternative to Methyldopa in pregnancy-induced HTN
 - ✓ IV administration in ER, fast onset
- **Carvedilol** *also used* to prevent cardiovascular mortalities in patients with stable chronic heart failure
- ❖ Orthostatic hypotension and dizziness are associated with α_1 blockade

DRUGS AFFECTING NEUROTRANSMITTER RELEASE OR UPTAKE

- Historical value, seldom use

Reserpine

- A plant alkaloid
- Blocks the Mg^{2+} /adenosine triphosphate–dependent transport of biogenic amines, (Norepinephrine, Dopamine, and Serotonin) from the cytoplasm into storage vesicles in the adrenergic nerves of all body tissues.
- Decreases NE release and impairment in SNS
- Slow onset of action, long duration
- Old anti HTN medication

Guanethidine

- ☐ Blocks the release of stored norepinephrine as well as displaces norepinephrine from storage vesicles (thus producing a transient increase in blood pressure)
- ☐ Leads to NE depletion peripherally
- ☐ causes Orthostatic Hypotension

- End of unit II regarding ANS drugs!!!!!!