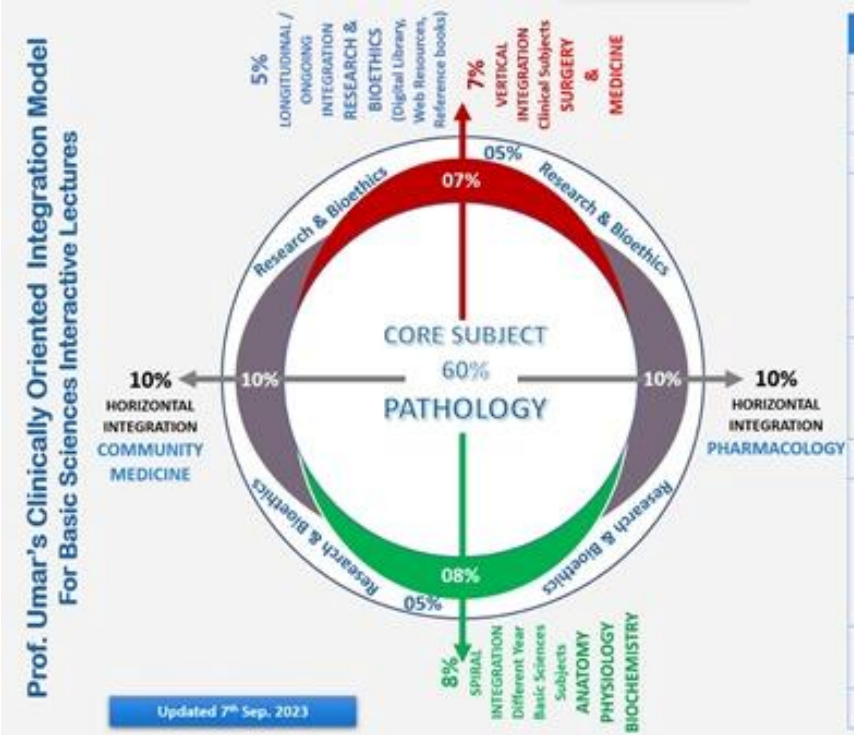
SYMPATHOMIMETICS

- Katzung's Basic & Clinical Pharmacology, 16th Edition
- Goodman and Gilmans The Pharmacological Basis of Therapeutics, 13th Edition

MOTO AND VISION

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

UMAR'S MODEL OF INTEGRATION



Model 3rd Year Pathology LGIS (≈30 slides)	
Core Subject – 60% (≈ 18-20 slides)	
Pathology (≈ 18-20 slides)	
Horizontal Integration – 20% (≈ 5-6 slides)	
Same Year Subjects	• Pharmacology (10%) (≈ 2-3 slides) • Community Medicine (10%) (≈ 2-3 slides)
Vertical Integration – 07% (≈ 2-3 slides)	
Clinical Subjects	• Medicine (3-5%) (≈ 1-2 slides) • Surgery (3-5%) (≈ 1-2 slides)
Spiral Integration – 08% (≈ 2-3 slides)	
Different Year Basic Sciences Subjects	• Anatomy (1-3%) (≈ 1-2 slides) • Physiology (1-3%) (≈ 1-2 slides) • Biochemistry (1-3%) (≈ 1-2 slides)
Longitudinal / Ongoing Integration – 05% (≈ 1-2 slides)	
Research & Bioethics (≈ 1-2 slides)	

PROF. UMAR'S MODEL OF TEACHING STRATEGY

- Self Directed Learning Assessment Program

- Objectives :To cultivate critical thinking, analytical reasoning, and problem-solving competencies.
- To instill a culture of self-directed learning, fostering lifelong learning habits and autonomy.
- How to Assess?
- Ten randomly selected students will be evaluated within the first 10 minutes of the lecture through 10 multiple-choice questions (MCQs) based on the PowerPoint presentation shared on Students Official WhatsApp group, one day before the teaching session.
- The number of MCQs from the components of the lecture will follow the guidelines outlined in the Prof. Umar model of Integrated Lecture.

Component of LGIS	Core Knowledge	Horizontal Integration	Vertical Integration	Spiral Integration
No of MCQs	6-7	1-2	1	1

PRELECTURE ASSESSMENT

A drug that stimulates beta1- and beta2-adreneceptors can be expected to cause:

A. a. decrease in heart rate
B. a decrease in total peripheral resistance
C. a constriction of airway smooth muscle resistance
D. a decrease in renin release
E. Decrease in blood pressure

Clonidine and alpha-methyldopa act as agonists at alpha2-adrenoceptors to cause:

A. sustained increase in mean arterial pressure
B. an increase in intestinal motility
C. a CNS-mediated decrease in blood pressure
D. an increase in myocardial contractility
E. Bronchoconstriction

Phenylephrine is applied to the nasal mucosa in order to?

A. block histamine receptors
B. block beta-adrenergic receptors
C. induce vasodilation
D. induce vasoconstriction
E. Block reuptake of norepinephrine

PRE-LECTURE ASSESSMENT

The sympathomimetic which may promote diuresis by a direct effect on the kidney is

A. Isoproterenol
B. dobutamine
C. norepinephrine
D. dopamine
E. Epinephrine

A 20-year-old man has been self-treating his nasal congestion with a nonprescription alpha agonist nasal spray for 2 weeks. When he stopped using it he found that he experienced:

A)Increased nasal congestion

B) Decreased nasal discharge

C) Improvement in breathing

D) Reduction in headache

E) Enhanced sense of smell

Which one of the following drugs would decrease release of norepinephrine from noradrenergic nerves?

A. Prazosin
B. Atropine
C. Phenylephrine
D. Clonidine
E. Dopamine

PRE-LECTURE ASSESSMENT

Drug X causes an increase in blood pressure and a decrease in heart rate when administered iv. If an antagonist at ganglionic nicotinic receptors is administered first, drug X causes an increase in blood pressure and an increase in heart rate. Drug X most likely is?

A. Propranolol
B. Norepinephrine
C. Isoproterenol
D. Terbutaline
E. Curare

Which of the following is a selective beta agonist and a potent bronchodilator?

A. Epinephrine and ephedrine
B. Salbutamol and orciprenaline
C. Amphetamine and ephedrine
D. Isoprenaline and pronalterol
E. Phenylephrine and salbutamol

PRE-LECTURE ASSESSMENT

An 8-year-old boy diagnosed with attention-deficit hyperactivity disorder is placed on a CNS stimulant that increases synaptic levels of neurotransmitter by inhibiting vesicular monoamine transporters and inhibiting reuptake by blocking the monoamine transporters. The doctor tells the boy and his mother that the drug might cause:

A. Lack of appetite
B. Increase appetite
C. Increase sleep
D. Lethargy
E. Hypertension

Which of the following sympathomimetics is preferable for the treatment of chronic orthostatic hypotension?

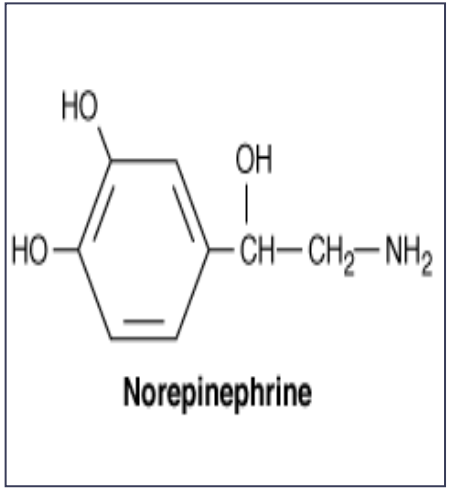
A. Epinephrine
B. Norepinephrine
C. Ephedrine
D. Salmeterol
E. Dobutamine

Learning Objectives

At the end of the lecture, students of 3rd Year MBBS will be able to ;

- **Recall classification of sympathomimetic drugs**
- **Discuss clinical pharmacology of catecholamines in relation with epinephrine**
- **Describe the mechanism of action of indirectly acting sympathomimetic drugs**
- **Discuss important clinical indications of indirectly acting sympathomimetics**

Norepinephrine
(Levarterenol ,Noradrenaline)



Norepinephrine

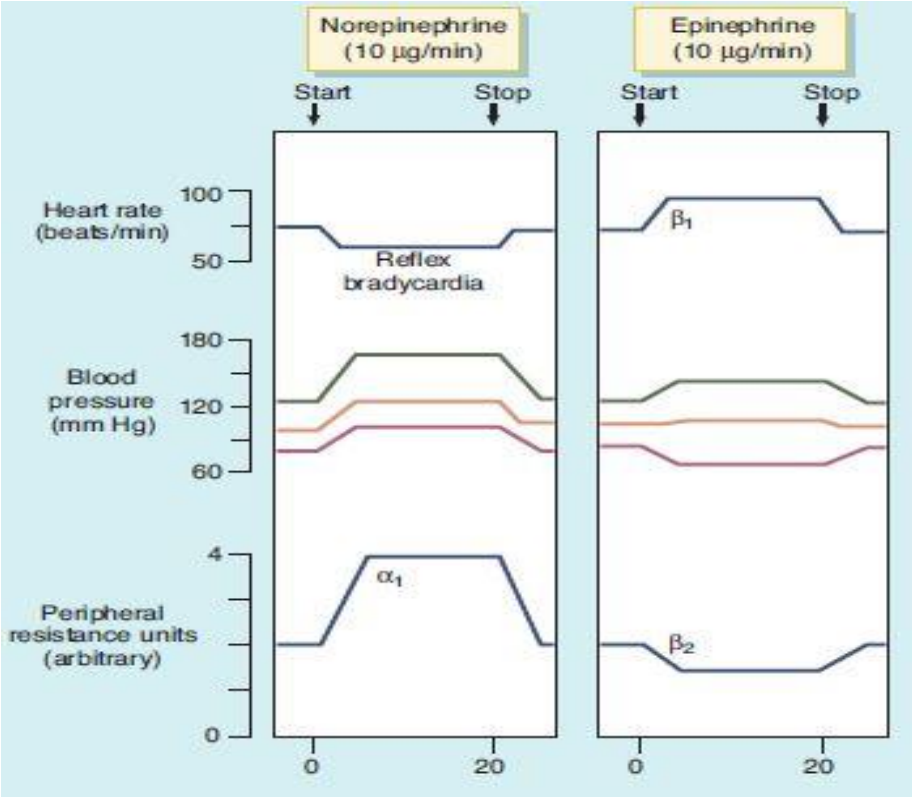
- Catecholamine
- Naturally produced in postganglionic sympathetic nerves and adrenal medulla (10-20%)
- Receptor affinity

$$\alpha_1 = \alpha_2 ; \beta_1 >> \beta_2$$

Droxidopa , prodrug converted by AAAD into NE

Norepinephrine

- **Blood vessels**
  Vasoconstriction----- PVR ⇧
- **Heart**
  Positive ionotropic
  Reflex bradycardia ✸
  (compensatory baroreceptor reflex)
- **Blood pressure**
  SBP
  DBP ⇧



Norepinephrine

- **Therapeutic uses (Limited)**

❖ May be used for treatment of hypotensive emergency to preserve cerebral or coronary blood flow

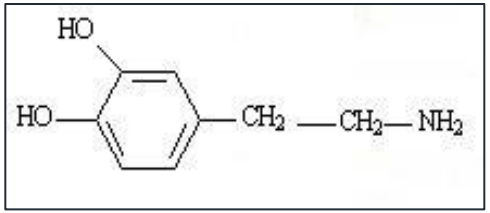
(Drug of choice is Dopamine & Dobutamine).

- **Adverse Effects:**

❖ Necrosis → Gangrene of extremities

❖ Severe hypertension

Dopamine



- Catecholamine
- Naturally and synthetically prepared
- Immediate precursor of epinephrine & norepinephrine
- Central neurotransmitter
- Receptor affinity

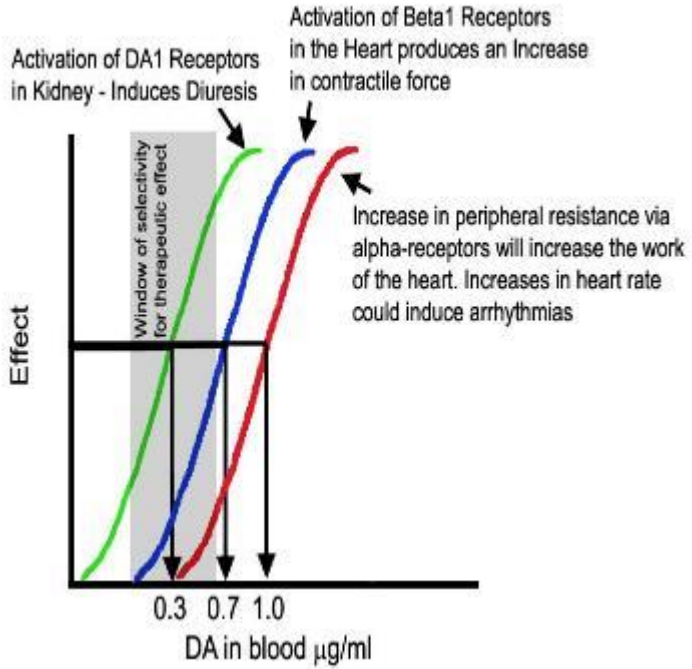
D1=D2>>β>>α

- Selectivity is lost at high doses

Dopamine

Pharmacological action

- At lower concentration (≤2µg/kg), only vascular dopamine receptors are stimulated (renal, mesenteric & coronary beds)
- At moderate levels (2-5µg/kg) beta receptors are stimulated (heart)
- At higher concentrations (5-15µg/kg), vascular alpha receptors are stimulated



Dopamine

Therapeutic uses

- Cardiogenic shock/hypovolemic shock/CCF with oliguria

Adverse effects

- Tachycardia, hypertension, arrhythmias, angina pain
- Necrosis or sloughing of tissue

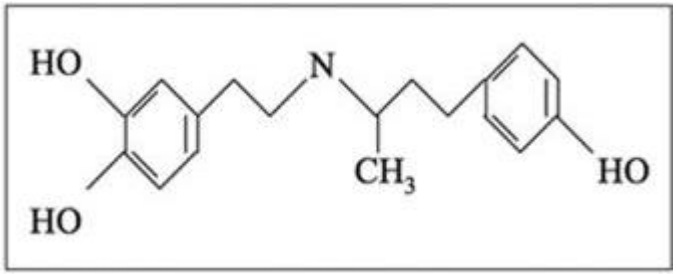
Precautions

- Correction of hypovolemia
- Dose reduction with MAO inhibitors

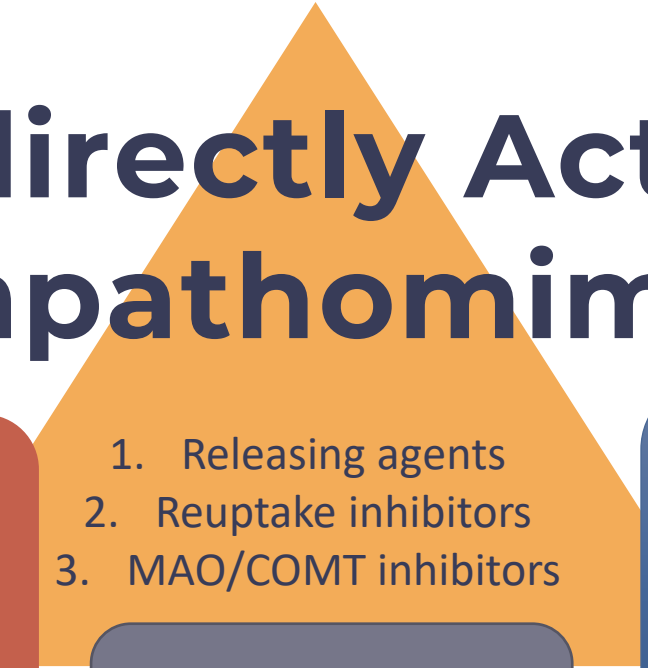
Dobutamine

- Semi synthetic catecholamine
- Receptor affinity=$\beta_1 > \beta_2 >>>> \alpha$
- More inotropic than chronotropic effect
- Shorter duration of action, $t_{½}$ is 2 min
- **Therapeutic uses:**

❖ Short term treatment of cardiac decompensation(cardiac surgery, CCF, MI, cardiogenic shock)



Indirectly Acting Sympathomimetics



1. Releasing agents
2. Reuptake inhibitors
3. MAO/COMT inhibitors

- Cocaine
- Tricyclic antidepressants

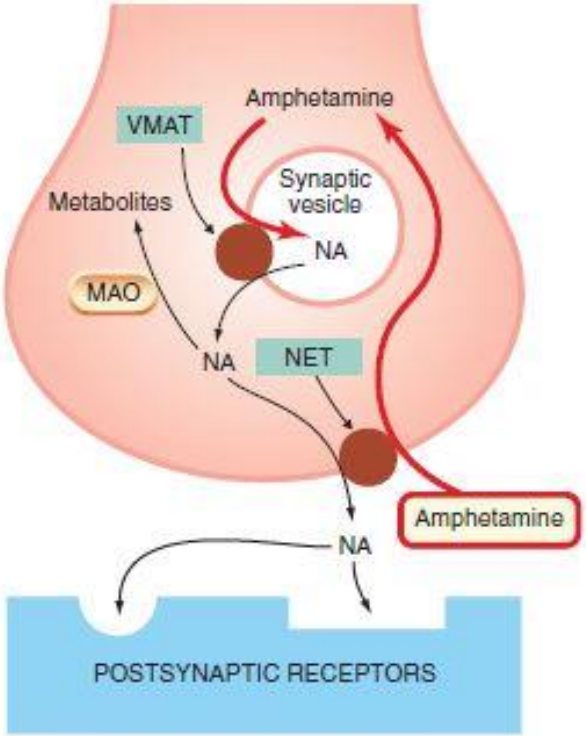
- Amphetamine
- Methamphetamine
- Dextroamphetamine
- Phenmetrazine
- Modafinil
- Methylphenidate
- Tyramine

- Selegiline
- Rasagiline
- Entacapone

Amphetamine

MOA

- Indirect same as ephedrine



Effects

- **CNS** :Euphoria
  Excitement
  Increase attentiveness
  Appetite suppressant
  Abused drug due to its euphoric effect
- **Respiration:** Increase rate & depth at higher doses
- **CVS:** increase BP & contractility
  reflex bradycardia

Amphetamine

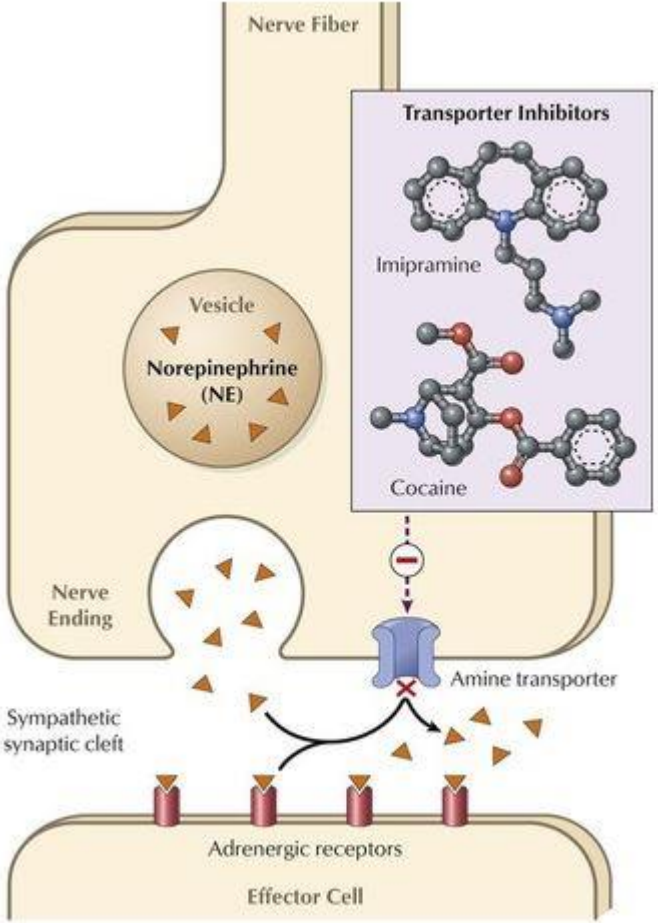
Therapeutic Uses of Amphetamine variants:

- **Methamphetamine:** Narcolepsy (abused drug)
- **Phenmetrazine** : Weight reduction
- **Methylphenidate & Pemoline**: Attention deficit hyper activity disorder (ADHD) in children
  Pemoline can produce hepatic failure
- **Modafinil**: Narcolepsy, ADHD, less abuse potential.
  Also affects central α_{1B} receptors, GABAergic , Glutaminergic & Serotonergic synapses
- **Phenylpropolamine:** weight reduction. **Withdrawn**– Hemorrhagic stroke

Tyramine

- Non-catecholamine
- Normal by-product of tyrosine metabolism in body
- High concentration in fermented food i.e Cheese or yeast
- Parenteral Indirect acting sympathomimetic
- Ineffective orally due to high first pass metabolism by MAO-A in liver
- In Patients on MAO-A inhibitors, hypertensive crises can occur if foods rich in tyramine are taken ,due to increased bioavailability.

Cocaine



- A local anaesthetic
- Indirectly acting sympathomimetic drug
- Inhibits reuptake of released Nor-epinephrine at peripheral Nor-adrenergic synapses.
- In the CNS it inhibits dopamine reuptake into neurons in the “pleasure centers” of the brain.
- It is heavily abused drug.

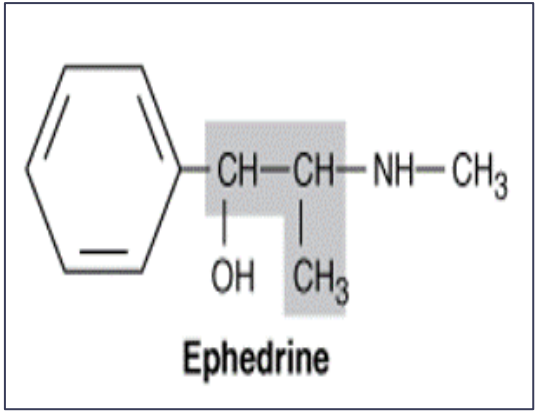
Mixed Agonists

EPHEDRINE

Source: alkaloid obtained from plants of the genus
Ephedra vulgaris (ma huang)

Pharmacokinetics:

- Weak base
- Good oral bioavailability
- Lipid soluble, crosses BBB
- Urinary excretion



EPHEDRINE

Mechanism of action:

❖ Indirect (majorly)------tachyphylaxis

- Promotes release of stored Nor-epinephrine
- This does not require action potential & exocytosis
- Released Nor-epinephrine enters the synaptic cleft via Reuptake – 1

❖ Direct

- Directly on receptors (α & β)

EPHEDRINE

Uses:

- Chronic orthostatic hypotension
- Acute hypotensive states associated with spinal anesthesia
- Bronchial asthma
- Nasal decongestant
- Urinary continence

S/E:

- **Tachyphylaxis**
- **CNS:**Restlessness, insomnia, nervousness
- **CVS:** Tachycardia, HTN, arrhythmias
- **GIT :** Nausea ,vomiting

RESEARCH

Ippolito M, Benovic JL. Biased agonism at β-adrenergic receptors. Cell Signal. 2021 Apr;80:109905. doi: 10.1016/j.cellsig.2020.109905. Epub 2020 Dec 29. PMID: 33385503; PMCID: PMC7878421.

ARTIFICIAL INTELLIGENCE

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BIOETHICS

Suissa, K., Schneeweiss, S., Kim, D.W. and Patorno, E., 2021. Prescribing trends and clinical characteristics of patients starting antiobesity drugs in the United States. *Diabetes, Obesity and Metabolism*, *23*(7), pp.1542-1551.

FAMILY MEDICINE

Abdullahi S, Cruz EV, Freeman L, Tanlaka E. Anti-obesity Medications Prescribing Measures Utilized by Primary Care Practitioners: Scoping Review.


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