SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENT OF CARDIO PULMONARY PERFUSION CARE TECHNOLOGY

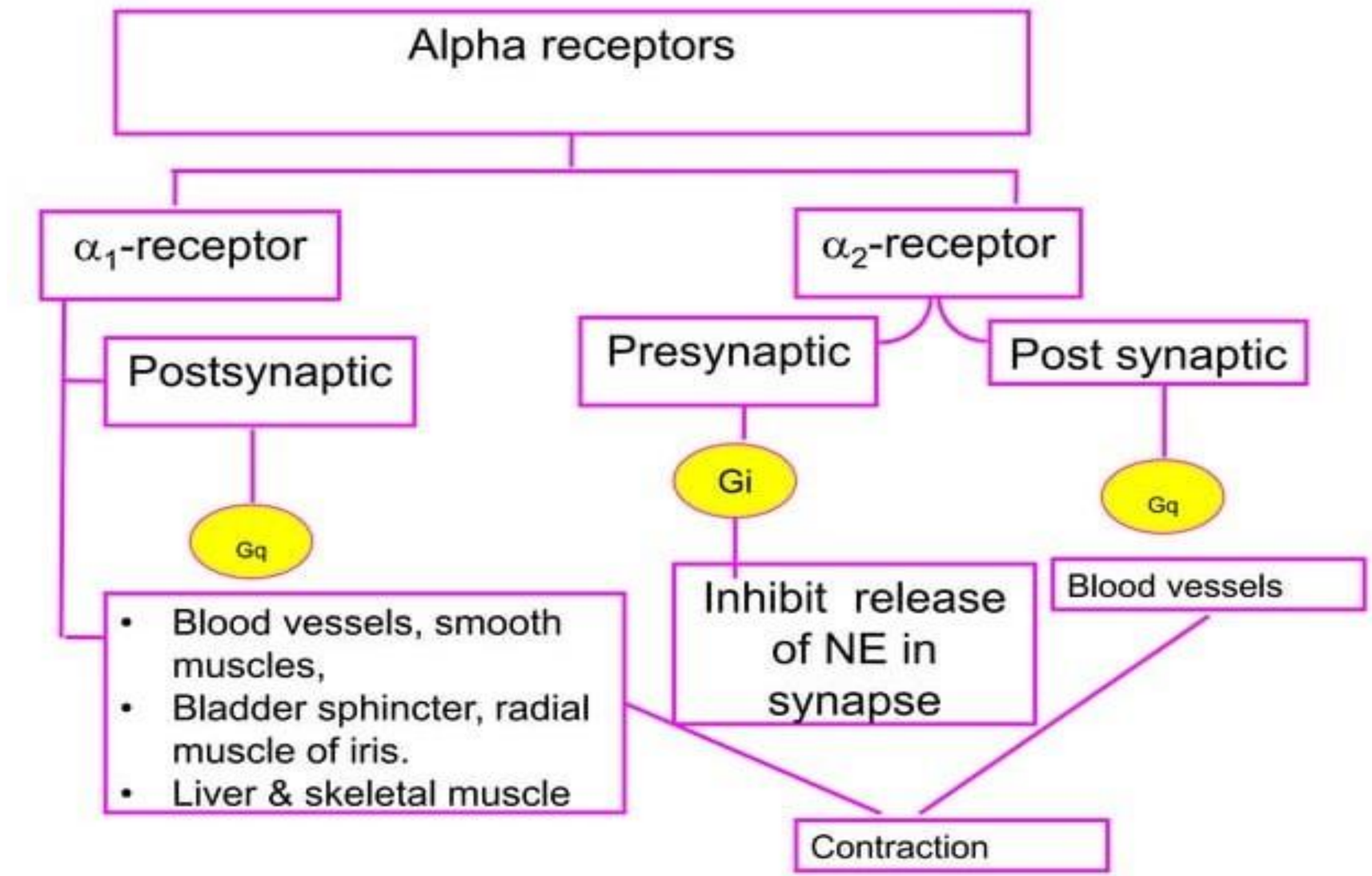
COURSE NAME : Pharmacology Pathology and Clinical Microbiology

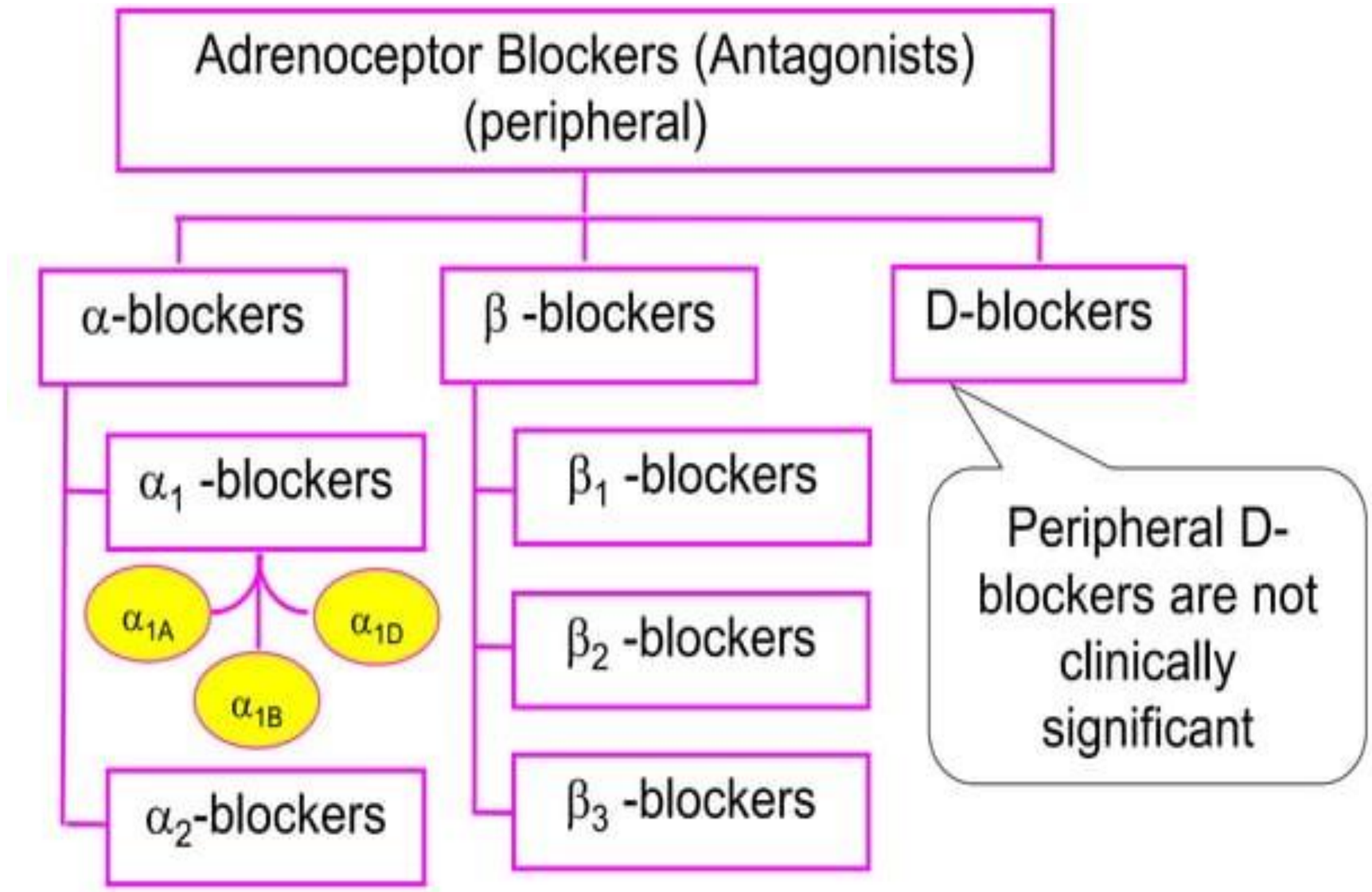
II nd YEAR

TOPIC : ALPHA BLOCKERS

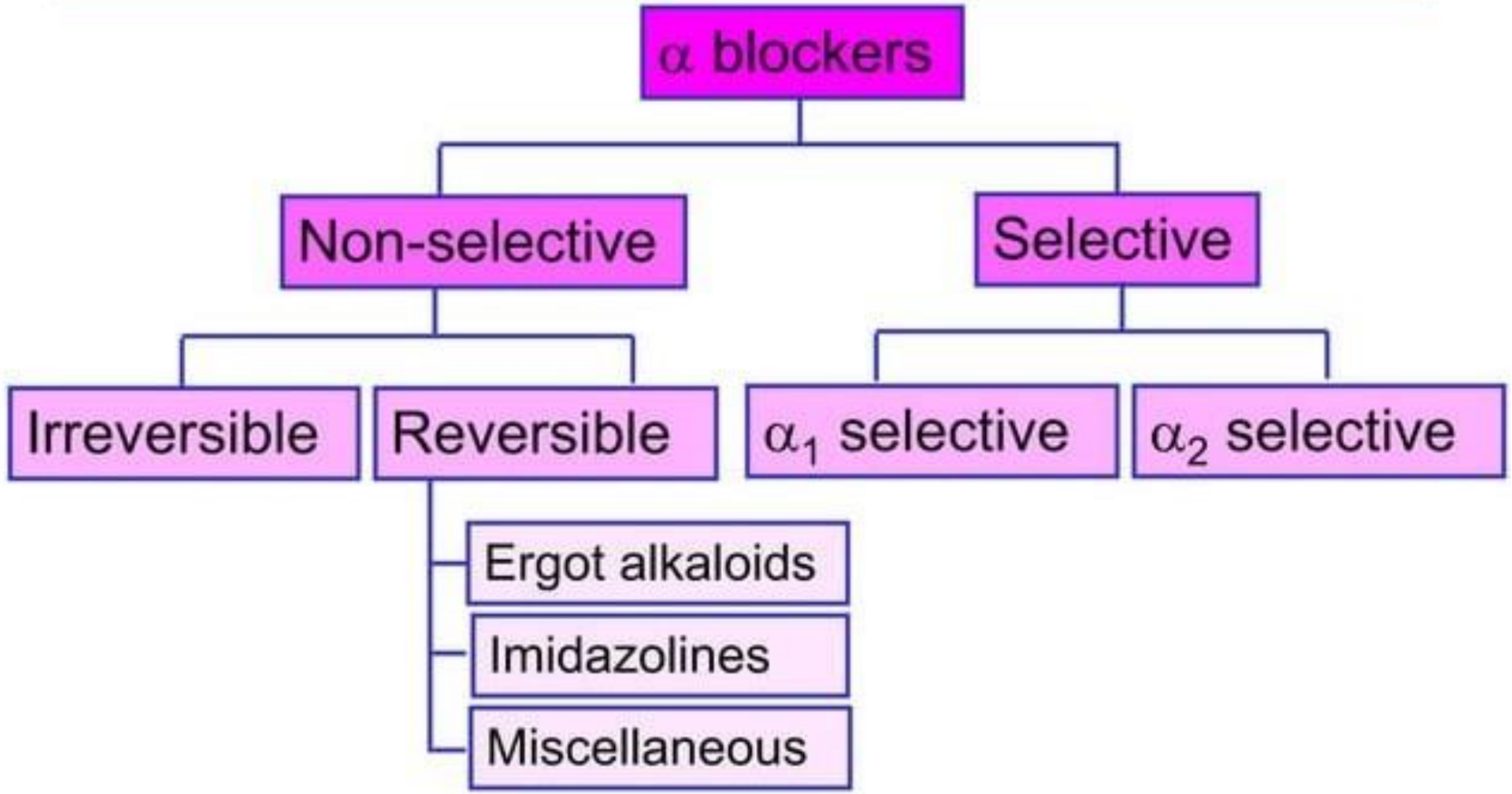
Objectives

- Classify alpha blockers according to the selectivity of receptor subtype
- Describe the mechanism of action and pharmacological actions of alpha blockers
- Discuss the clinical uses and important adverse effects
- Briefly describe individual alpha blockers


Alpha receptors
α_1-receptor
α_2-receptor
Postsynaptic
Presynaptic
Post synaptic
Gq
Gi
Gq
Blood vessels, smooth muscles,
Bladder sphincter, radial muscle of iris.
Liver & skeletal muscle
Inhibit release of NE in synapse
Blood vessels
Contraction


Adrenoceptor Blockers (Antagonists) (peripheral)
α-blockers
β -blockers
D-blockers
α1 -blockers
α1A
α1D
α1B
α2-blockers
β1 -blockers
β2 -blockers
β3 -blockers
Peripheral D-blockers are not clinically significant

Classification of α blockers



Non-selective

Irreversible (Non-equilibrium) type

- β -Haloalkylamines
  - Phenoxybenzamine.

Reversible (Equilibrium type)

Ergot alkaloids

- Ergotamine, ergotoxine
- Dihydroergotamine (DHE),
- Dihydroergotoxine

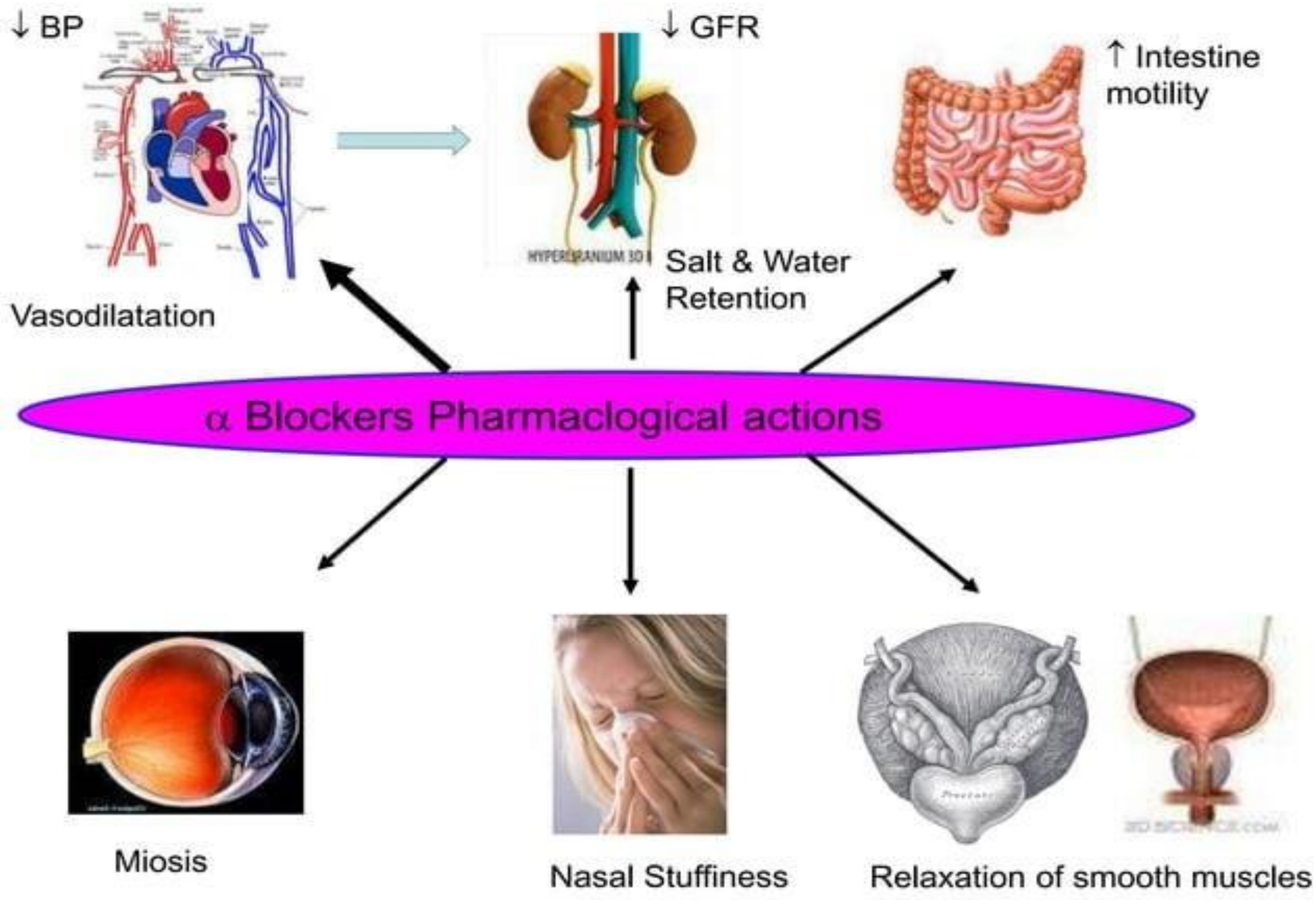
- Imidazolines (α1 = α2)
  - Tolazoline,
  - Phentolamine
- Miscellaneous
  - Chlorpromazine,
  - Ketanserin

Selective (α1-selective)

- Prazosin,
- Terazosin,
- Doxazosin
- Alfuzosin
- Tamsulosin
- Bunazosin
- Urapidil
- Indoramine

Selective (α2-selective)

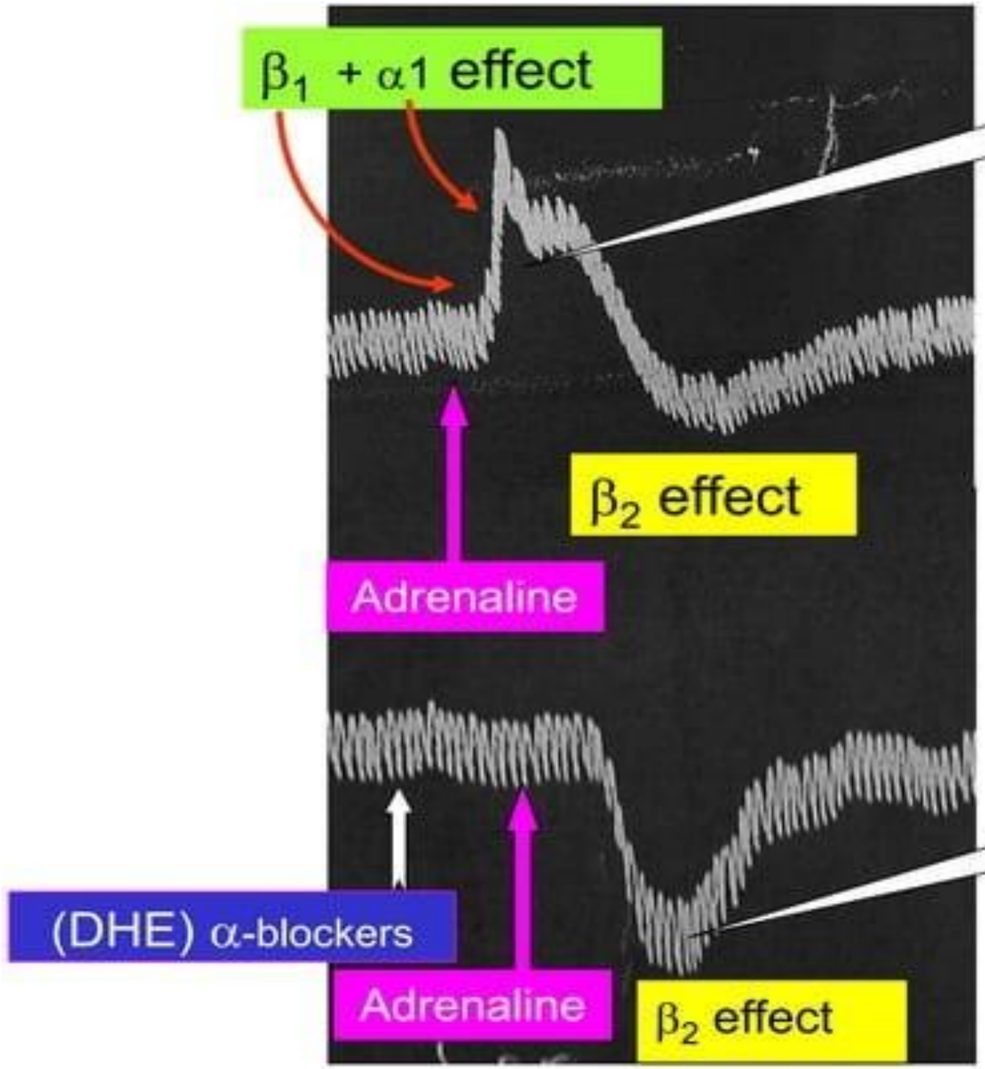
- Yohimbine
- Idazoxan


↓ BP
↓ GFR
↑ Intestine motility
Vasodilatation
Salt & Water Retention
α Blockers Pharmaclogical actions
Miosis
Nasal Stuffiness
Relaxation of smooth muscles

Reversible non selective α blockers

Phentolamine and tolazoline

- Similar affinities for α-1 and α-2
- Cardiovascular effects
  - Vasodilation & reflex tachycardia
  - Postural hypotension
- Other effects
  - Nasal stuffiness
  - Miosis
  - Improved urinary flow rates
  - Failure of ejaculation & impotence
  - Nausea, vomiting and diarrhea



Sir Henry Dale
(1906)

Dales Vasomotor reversal phenomenon

Reversible non selective α blockers

Therapeutic Uses of **Phentolamine**

- Diagnosis & intraoperative management of phaeochromocytoma
- Hypertensive crisis
  - Control hypertension in clonidine withdrawal
  - Cheese reaction
- Peripheral vascular disease (Raynaud`s syndrome & frost bite)
- Extravasation of Noradrenaline / dopamine
- Erectile dysfunction

Tolazoline: less potent, better absorbed from GIT

Irreversible non selective α blockers

Phenoxybenzamine Pharmacological actions

- Slow onset & long duration of action 3-4 days
- Inhibits NE reuptake & also blocks muscarinic, histamine and 5-HT receptors
- CVS effects
  - Similar to phentolamine: ↓BP, tachycardia etc
  - Na^+ & fluid retention
  - CVS effects are not reversed by Catecholamine
- Other effects:
  - Similar to phentolamine
  - Sedation, Fatigue

Therapeutic Uses of Phenoxybenzamine

- Phaeochromocytoma
  - Intraoperatively
  - Treatment of inoperable cases (with metyrosine)
- To treat peripheral vascular disease like Raynaud`s syndrome and frost bite

Reversible, Selective α_1 receptor blockers

- Prazosin,
- Terazosin, Doxazosin
- Bunazosin, Alfuzosin
- Tamsulosin, silodosin (α_{1A}-α_{1D})
- Indoramine, Urapidil

Prazosin

- Cardiovascular effects
  - Vasodilatation → Hypotension
  - Inhibits cyclic phosphodiestase enzyme → ↑cAMP in vascular smooth muscle
  - Less tachycardia than non-selective blockers
    - Does not block pre-synaptic α_2 autoreceptor
    - Decrease cardiac pre-load
    - Suppresses sympathetic outflow from CNS

Pharmacological Effects

Prazosin

- Lipid Profile
  - Rise in HDL level
  - Lowers LDL and triglyceride level
- Genito-urinary System
  - Relaxes smooth muscles in bladder neck, prostate capsule and prostatic urethra → improve in urine flow in benign prostatic hypertrophy.

Therapeutic Uses of prazosin

1. Hypertension

   Advantage: Favorable lipid profile

   Disadvantage: First dose effect

   (1 mg at bed time – titrated upwards)

2. Benign prostatic hyperplasia: symptomatic treatment

   Disadvantage

   - Twice daily dose
   - Postural hypotension

3. Raynaud's Disease

Adverse Effects of prazosin

- Postural hypotension at initial dose (First dose effect) – syncopal attack
- Impotence
- Nasal congestion
- GI Tract upset
- Sodium and Water retention

Terazosin and doxazosin

- Selective alpha 1 blockers with longer duration of action
- Terazosin t ½ = 12 hrs, doxazosin =18 hrs
- Well absorbed orally
- Use:
  - Benign prostatic hyperplasia
    - Preferred due to once daily dosing
    - Apoptosis promoting effect on prostrate
    - Faster action than finasteride

Alfuzosin

- Similar to prazosin
- Used for symptomatic treatment of Benign prostatic hyperplasia

Tamsulosin & sildosin

Tamsulosin

- Relatively uroselective $\alpha 1_A$ / $\alpha 1_D$ blocker
- lacks prostatic apoptosis promoting property
- More efficacious in BPH treatment with little effect on Blood pressure
- Adverse effects:
  - Intraoperative floppy iris during cataract surgery
  - Abnormal ejaculation

Sildosin

  - Selective $\alpha 1_A$ blocker
  - Weaker but longer acting analog of tamsulosin

Subdivision of α_1 Blockers

	α_{1A}	α_{1B}
Location	Bladder neck and urethra	Blood vessels
Block	Relaxation of smooth muscles and opening of urethral urine flow	Relaxation of smooth muscle of blood vessels → vasodilatation

α_2 Adrenergic receptor blocker

Yohimbine

- Natural alkaloid
- Also blocks 5 HT receptors

<u>Therapeutic Use: (Off label)</u>

- Diabetic neuropathy
- Treatment of postural hypertension
- Male sexual dysfunction

Therapeutic uses of Alpha Blockers

- Phaeochromocytoma
- Hypertension
- Benign prostatic hyperplasia
- Peripheral vascular disease
- Papaverine/ phentolamine induced penile erection therapy for impotence

THANK YOU