



KING SAUD UNIVERSITY
COLLEGE OF MEDICINE
1ST YEAR, 3RD BLOCK

Adrenergic Agonists

2

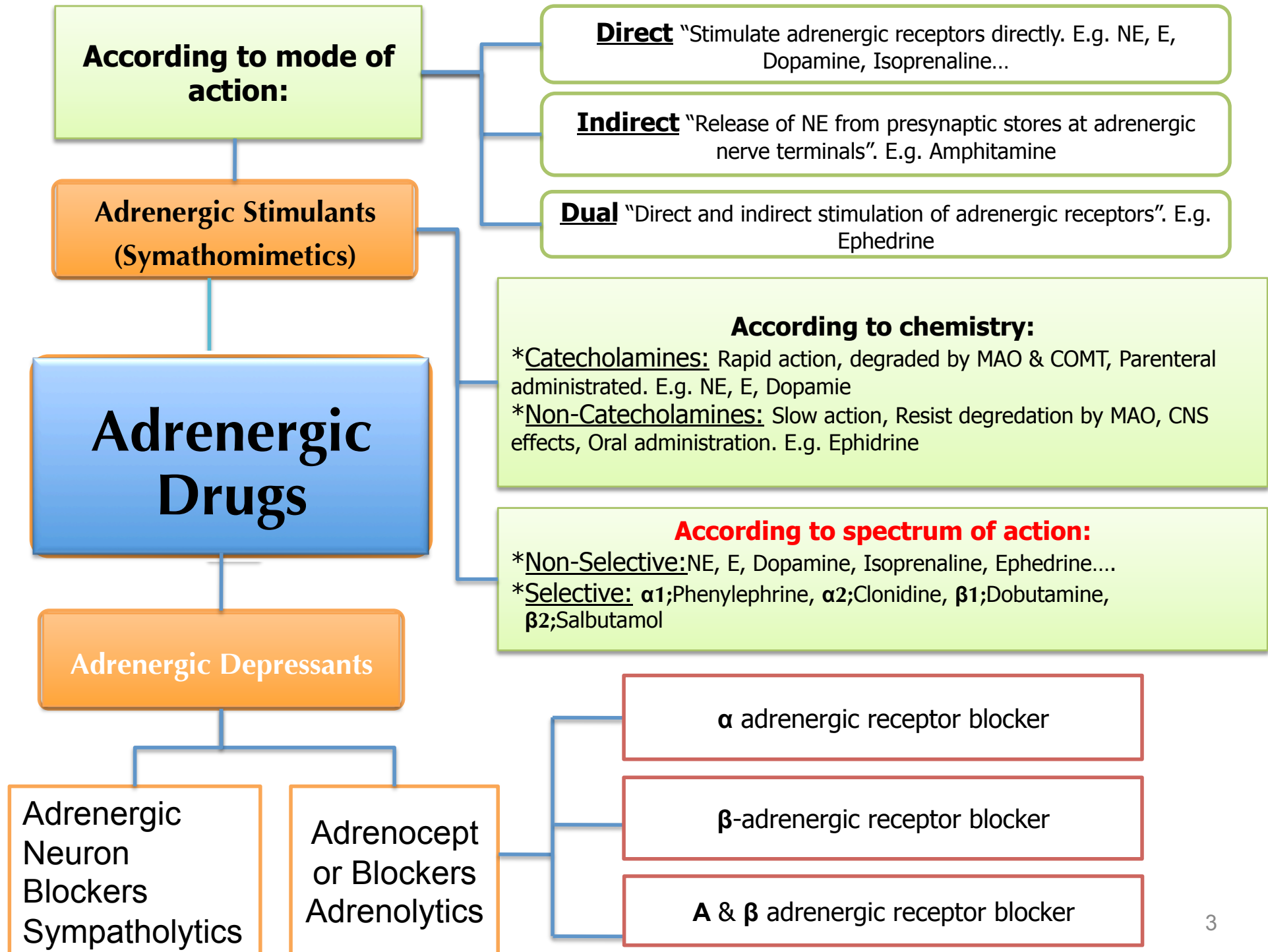


RESPIRATORY BLOCK



***Before you study this lecture, study the Physiology of the Sympathetic NS.**

***Adrenaline is the same as Epinephrine (E), and Noradrenaline is the same as Norepinephrine(NE). And both of them are natural hormones in the Human body, but what we study here are synthetic medications for certain conditions.**



Adrenaline

Overview :

- *Naturally released from adrenal medulla
“secondary to stress, hunger, fear...”
- *Inactivated by intestinal enzymes (MAO and COMT).
- *Given parenteral and by inhalation.
- *Acts on all Adrenoceptors (**Beta more than Alpha**).

Classification :

- *Chemistry\ Catecholamines
- *Spectrum of action\ Non-selective
- *Mode of action\ Direct

Adrenaline: Pharmacological actions :

Organ	Actions	Receptor
Heart	Excitability of all properties of the heart	β_1
Blood Pressure	1-increase systolic. 2-decrease diastolic (if low dose). 3-increase diastolic (if high dose)	1- β_1 2- β_2 3- α_1
Vascular Smooth Muscle cells	1-constrict skin and peripheral 2-dilate coronary and skeletal	1- α_1 2- β_2
Non-vascular smooth muscle cells	1-Lung: bronchodilatation 2-GIT: decrease motility, contract sphincter 3-Bladder: decrease detrusor muscles, contract sphincter 4-Pregnant uterus: tocolytic 5-Eye: mydriasis	1- β_2 2- β_2, α_1 3- β_2, α_1 4- β_2 5- α_1
Metabolism	1- decrease insulin 2-increase glucagon 3-increase liver glycogenolysis and skeletal muscles glycolysis 4-increase adipose lipolysis	1- α_2 2- β_2 3- β_2 4- $\beta_2 \setminus \beta_3$
CNS	Little effects; headache, tremors, restlessness	

Adrenaline:

Indications:

*Locally\

- As haemostatic (in epistaxis"nose bleeding").
- As decongestant (by α_1 receptor).
- With local anesthetics: decreases the absorption, decreases the toxicity, increases the duration of action, decreases the bleeding from incision.

*Systemically\ treatment of:

- Allergic reactions** : **anaphylactic shock** (because it is the physiological antagonist of Histamine), Urticaria, Angioneurotic edema, Hypersensitivity reactions.
- Status Asthmatics : (given parentally) causes bronchodilatation (β_2) and decreases mucosal edema (α_1)
- Cardiac arrest: direct but now through central line.

Adverse effects :

- Tachycardia, palpitation, arrhythmias, angina pains.
- Headache, weakness, tremors anxiety and restlessness.
- Hypertension → cerebral hemorrhage and pulmonary edema.
- Coldness of extremities → tissue necrosis and gangrene if extravasation.
- Nasal stuffiness; rebound congestion if used as decongestion.

Contraindications:

- Coronary heart disease, hypertension, peripheral arterial disease.
- Hyperthyroidism.
- Closed-angle glaucoma → may increase IOP

Noradrenaline

Overview	Classification	Indications
<p>*Naturally released from postganglionic adrenergic fibers.</p> <p>*Not used much therapeutically because it causes severe vasoconstriction.</p> <p>*Administered only by IV (No intramuscular nor subcutaneous because it may cause necrosis).</p> <p>*Increases BP (systolic and diastolic) → reflex bradycardia.</p>	<p>*Chemistry → Catecholamines</p> <p>*Spectrum of action → Non-selective [Acts on the α receptors better than β_1 (No action on β_2 and very weak action on β_3)].</p> <p>*Mode of action → Direct. (Same as Adrenaline)</p>	<p>*Systemically: Hypotensive states (in spinal anesthesia, in septic shock, if fluid replacement and inotropics fail).</p> <p>*Topically (locally); as a local haemostatic with local anesthetic.</p>

Dopamine

*Overview:

- Natural CNS transmitter.
- Released from postganglionic adrenergic fibers.
- Releases NE from postganglionic adrenergic fibers.

*Pharmacological actions:

-Acts on $D1 > \beta1 > \alpha1$

D1: On the kidneys → vasodilatation and diuresis (increase excretion of urine).

$\beta1$: On the heart → increase the force (inotropic), no chronotropic effect.

$\alpha1$: On the blood pressure (according to the dose; first decrease D1, then it will increase due to $\beta1$ effect, then $\alpha1$ will produce its action.)

*Indications:

- Given parentally by infusion.
- Drug of choice for all kind of shocks; septic, hypovolaemic, cardiogenic.** “It increases the BP by $\beta1$ receptor but without causing renal impairment D1”
- Can be given in acute heart failure, but Dobutamine is better.

Isoprenaline

*Synthetic, shows no presynaptic uptake nor breakdown by MAO → longer duration of action.

*Acts on $\beta > \alpha$

***Makes bronchodilatation, so it is used in acute asthma by inhalation.**

*Used also in cardiac arrest.

*Contraindicated in Hyperthyroidism and congestive heart failure.

Dobutamine

*Synthetic drug

*Given I.V.

*Direct acting

Acts on $\beta_1 > \beta_2 > \alpha_1$

-On heart: Inotropic with little chronotropic effect

-On BP: No or little effect decrease in therapeutic dose (β_1 and β_2 counterbalance, and no α_1)

Indications:

*Given parentally by infusion for short term management of **cardiac decompensation** (inability of the heart to maintain adequate circulation)

*It is preferred because it does not increase the oxygen demand.

	Phenylphrine , Midodrine	*Phenylethylamines : Pseudoephedrine , Phenylephrine, Methoxamine
		*Imidazoline: Naphazoline, Oxymetazoline, Xylometazoline
Overview	<p>It's synthetic, noncatecholamine, given orally</p> <p>Has long duration of action.</p> <p>Acts as selective α_1.</p>	-
Indications	<p>-Systemically :</p> <ul style="list-style-type: none"> *Pressor agent in hypotensive states. *Infusion Terminate atrial tachycardia (reflex bradycardia). *Nasal decongestant. <p>-Topically:</p> <ul style="list-style-type: none"> *Local Haemostatic, with Local anesthesia. *Decongestant (nasal & ocular). *Mydriatic (no cycloplegia). 	<p>(Nasal & Ocular Decongestants)</p> <p>Used for treatment of nasal stuffiness</p>

	Salbutamol	Terbutaline	Ritodrine
overview	<p>*It is synthetic.</p> <p>*Given orally or parenteral but mainly by inhalation.</p> <p>*Acts selectively on b_2 → on bronchi.</p> <p>*Hardly effect on heart (b_1) (if you inhale to much)</p>	Selective b_2 agonists	Selective b_2 agonists
Indications	<p>Bronchodilator → asthma & chronic obstructive airway disease (COPD).</p> <p>N.B. Because $t_{1/2}$ is 4 hrs, longer acting preparations exist : Salmeterol & Formoterol.</p>	* Bronchodilator & Tocolytic.	<p>*Tocolytic → postpone premature labour (labour that begins before the 37th week of gestation).</p>

CLONIDINE:

*It is Imidazoline, Given orally or as patch.

***Acts selectively on presynaptic α_2 .**

***(Antihypertensive agent) decrease BP** → by its action on (α_2) at nucleus tractus solitarius to decrease sympathetic outflow to heart & vessels.

(N.B. **Brimonidine** is an imidazoline → α_2 agonist used in **glucoma**)

Indirect acting sympathomimetics : Amphetamine

*Releases NE from adrenergic nerve endings → Blocking of its reuptake
(Because it depletes vesicles from stored NE → **Tachyphylaxis**)

Pharmacokinetics	<ul style="list-style-type: none">*Absorbed orally*not destroyed by MAO*The excretion is increased by acidification of urine.
Action	<p>Acts on α & β “similar to Epinephrine but has CNS stimulant effects”</p> <ul style="list-style-type: none">*Increase mental alertness.*wakefulness.*concentration and self-confidence, followed by depression & fatigue on (when used continuously).*Increase euphoria (intense happiness) → causes its abuse.
Side effects	<ul style="list-style-type: none">*Decrease weight.*Decrease appetite.*Increase energy expenditure.

No more used therapeutically (because it induces psychic and physical dependence and psychosis.
And it has CVS side effects

Dual acting sympathomimetics : Ephedrine

Overview

- Plant alkaloid, synthetic, mixed sympathomimetic;
- Prolonged direct action on receptors → receptor down regulation
- Release NE from adrenergic nerve endings → depletes stores (**Tachyphylaxis**)

Pharmacokinetics

- *Absorbed orally
- *Not destroyed by MAO or COMT → prolonged action

Action

- Acts on α & β :
- 1) Facilitation of neuromuscular transmission & retention of urine.
 - 2) Has CNS stimulant effects (less than Amphetamine).

Uses

- *No more therapeutically used (but is abused by athletes and prohibited during games).

Dual acting sympathomimetics : Pseudoephedrine

Overview

No CNS effect compared to Ephedrine.

Uses

Used as nasal & ocular decongestant and **in flue remedies**. Increase hypertension.

SUMMARY

Drug	Receptors acting on	Uses	Other notes
Adrenaline	Act on All receptors	*Status asthmatics *Cardiac arrest	-Drug of choice in anaphylactic shock, -Never giving for Hyperthyroidism and Glaucoma.
Noradrenaline	Acts on $\alpha > \beta 1$	Hypotensive status, Haemostatic	Causes gangrene if administrated intramuscularly.
Isoprenaline	Acts on $\beta > \alpha$	Cardiac arrest	Contraindicated in Hyperthyroidism and congestive heart failure.
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	Selective $\alpha 1$	Hypotension, tachycardia	Used locally as decongestant, haemostatics, mydriatic
Clonidine	Selective $\alpha 2$	Hypotension	IMIDAZOLINE Giving orally or as patch
Brimonidine	Selective $\alpha 2$	Glaucoma	IMIDAZOLINE
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	

M C Q S

1-Which of the following is contraindicated in hyperthyroidism?

- A-Dopamine
- B-Epinephrine
- C-Norepinephrine
- D-Ephedrine

2-A woman comes to the emergency room with a 7-month pregnancy and her contractions have started. Which of the following drugs should we give her to put off her labor?

- A-Salmeterol
- B-Formotrol
- C-Salbutamol
- D-Ritodrine

3-Which of the following is indicated for bronchial asthma?

- A. Salbutamol
- B. Clonidine
- C. Epinephrine
- D. Norepinephrine

4-Which of the following is a selective β_2 agonist?

- A. Clonidine
- B. Terbutaline
- C. Phenylephrine
- D. Dobutamine

5-A man came to the emergency room with hypotension so they gave him an antihypotensive drug subcutaneously which caused him tissue necrosis and gangrene. Which of the following is most probably this drug?

- A. Ephedrine
- B. Norepinephrine
- C. Dopamine
- D. Isoprenaline

6. Which of the following causes psychosis as a side effect?

- A. Dopamine
- B. Isoprenaline
- C. Amphetamine
- D. Terbutaline

7. Which of the following is not used therapeutically anymore due to its severe CNS effect?

- A. Ephedrine
- B. Epinephrine
- C. Isoprenaline
- D. Dobutamine

8. A man had a severe infection and underwent a septic shock. Which of the following drugs should we give him?

- a. Dobutamine
- b. Dopamine
- c. Salbutamol
- d. Ritodrine

9. A football player was suspected for being on stimulants because of his increased alertness, endurance and productivity. A test was conducted and found positive for one of the adrenergic agonists. Which of the following is probably this drug?

- A. Phenylephrine
- B. Epinephrine
- C. Ephedrine
- D. Naphazoline

1-B 2-D 3-A 4-B 5-B
6-C 7-A 8-B 9-C

We hope we made this lecture easier for you
Contact us for any questions or comments
Good Luck !

Nada Dammas
Ghada AlHindi
Latifa AlAnazi
Maha Alrajhi
Lamees al-mezaini

Ahmed Aldakhil
Abdulrahman Althaqib



Pharma_433@yahoo.com



[@pharma_433](https://twitter.com/pharma_433)



PHARMACOLOGY

433