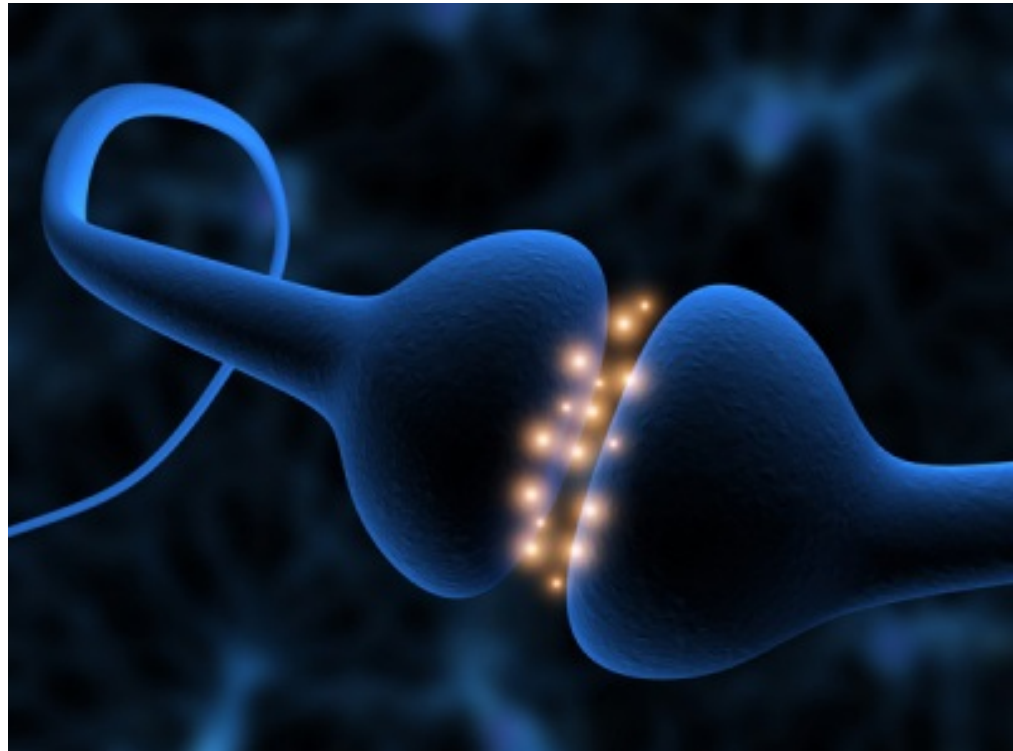
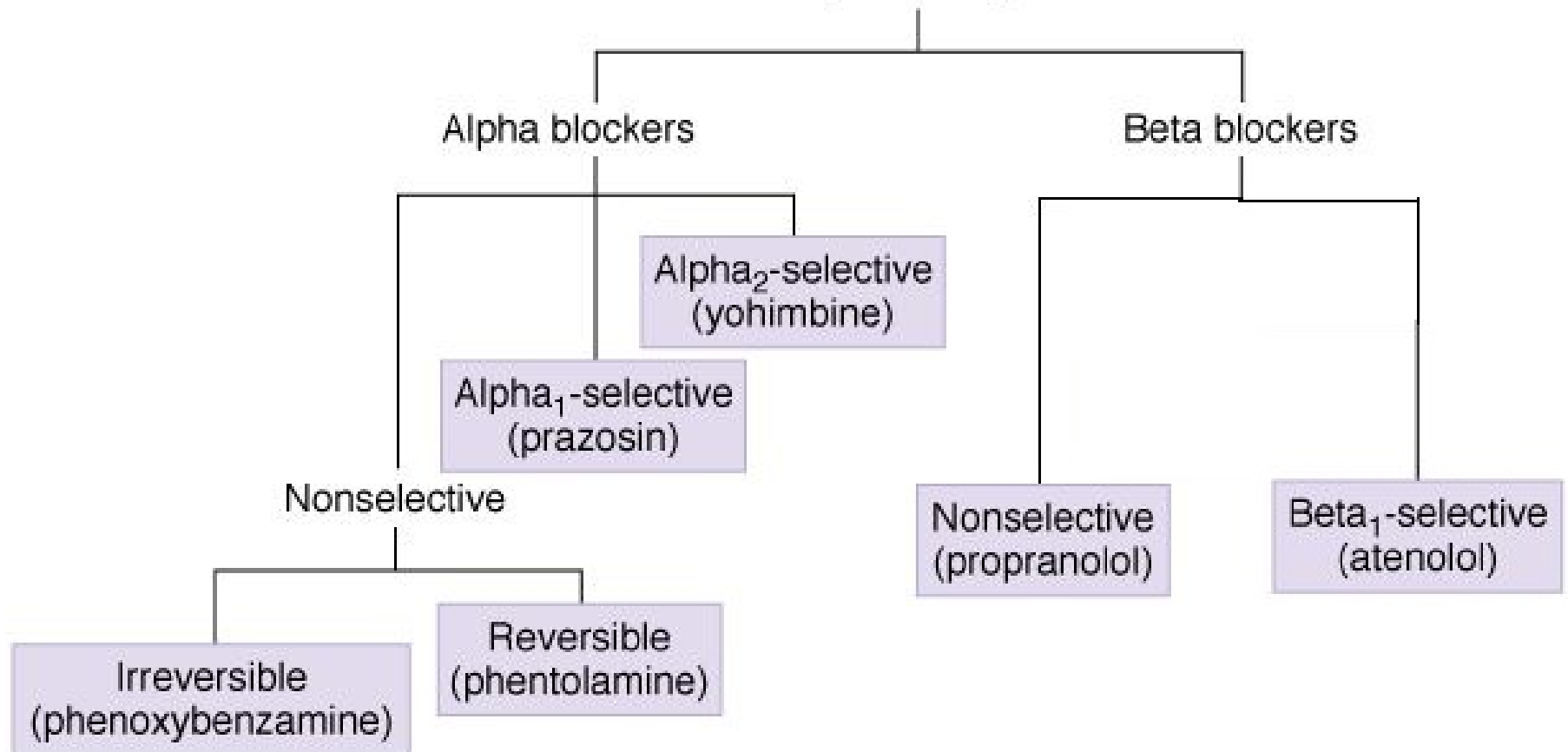


Adrenergic antagonists

Ahmed Shubbar



Adrenoceptor antagonists



α -blockers

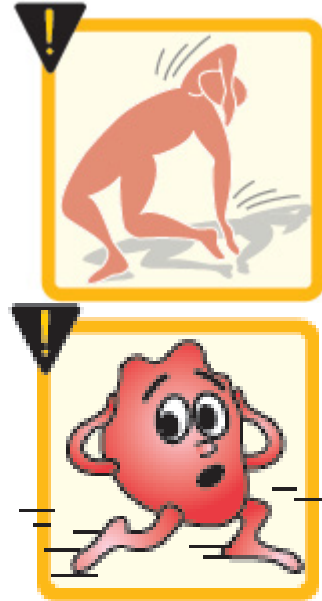
Receptor Affinity	
Alpha antagonists	
Prazosin, terazosin, doxazosin	$\alpha_1 \gg \gg \gg \alpha_2$
Phenoxybenzamine	$\alpha_1 > \alpha_2$
Phentolamine	$\alpha_1 = \alpha_2$
Yohimbine, tolazoline	$\alpha_2 \gg \alpha_1$

Pharmacological Effects

1. CVS

↓ BP >>> orthostatic hypotension & reflex tachycardia.

Reflex tachycardia is higher with non-selective α blockers, why ?



2. Bladder & Prostate

↓ resistance to urine flow.

Phenoxybenzamine

- Irreversible slightly selective α_1 -blocker used in management of *pheochromocytoma*.

Phentolamine

- Competitive , non-selective α -blocker used in management of *pheochromocytoma* and *erectile dysfunction*.

Prazosin, Alfuzosin, Terazosin, Doxazosin, Indoramin and Urapidil

- α_1 -selective blockers.
- Less reflex tachycardia as compared with phenoxybenzamine and phentolamine, why?

Indications: Hypertension and BPH.

Tamsulosin and Silodosin

- α_1 -selective blockers.
- Higher selectivity to α_{1A} (prostatic) than α_{1B} (vascular).

Indications: BPH (least effects on BP).

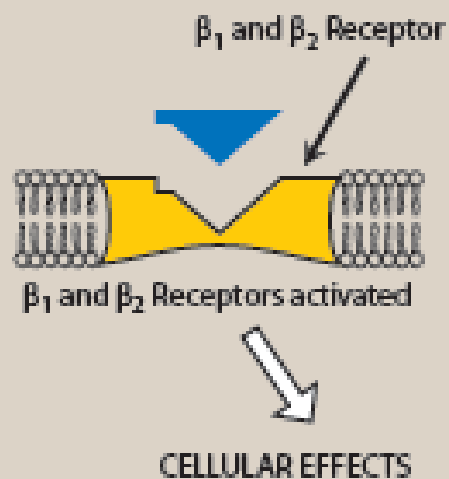
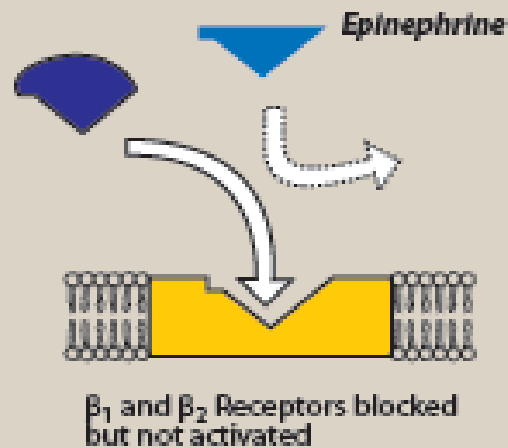
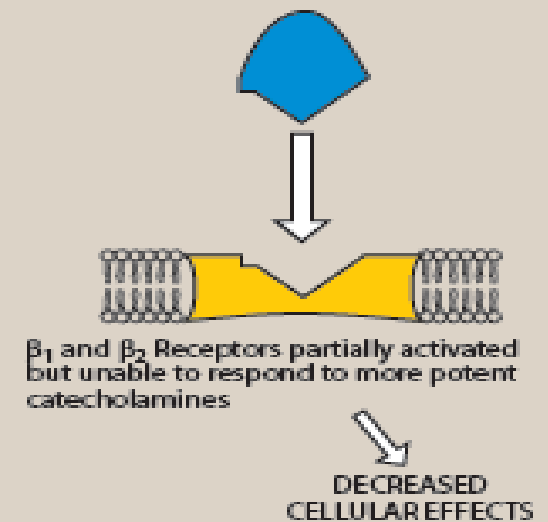
Yohimbine

- α_2 -selective blocker.

Indications: Orthostatic hypotension and erectile dysfunction.

β -blockers

- Are of two types: ***non-selective blockers*** & **β_1 -selective blockers**.
- No absolute β_1 selectivity.
- Selectivity is lost with dosage increase.

A**Agonists**(for example, *epinephrine*)**B****Antagonists**(for example, *propranolol*)**C****Partial agonists**(for example, *pindolol* and *acebutolol*)

	Selectivity	Partial Agonist Activity	Lipid Solubility
Acebutolol	β_1	Yes	Low
Atenolol	β_1	No	Low
Betaxolol	β_1	No	Low
Bisoprolol	β_1	No	Low
Carteolol	None	Yes	Low
Carvedilol ¹	None	No	Moderate
Celiprolol	β_1	Yes	Low
Esmolol	β_1	No	Low
Labetalol ¹	None	Yes	Low
Metoprolol	β_1	No	Moderate
Nadolol	None	No	Low
Nebivolol	β_1	? ²	Low
Penbutolol	None	Yes	High
Pindolol	None	Yes	Moderate
Propranolol	None	No	High
Sotalol	None	No	Low
Timolol	None	No	Moderate

Pharmacological Effects

1. CVS

- ↓ BP (- inotropic and chronotropic effects, ↓ renin release).
- ↓ AV conduction >>> PR interval prolongation.

2. Respiratory System

β_2 -blockade >>> bronchoconstriction

- All β -blockers should generally be avoided in patients with asthma (even β_1 selective).

3. Eye : ↓ aqueous humor production >>> ↓ IOP

4. Metabolic

- β -blockers may impair recovery from hypoglycemia because they inhibit glucagon secretion and glycogenolysis (this occurs less frequently with β_1 selective blockers).
- ↑ VLDL and ↓ HDL (less with those with ISA).

Propranolol

- Prototype non-selective β blocker.
- Low and dose-dependent bioavailability , why?

Esmolol

- Ultra-short acting ($t_{1/2}$ is about 10 minutes) used in treatment of cardiac arrhythmias.

Nebivolol

is the most highly selective β_1 -blocker & additional advantages over other β -blockers include:-

- ✓ Stimulates eNOS >>> vasodilation.
- ✓ May \uparrow insulin sensitivity.
- ✓ Does not adversely affect lipid profile.

Metoprolol , Atenolol and other β_1 selective blockers

More preferred in patients with :

1. DM.
2. Who experience bronchoconstriction with non-selective β blockers
3. Peripheral vascular disease.

Pindolol, Acebutolol and other β blockers with ISA

- Less likely to cause bradycardia and abnormalities in lipid profile.
- Overall clinical significance is uncertain.

Timolol, Betaxolol, Carteolol and Levobunolol

- Used topically in treatment of glaucoma.

Mixed α and β blockers

Carvedilol, Labetalol, Medroxalol and Bucindolol

- α_1 and β blockers.
- ***Labetalol*** is used in emergency/pregnancy HTN.
- ***Carvedilol*** appears to \downarrow free radical–initiated lipid peroxidation and to inhibit vascular smooth muscle mitogenesis independently of adrenoceptor blockade.

Clinical Uses of β -blockers

1. **Hypertension, Ischemic heart disease** (\downarrow oxygen demand) **and arrhythmias.**
2. **Heart failure:** \downarrow myocardial remodeling and risk of sudden death (*Metoprolol Succinate, Carvedilol & Bisoprolol*).
3. **Hyperthyroidism:** \downarrow HR through β blockade and they also \downarrow peripheral conversion of levothyroxine to T_3 .

4. Neurological applications

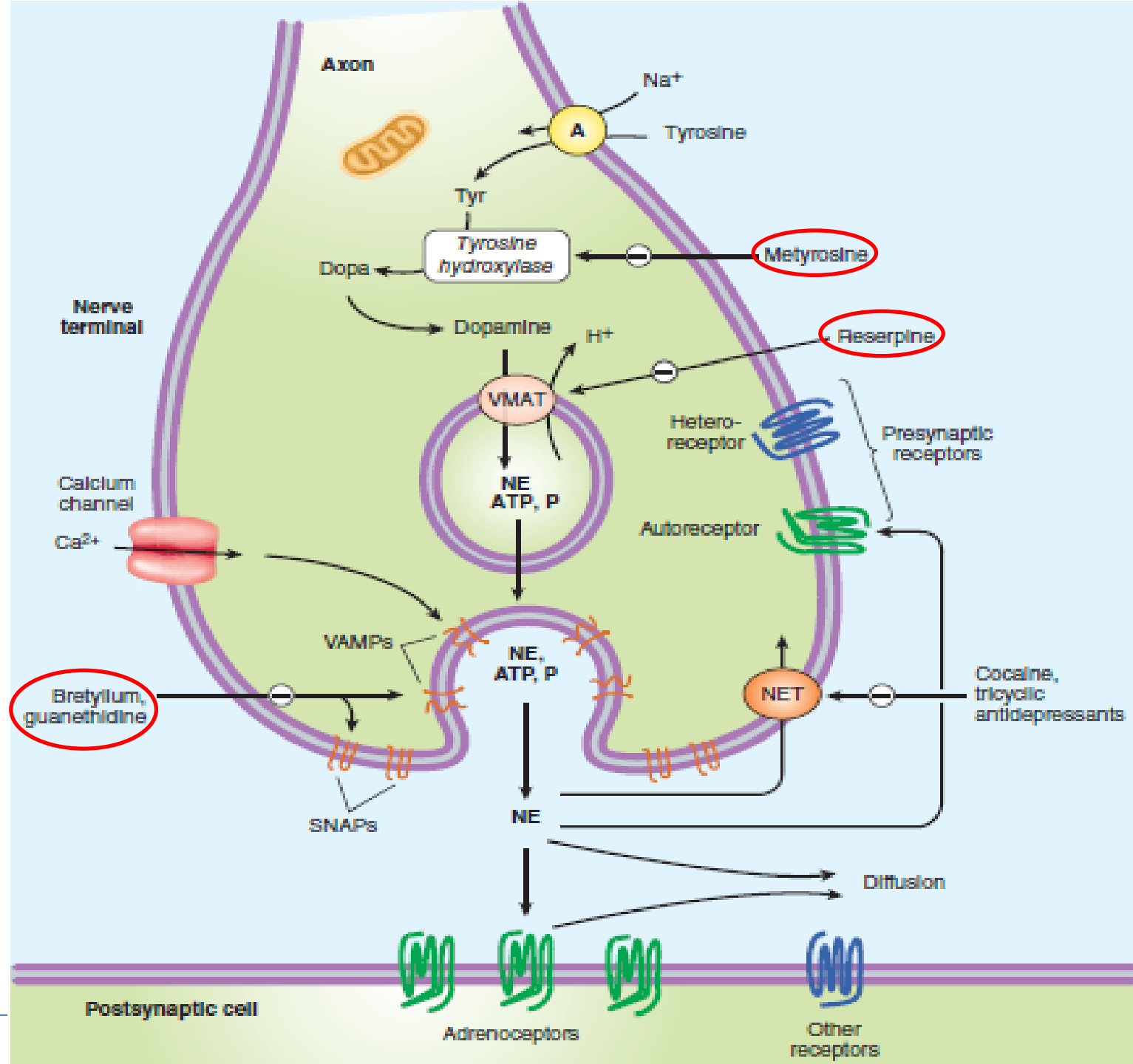
- Migraine prophylaxis (***Propranolol & Nadolol***).
- Tremors.
- Performance anxiety.

5. Other

Propranolol & Nadolol :

- ↓ portal vein pressure in patients with cirrhosis.
- ↓ bleeding from esophageal varices.

Interference with the Synthesis or Release of the Transmitter



References

- Lippincott's Illustrated Reviews: Pharmacology , 6th edition.
 - Basic & Clinical Pharmacology , Bertram G. Katzung 12th edition .
 - Goodman & Gilman's The Pharmacological Basis of Therapeutics, 12th edition.
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