



Lecture 2

Pharmacology of SNS

- Additional Notes
- **Important**
- Explanation –Extra-

For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com

Adrenergic drugs

Adrenergic Depressants

Adrenoceptor Blockers (Adrenolytic)

Adrenergic Neuron Blockers (Sympatholytic)

α adrenergic receptor blockers

β adrenergic receptor blockers

α and β adrenergic receptor blockers

According to mode of action

Direct

Indirect

Dual

Adrenergic stimulants (sympathomimetic)

According to spectrum of action

Non-Selective

Norepinephrine

Epinephrine

Dopamine

Isoprenaline

ephedrine

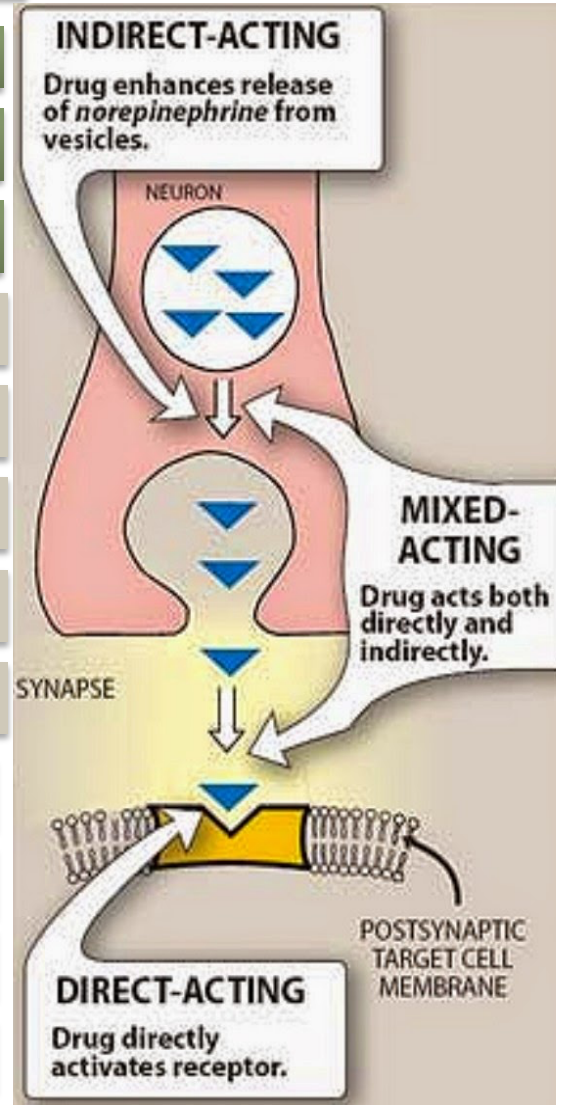
Selective

α_1 ; Phenylephrine

α_2 ; Clonidine

β_1 ; Dobutamine

β_2 ; Salbutamol



- Sympatholytic affect the release and synthesis of the transmitters. While Adrenolytic blocks the receptors.
- Most of adrenergic stimulation drugs are direct.

Direct Acting	ADRENALINE	NORADRENALINE
overview	<ul style="list-style-type: none"> - Naturally released from adrenal medulla → 2ndry to stress, hunger, fear - Inactivated by intestinal enzymes (MAO and COMT). 	Naturally released from postganglionic adrenergic fibers
Administration	given parenteral & by inhalation.	Only administered IV <u>Not</u> IM or Subcutaneous → <u>necrosis</u>
Spectrum of action	<p style="text-align: center;">Non-selective (Acts on all Adrenoceptors , but β more than α)</p>	<p style="text-align: center;">Non-selective (Acts on α mainly and β1)</p>
Indications	<p>1-Used locally:</p> <ul style="list-style-type: none"> - as haemostatic (in epistaxis – الرعاف). - with local anesthetics, it will decrease its absorption and toxicity and prolong action + decrease bleeding from incision. (e.g. tooth extraction) <p>2-Used systemically:</p> <ul style="list-style-type: none"> - Allergic reactions → drug of choice in anaphylactic shock, angioneurotic edema –sudden swelling of the dermis due to allergen- as it is the physiological antagonist of histamine. (i.e. ↑ BP & cause vasoconstriction) - In status asthmatics → given parentally → Bronchodilatation (β2) + → ↓ mucosal edema (α1). (N.B. Selective β2 are better by inhalation) - In cardiac arrest → direct, but now (NOT) through central line. (N.B. Selective β1 are better → Less side affects & stronger action) 	<p>1-Used systemically:</p> <p>Hypotensive states (in spinal anesthesia, in septic shock, if fluid replacement and inotropics fail). – means when there’s a leakage the anesthetic substance from the spinal cord it will cause severe Hypotension-</p> <p>2-Used locally:</p> <p>as a local haemostatic with local anesthetic.</p>
Side effects	<ul style="list-style-type: none"> - Tachycardia, palpitation, arrhythmias, angina pains - Headache, weakness, tremors anxiety and restlessness. - Hypertension → cerebral hemorrhage and pulmonary edema (So it should be given by infusion NOT injection) - Coldness of extremities (Never inject it in extremities) - Tissue necrosis and gangrene if extravasation - Nasal stuffiness → rebound congestion. (At the beginning it causes vasoconstriction in nasal cavity, but then the air entering the lungs will become cold, so it will cause rebound dilatation & you’ll feel your nasal swollen) 	The drug isn’t much used nowadays because it causes a severe vasoconstriction
Contraindications	<ul style="list-style-type: none"> - CHD (coronary heart disease), hypertension, peripheral arterial disease - Hyperthyroidism. (Cause the gland is already over stimulated) 	-
Pharmacological actions	see physiological actions of the SNS	-

Direct Acting	DOPAMINE	DOBUTAMINE	Isoprenaline
overview	<p>-Natural CNS transmitter.</p> <p>-Released from postganglionic adrenergic fibers (> renal vessels) –causes renal vasodilation so it's preferred to be used in shocks, because it protects the kidney from renal failure which could be caused by vasoconstriction-</p> <p>-Releases NE from postganglionic adrenergic fibers.</p>	Synthetic.	-Synthetic; show no presynaptic uptake nor breakdown by MAO → longer action.
administration	Given parentally by infusion	Given IV.	inhalation
Spectrum of action	Acts on D1, α_1 and β_1	Acts on β_2 , α_1 and β_1	Acts on β_1 and β_2 . (but in the slides the doctor wrote that it Acts on α and β).
Indications	<p>Drug of choice in treatment of shocks; septic, Hypovolemic (after fluid replacement), cardiogenic.</p> <p>It increases the BP by β_1 receptor but <u>without causing renal impairment D1.</u></p> <p>Can be given in acute heart failure (HF) but Dobutamine is better.</p>	<p>-Given parentally by infusion for short term management of Cardiac decompensation after cardiac surgery, in acute heart failure [AHF].</p> <p>-It does not ↑ oxygen demand</p>	<p>- Cardiac arrest.</p> <p>- Bronchodilatation → Was used by inhalation in acute asthma.</p>
Contra-indications	-	-	In hyperthyroidism & congestive heart failure.
Pharmacological actions	<p>D1: On the kidneys → vasodilatation and diuresis (increase excretion of urine).</p> <p>β_1: On the heart → increase the force (inotropic).</p> <p>α_1: On the blood pressure (according to the dose; first decrease D1, then it will increase due to β_1 effect, then α_1 will produces its action."at high dose").</p>	<p>-On heart → Inotropic with little chronotropic effect.</p> <p>-On BP → Hardly any effect; β_1 & β_2 counterbalance + no α_1.</p>	-

Direct	Phenylephrine & MIDODRINE	CLONIDINE	SALBUTAMOL	Terbutaline	Ritodrine
Over-view	- Synthetic & has prolonged duration of action. - Midodrine : Peaks in 20 min. $t_{1/2}$ 30 min	Synthetic.		-	
Administration	Given orally	Given orally or as patch.	Given orally.	-	
Spectrum of action	selective (Acts on α_1 and α_2 but selectively on α_1).	Selective on presynaptic α_2	Selective on β_2 .		
Indications	<p>1-Used systemically:</p> <ul style="list-style-type: none"> -Pressor agent in hypotensive states. -Infusion Terminate atrial tachycardia (reflex bradycardia). -Nasal decongestant. <p>2-Used locally(topically):</p> <ul style="list-style-type: none"> -Local Haemostatic, with Local anesthesia. -Decongestant (nasal & ocular). <p>Midodrine is more selective on α_1 than phenylephrine : used In hypotension. And it's safer.</p>	- N.B. Brimonidine → α_2 agonist used in glucoma .	- Bronchodilator → asthma & chronic obstructive airway disease (COPD). N.B. Salmeterol & Formoterol are longer acting preparations	Bronchodilator & Tocolytic (pre-mature labor)	Tocolytic → postpone premature labour (labour that begins before the 37 th week of gestation)
Pharmacological actions	-On heart → reflex Bradycardia -On BP → ↑ due to vasoconstriction (α_1)	(Antihypertensive agent) decrease BP by its action on (α_2) at nucleus tractus solitarius to decrease sympathetic outflow to heart & vessels.	-		

- Any selective drug given in a high dose turn to be non selective.

- In the human brain **nucleus tractus solitarii** is a series of nuclei (clusters of nerve cell bodies) forming a vertical column of grey matter embedded in the medulla oblongata.

Nasal & Ocular Decongestants

Direct	Phenylephrine	Methoxamine	Naphazoline	Oxymetazoline HCl (Afrin)	Otrivine -Xylometazoline HCl-
Indications	-Used for treatment of nasal stuffiness.				
Side effects	-can cause Rebound nasal stuffiness (overdose).				

- **Pseudoephedrine** is dual Sympathomimetic that works the same way as the drugs mentioned above (**Nasal & Ocular Decongestants**).

- **Nasal rebound**: - Patients often try increasing both the dose and the frequency of nasal sprays upon the onset of RM, worsening the condition. The swelling of the nasal passages caused by rebound congestion may eventually result in permanent turbinate hyperplasia, which may block nasal breathing until surgically removed.

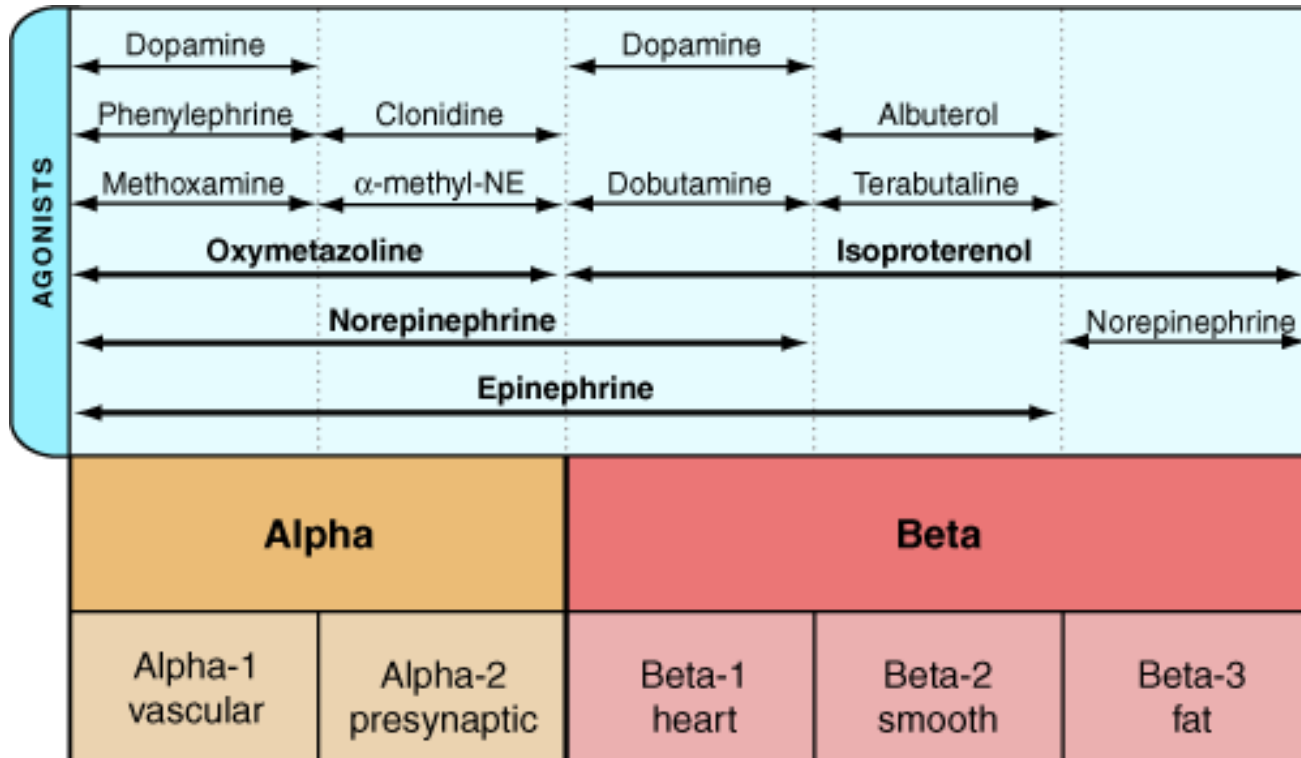
Adrenergic stimulants (Indirect): Release of NE from presynaptic stores at adrenergic terminals.		Adrenergic stimulants (Dual): Direct and indirect stimulation of adrenergic receptors
Drug	AMPHETAMINE	EPHEDRINE
spectrum of action	Non-selective Acts on α & β + CNS stimulant effects	Non-selective Acts on α & β + CNS stimulant effects less than amphetamine
Mechanism of action	<ul style="list-style-type: none"> It acts indirectly Release of NE from presynaptic stores at adrenergic terminals → depletes stores → Tachyphylaxis 	<ul style="list-style-type: none"> mixed sympathomimetic: Direct and indirect stimulation of adrenergic receptors. Prolonged direct action on receptors → receptor down regulation. Release of NE from presynaptic stores at adrenergic terminals → depletes stores → Tachyphylaxis facilitate neuromuscular transmission & retention of urine Has CNS stimulant effects less than amphetamine.
Side effects	<ul style="list-style-type: none"> Drugs of abuse Bi folded effect: activation followed by dropping Because it depletes vesicles of stored NE it cause tachyphylaxis CNS stimulant effects → cause euphoria ↓ Weight → ↓ appetite ↑ increase energy expenditure 	<ul style="list-style-type: none"> Drugs of abuse by athletes and prohibited during games. Bi folded effect: activation followed by dropping Because it depletes vesicles of stored NE it cause tachyphylaxis
Pharmacokinetics and other notes	Not used anymore → induces psychic & physical dependence	Absorbed orally, not destroyed by MAO or COMT → prolonged action

- **Cocaine** is an Indirect Adrenergic stimulants that inhibits the uptake of norepinephrine so it increases its availability in synapse.

★ Summary

Drug	Receptors	Uses	Other notes
Adrenaline	Act on All receptors	Status asthmatics, Cardiac arrest, haemostatic, with local anesthetics	Drug of choice in anaphylactic shock, Never giving for Hyperthyroidism, CHD and Glaucoma.
Noradrenaline	Acts on $\alpha > \beta 1$	Hypotensive status, Haemostatic	Causes gangrene if administrated intramuscularly.
Isoprenaline	Acts on $\beta > \alpha$	Cardiac arrest & Bronchodilator	Contraindicated in Hyperthyroidism and congestive heart failure – Has long action.
Dopamine	Acts on $D1 > \beta 1 > \alpha 1$	Treatment of shock	Used in intensive care to protect kidney
Dobutamine	Acts on $\beta 1 > \beta 2 > \alpha 1$	Acute heart failure, cardiac decompensation	Giving parentally, it's better than Dopamine
Midodrine & Phenylephrine	Selective $\alpha 1$	Hypotension, tachycardia	Used locally as decongestant, haemostatics, mydriatic
Clonidine	Selective $\alpha 2$	Hypotension	Given orally or as patch, acts on nucleus tractus solitarius
Brimonidine	Selective $\alpha 2$	Glaucoma	-
Salbutamol	Selective $\beta 2$	Asthma and COPD	Has a longer duration forms which are : Salmeterol and Formoterol
Terbutaline	Selective $\beta 2$	Bronchodilator, Tocolytic	-
Ritodrine	Selective $\beta 2$	Tocolytic	-
Amphetamine	Non-selective + CNS	Tachyphylaxis, euphoria	Indirect, drug of abuse, bi folded effect
Ephedrine		Tachyphylaxis, urine retention,	Dual, drug of abuse, bi folded effect

★ Summary



-Name the important α -selective direct-acting agonist?

1. Midodrine & Phenylephrine
2. Clonidine
3. Brimonidine

-Name the important β -selective direct-acting agonist?

1. Dobutamine
2. Salbutamol
3. Terbutaline
4. Ritodrine

-List the major non-selective direct-acting agonist?

1. Adrenaline
2. Noradrenaline
3. Dopamine

★ MCQs

Q1-An example of an indirect drug that releases NE from presynaptic at adrenergic term?

- A. Cocaine
- B. Amphetamine
- C. Ephedrine

Q2-Adrenergic stimulant that it direct and indirect stimulation of adrenergic receptors?

- A. Salbutamol
- B. Ephedrine
- C. Clonidine

Q3-Which one of the following is not a selective drug?

- A. Dopamine
- B. Phenylephrine
- C. Dobutamine

Q4-Which of the following receptors work better on the heart?

- A. Beta 1
- B. Beta 2
- C. Beta 3

Q5-A 19 year old male came to the hospital with Status Asthmatics. He was given Adrenaline. Which one of the effects was shown after he took a therapeutic dose?

- A. Bronchoconstriction
- B. Decrease in the mucosal edema
- C. Mucus plug

Q6-Which nerve is stimulated when taking Adrenaline?

- A. Olfactory nerve
- B. Vagal nerve
- C. C fiber

Q7-Drug specifically indicated for Cardiac arrest?

- A. Salbutamol
- B. Ritodrine
- C. Dobutamine

Answers:
1-B
2-B
3-A
4-A
5-B
6-B
7-C

Good luck!

Done by Pharmacology team 434

Moneera Al draihem
Maha Al-Rabiah
Razan Alsubhi
Sara Alsuliman
Noura Al helali



For any correction, suggestion or any useful information do not
hesitate to contact us: Pharmacology434@gmail.com