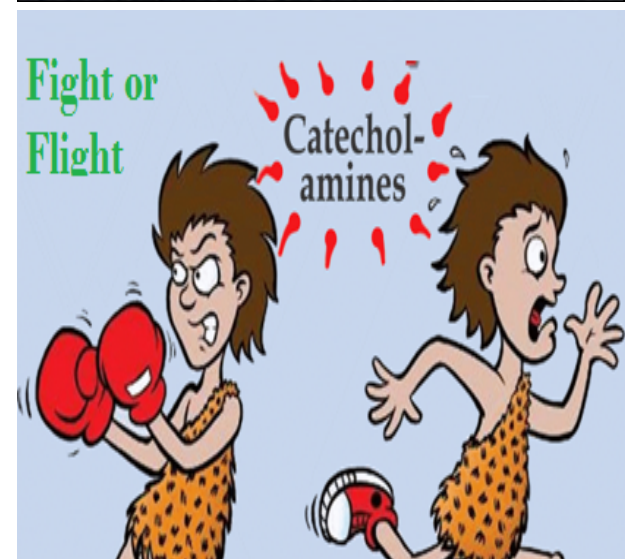
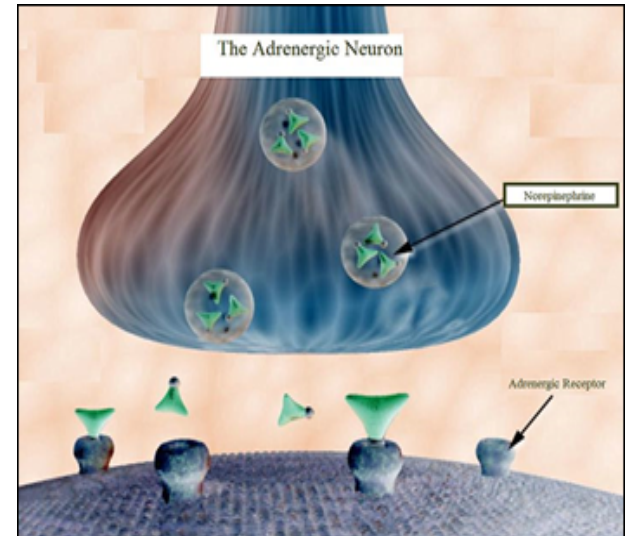


ADRENERGIC AGONISTS

ILOS

Classify adrenergic agonists according to chemical structure, receptor selectivity and mode of action

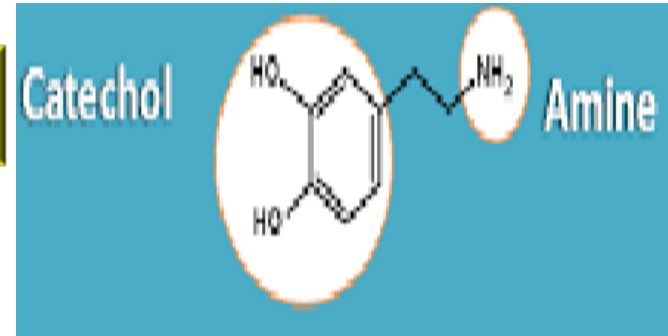
Discuss pharmacodynamic actions, ADRs, indications and contraindications of adrenergic agonists



ADRENERGIC AGONISTS

Classification

i-According to chemical structure



A- Catecholamines

1- Natural

Noradrenaline, adrenaline, dopamine

2-Synthetic

Isoprenaline

Degraded by MAO & COMT / Little CNS effects / Parenterally administered

B- Non Catecholamines

Ephedrine

Resist degradation by MAO / Prominent CNS effects / Orally administered

ADRENERGIC AGONISTS

ii-According to receptor selectivity

1-Selective

α_1 ; Phenylephrine

β_1 ; Dobutamine

α_2 ; Clonidine

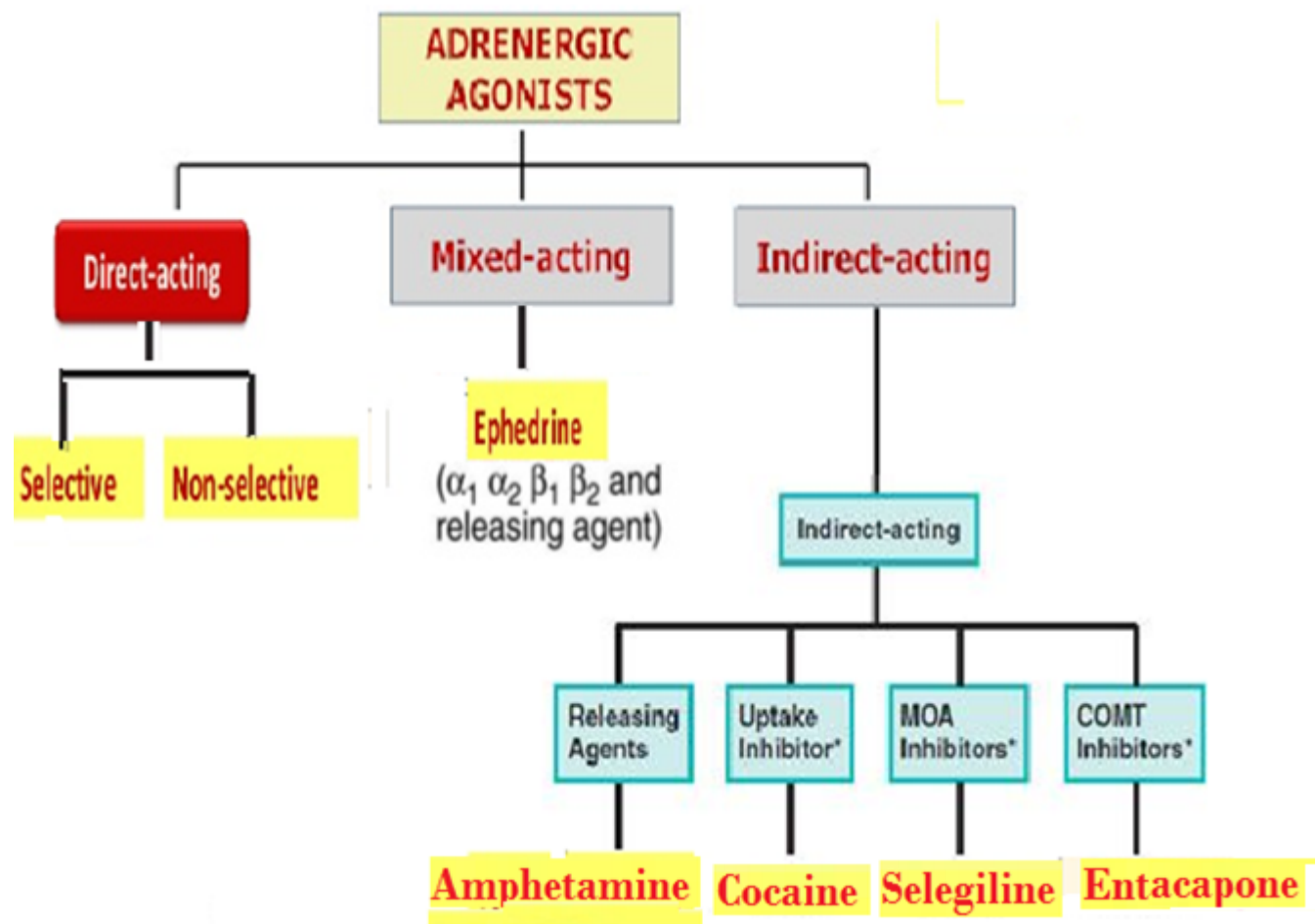
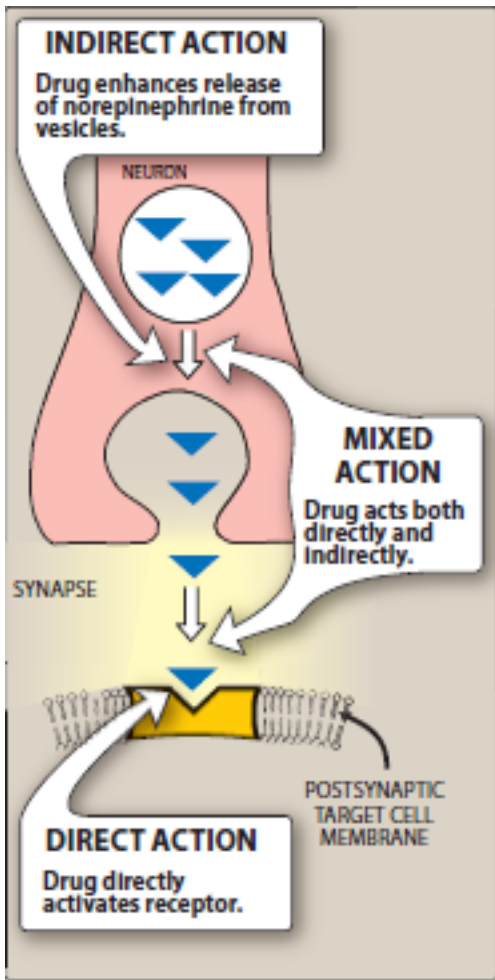
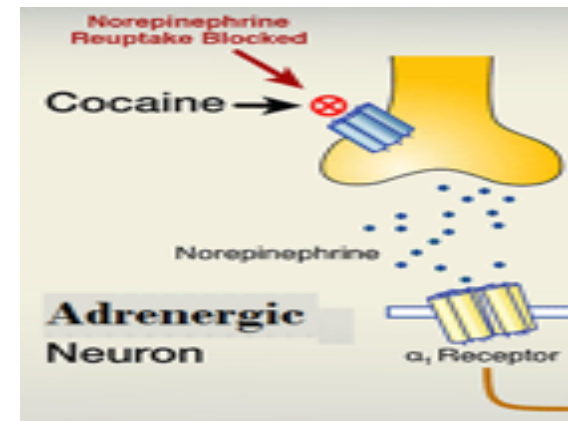
β_2 ; Salbutamol

2-Non-selective

Noradrenaline, adrenaline, dopamine, isoprenaline, ephedrine

ADRENERGIC AGONISTS

iii-According to mode of Action



DIRECT- ACTING

ADRENALINE

Naturally released from adrenal medulla
→ secondary to stress, hunger, fear

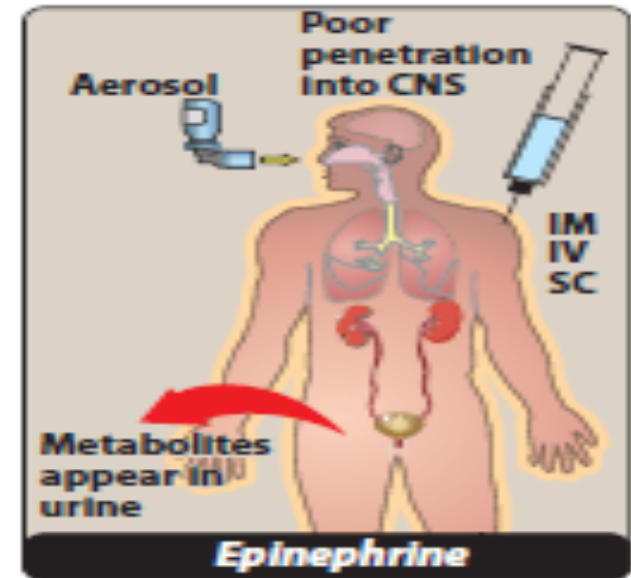
Inactivated by intestinal enzymes, so given parenterally or by inhalation

Acts on all adrenergic receptors; $\beta \neq / > \alpha$

Lung → bronchiodilatation (β_2)

Pregnant uterus → tocolytic (β_2), Eye → mydriasis (α_1)

CNS → little, headache, tremors & restlessness

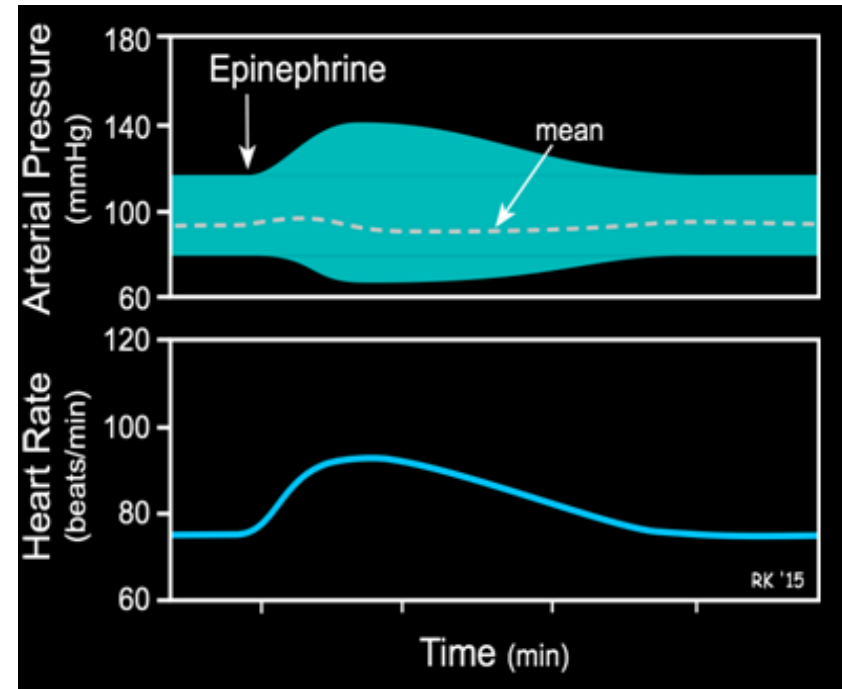


ADRENALINE

PHARMACOLOGICAL ACTIONS

Heart → +inotropic, chronotropic, dromotropic (↑ excitability) (β_1)

BP → ↑ systolic (β_1) / ↓ diastolic . Low dose (β_2) , high dose (α_1)



Vascular SMC:- Constricts skin & peripheral vessels (α_1) . Dilates coronary & skeletal vessels (β_2)

ADRENALINE

INDICATIONS



Used locally; as haemostatic (in epistaxis) & as decongestant (α_1)

With local anesthetics → to reduce absorption, toxicity & bleeding from incision

Used systemically for treatment of:-

Allergic reactions → drug of choice in anaphylactic shock as it is the physiological antagonist of histamine → ↑ BP & cause vasoconstriction

In status asthmatics → given parenterally → bronchodilatation (β_2) + → ↓ mucosal edema (α_1)

⚡ In cardiac arrest → direct but now through central line
N.B. Selective β_1 agonists are preferred

ADRENALINE

ADRS

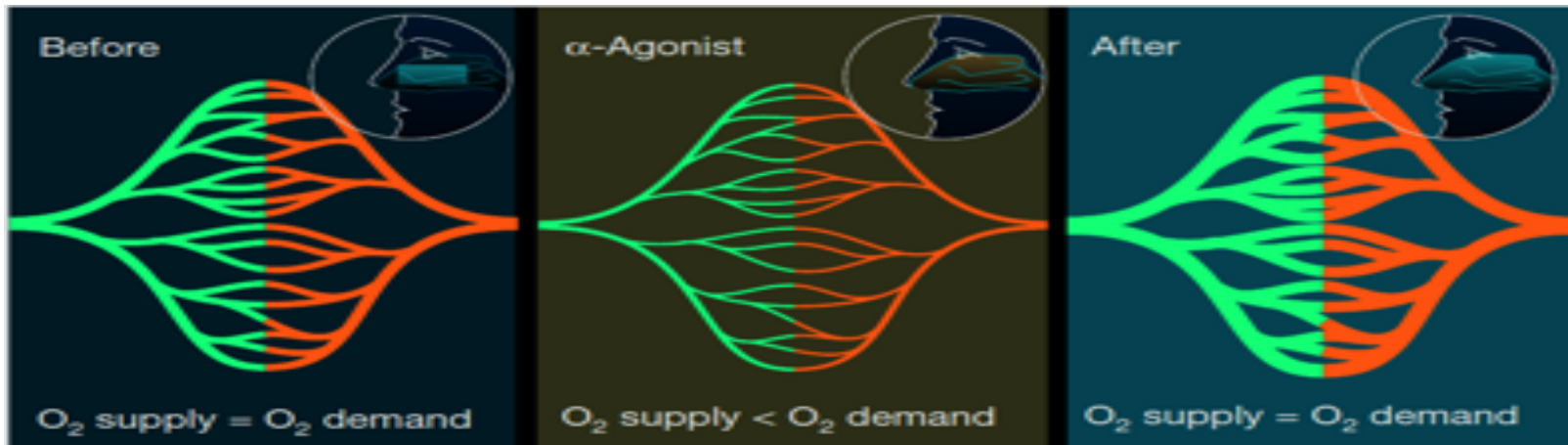
Tachycardia, palpitation, arrhythmias, angina pains

Headache, weakness, tremors anxiety and restlessness.

Hypertension → cerebral hemorrhage and pulmonary edema.

Coldness of extremities, tissue necrosis and gangrene if extravasations

Nasal stuffiness; rebound congestion if used as decongestion



ADRENALINE

CONTRINDICATIONS

✚ Coronary heart disease, hypertension, peripheral arterial disease.

Hyperthyroidism

Catecholamines are ineffective when taken orally because they're destroyed by digestive enzymes.



Closed-angle glaucoma

(Iris relaxation ↓ filtration angle → ↑ IOP)

NORADRENALINE

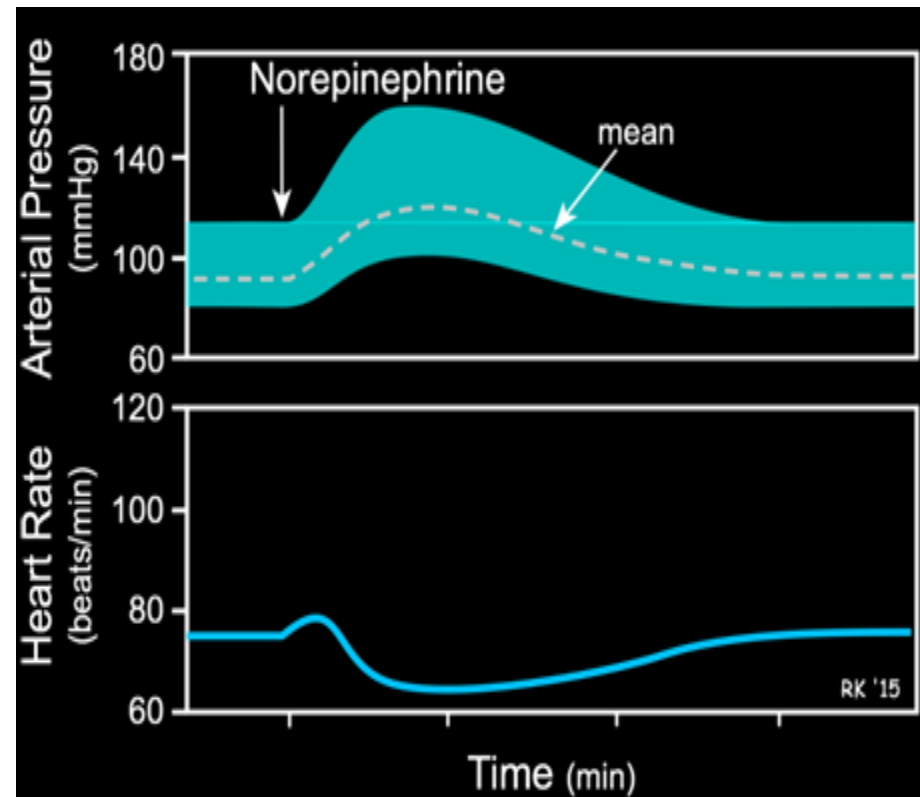
It is naturally released from postganglionic adrenergic fibers

Not much used therapeutically → severe vasoconstriction

Acts on $\alpha > \beta_1$

Only administered IV - Not IM or Subcutaneous
→ necrosis

It ↑ BP [systolic & diastolic]
→ reflex bradycardia (*vagal stimulation*)
→ CO not much changed



NORADRENALINE

INDICATIONS

Used systemically; hypotensive states

In spinal anesthesia, in septic shock if fluid replacement and inotropics fail

Used topically; as a local haemostatic with local anesthetic (< tachycardia & irritability & > necrosis & sloughing)

ISOPRENALINE

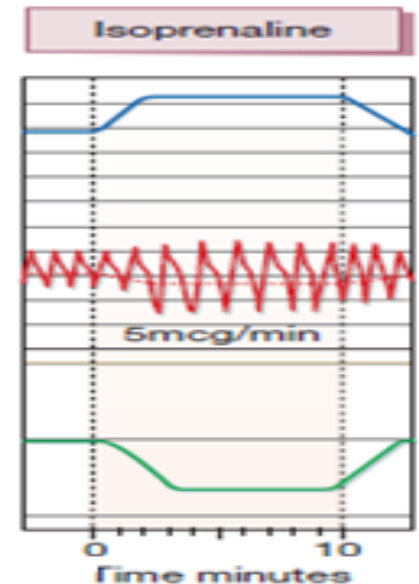
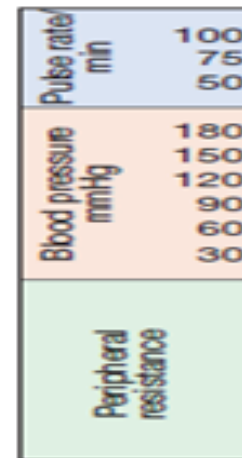
It is synthetic ; show no presynaptic uptake nor breakdown by MAO → longer action.

Acts on $\beta \gg \alpha$

Slightly ↑systolic pressure,
↓diastolic pressure , ↓PVR, ↑HR

Produce broncho-dilatation → Was used by inhalation **in acute asthma**

Used in **cardiac arrest** but contraindicated in hyperthyroidism & CHD



DOPAMINE

It is a natural CNS transmitter

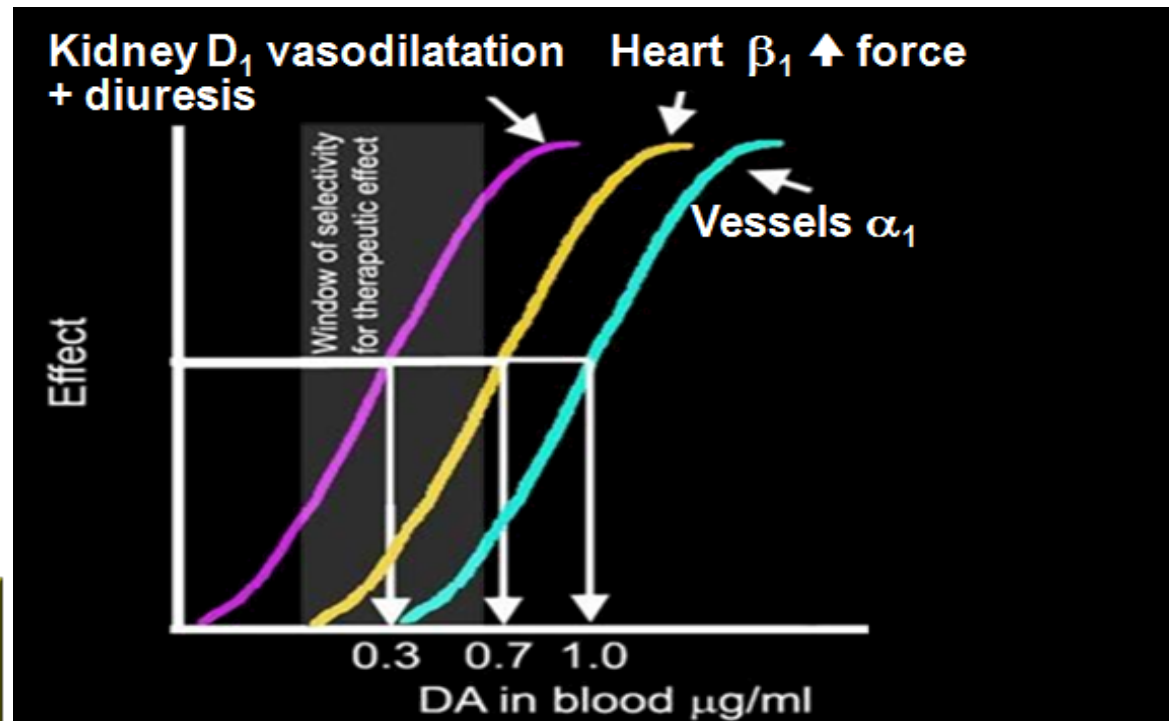
Released from postganglionic adrenergic fibers (> renal vessels)

Releases NE from postganglionic adrenergic fibers

Acts on $D_1 > \beta_1 > \alpha_1$

On BP → According to dose; first ↓ D_1 then ↑ due to β_1 followed by α_1 effect

On heart → Inotropic, no chronotropic effect



DOPAMINE

Indications

✚ Given parenterally by continuous infusion

✚ It is the **drug of choice in treatment of SHOCK** → septic, hypovolaemic (after fluid replacement), cardiogenic. It ↑ BP & CO (β_1), without causing renal impairment (D_1)

Can be given in acute heart failure (HF) but dobutamine is preferred

DOBUTAMINE

It is synthetic. Given IV.

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

On heart → Inotropic with little chronotropic effect

On BP → No or little ↓ in therapeutic dose (β_1 & β_2 counterbalance + no α_1)

Given parenterally by infusion for **short term management of cardiac decompensation** after cardiac surgery, in acute myocardial infarction (AMI) & HF

It is preferred because it does not ↑ oxygen demand

Dobutamine really helps me get a steady beat going!



PHENYLEPHRINE

It is synthetic, noncatecholamine

Given orally & has prolonged duration of action

Systemically; **Pressor agent** in hypotensive states. *Infusion*. **Acts as selective α_1** Peaks in 20 min. $t_{1/2}$ 30 min

Terminate atrial tachycardia (*reflex bradycardia*)

Nasal decongestant. *Oral*

Topically; Local Haemostatic, with Local anesthesia.

Nasal & Ocular Decongestants

Used for treatment of nasal stuffiness . But can cause Rebound nasal stuffiness

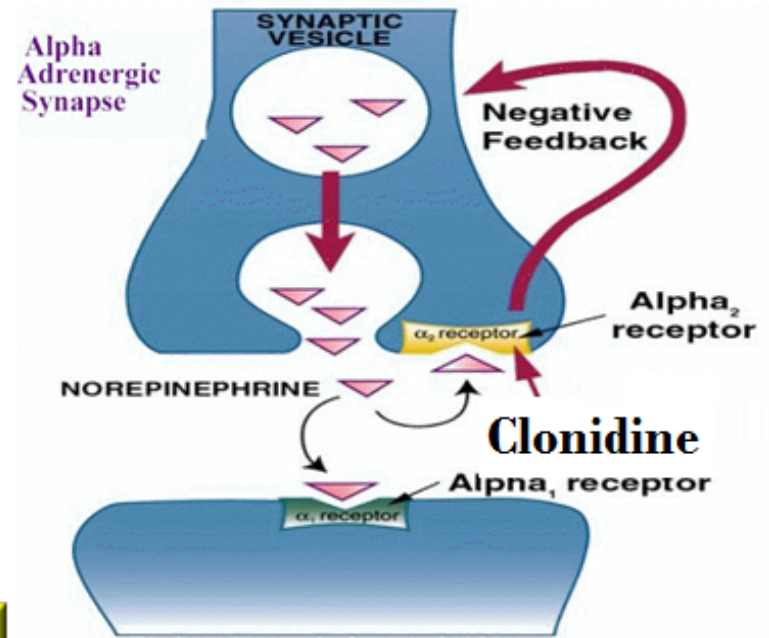
Mydriatic (*no cycloplegia so facilitate eye examination*)

CLONIDINE

It is synthetic, imidazoline

Given orally or as patch

Acts selectively on presynaptic α_2



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

Brimonidine is an imidazoline → α_2 agonist used in glaucoma

SALBUTAMOL

It is synthetic. Given orally, by inhalation or parenteral.

Acts *selectively* on β_2 \rightarrow on bronchi. *Little effect on heart* (β_1)

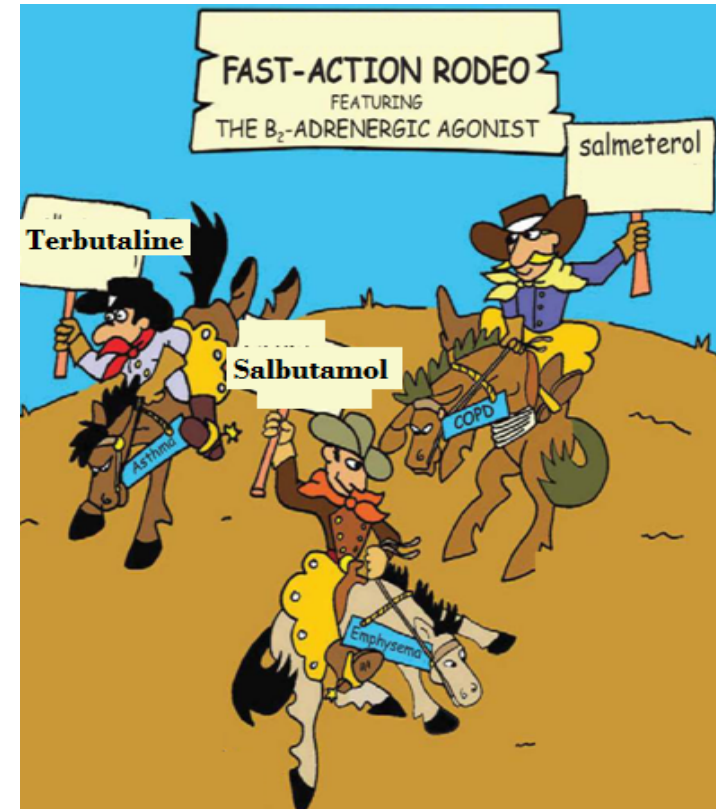
Bronchodilator \rightarrow asthma & chronic obstructive airway disease (COPD)

Because $t_{1/2}$ is 4 hrs longer acting preparations exist ; Salmeterol & Formoterol

Other selective β_2 agonists :

Terbutaline; **Bronchodilator & Tocolytic**

Ritodrine; **Tocolytic** \rightarrow postpone premature labour (labour that begins before the 37th week of gestation)



INDIRECTLY-ACTING SYMPATHOMIMETIC AMINES

AMPHETAMINE

It acts indirectly; Releasing NE from adrenergic nerve endings > Blocking of its reuptake

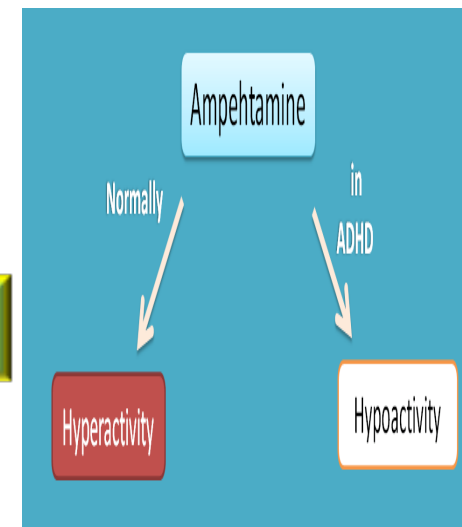
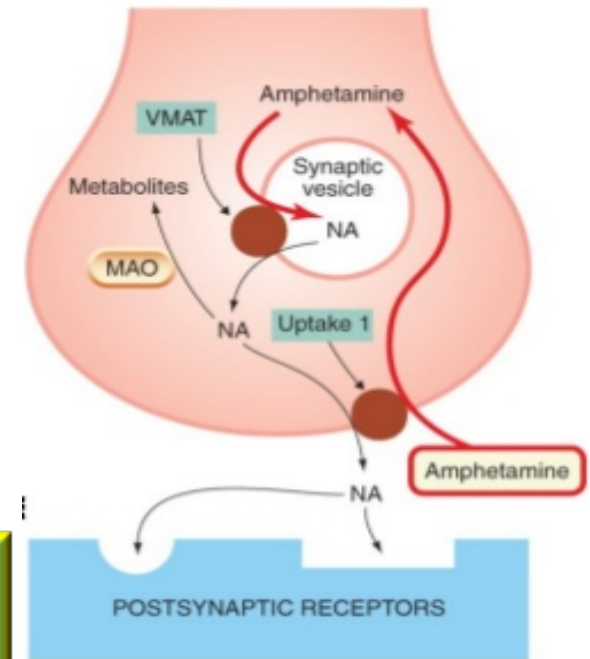
Because it depletes vesicles from stored NE
→ **tachyphylaxis**

Absorbed orally, not destroyed by MAO, excreted mostly unchanged (↑ *by acidification of urine*)

Acts on α & β → similar to epinephrine but has **CNS stimulant effects**; mental alertness, wakefulness, concentration & self-confidence / followed by depression & fatigue on continued use

↓ Weight → ↓ appetite ↑ increase energy expenditure

No more used therapeutically → **induces psychic & physical dependence** and psychosis + the CVS side effects



MIXED SYMPATHOMIMETICS

EPHEDRINE

Plant alkaloid, synthetic, mixed sympathomimetic



Prolonged direct action on receptors → receptor down regulation

Release NE from adrenergic nerve endings → depletes stores → tachyphylaxis

Absorbed orally, not destroyed by MAO or COMT → prolonged action

MIXED SYMPATHOMIMETICS

EPHEDRINE

Acts on α & β

Facilitation of neuromuscular transmission (myasthenia gravis) & retention of urine

Has **CNS stimulant effects** (*less than amphetamine*)

No more therapeutically used → but is abused by athletes and prohibited during games.

Pseudoephedrine, dual acting < CNS & pressor effects compared to ephedrine. Used as nasal & ocular decongestant & in flue remedies

