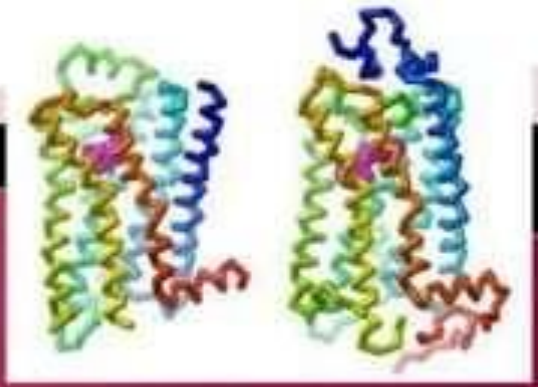
ADRENERGIC AND ANTI-ADRENERGIC DRUGS

BY

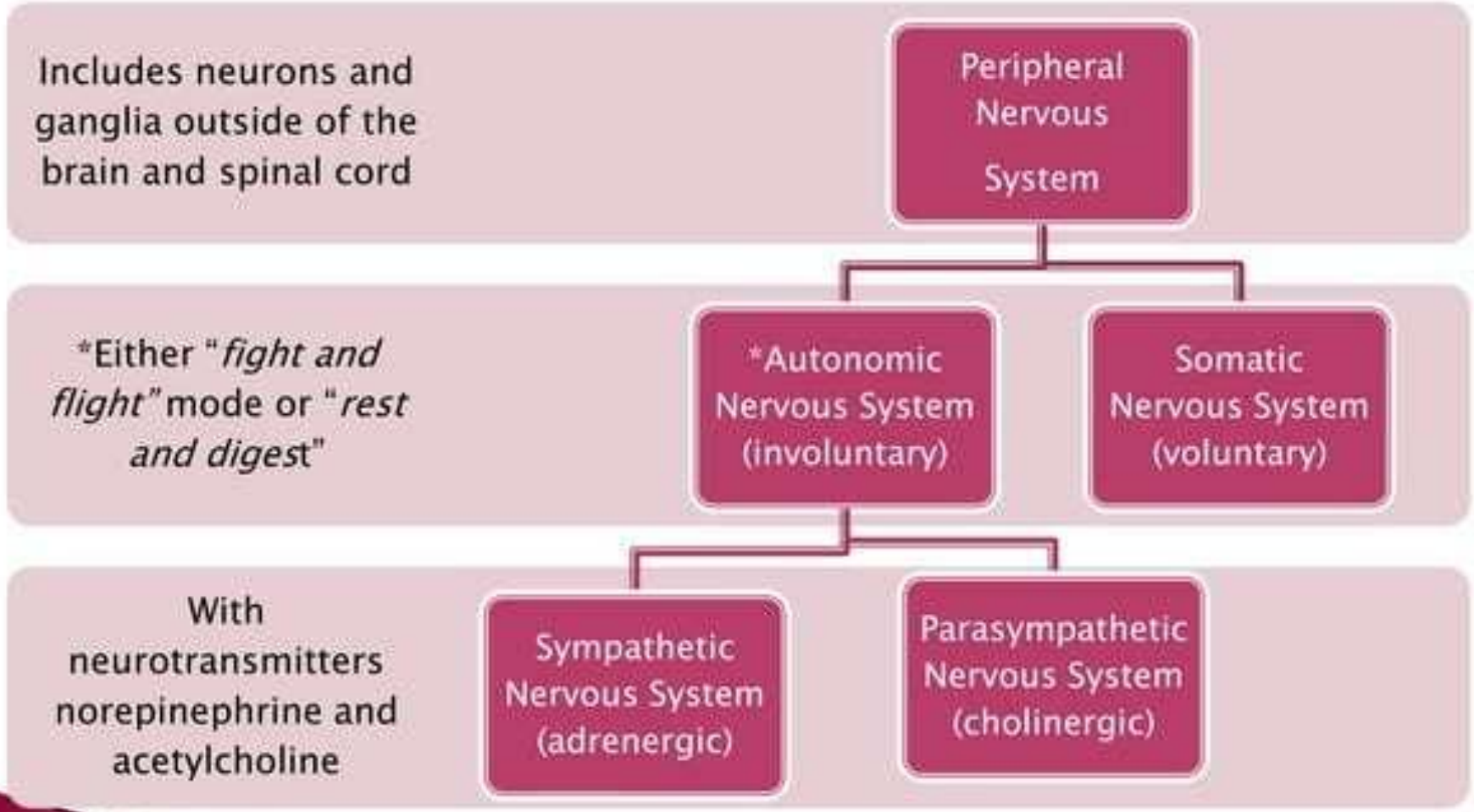
MR.BHAVESH BHARAT AMRUTE

(M.PHARM-PHARMACEUTICAL CHEMISTRY)



DIVISIONS OF HUMAN NERVOUS SYSTEM

NERVOUS SYSTEM



SYMPATHETIC NERVOUS SYSTEM

Fight or flight response results in:

1. Increased BP
2. Increased blood flow to brain, heart and skeletal muscles
3. Increased muscle glycogen for energy
4. Increased rate of coagulation
5. Pupil dilation

ADRENERGIC RECEPTORS

- Alpha—A1 and A2
- Beta—B1, B2, B3
- Dopamine—subsets D1-5

REVIEW OF FUNCTIONS OF SYMPATHETIC NERVOUS SYSTEM RECEPTORS

- Alpha 1—smooth muscle contraction
- Alpha 2-negative feedback causes less norepinephrine to be released so BP is reduced
- Beta 1—increased heart rate
- Beta 2—bronchodilation
- Beta 3—actual site for lipolysis

MECHANISMS OF ACTION AND EFFECTS OF ADRENERGIC DRUGS

- Direct adrenergic drug action
- Affects postsynaptic alpha 1 and beta receptors on target effector organs
- Examples: epinephrine, Isuprel, norepinephrine, phenylephrine

MECHANISMS OF ACTION CONT.

- 2. Indirect adrenergic drug action occurs by stimulation of postsynaptic alpha 1, beta 1 and beta 2 receptors.Cause release of norepinephrine into the synapse of nerve endings or prevent reuptake of norepinephrine.
- Examples include cocaine and TCAs

MECHANISMS OF ACTION CONT.

- 3. mixed action. Combination of direct and indirect receptor stimulation
- Examples are ephedrine and pseudoephedrine

MECHANISMS OF ACTION CONT.

- Stimulation of alpha 2 receptors in CNS is useful in decreasing BP
- Most body tissues have both alpha and beta receptors
- Effect occurs 2ndary to receptor activated and number of receptors in the particular body tissue

MECHANISMS OF ACTION CONT.

- Some drugs act on both receptors--dopamine
- Some are selective--Isuprel

INDICATIONS FOR USE

- Emergency drugs in treatment of acute cardiovascular, respiratory and allergic disorders
- In children, epinephrine may be used to treat bronchospasm due to asthma or allergic reactions
- Phenylephrine may be used to treat sinus congestion

INDICATIONS OF ADRENERGICS CONT.

- Stokes Adams
- Shock
- Inhibition of uterine contractions
- For vasoconstrictive and hemostatic purposes

CONTRAINDICATIONS TO USE OF ADRENERGICS

- Cardiac dysrhythmias, angina pectoris
- Hypertension
- Hyperthyroidism
- Cerebrovascular disease
- Distal areas with a single blood supply such as fingers, toes, nose and ears
- Renal impairment use caution

INDIVIDUAL ADRENERGIC DRUGS

- *Epinephrine*—prototype
- Effects include: increased BP, increased heart rate, relaxation of bronchial smooth muscle, vasoconstriction in peripheral blood vessels

EPINEPHRINE

- Increased glucose, lactate, and fatty acids in the blood due to metabolic effects
- Increased leukocyte and increased coagulation
- Inhibition of insulin secretion

EPINEPHRINE

- Affects both alpha and beta receptors
- Usual doses, beta adenergic effects on heart and vascular smooth muscle will predominate, high doses, alpha adrenergic effects will predominate
- Drug of choice for bronchospasm and laryngeal edema of anaphylaxis

EPINEPHRINE

- Excellent for cardiac stimulant and vasoconstrictive effects in cardiac arrest
- Added to local anesthetic
- May be given IV, inhalation, topically
- Not PO

EPINEPHRINE

- Physiologic antagonist to histamine
- Those on beta blockers may need larger doses
- Drug of choice in PEA. Vasopressin has now become drug of choice in ventricular tachycardia
- Single dose of Vasopressin, 40 units IV

OTHER ADRENERGICS

- Ephedrine is a mixed acting adrenergic drug. Stimulates alpha and beta receptors. Longer lasting than epinephrine.
- See in Primatene mist

PSEUDOPHED

- Used for bronchodilating and nasal decongestant effects

ISUPREL (ISOPROTERENOL)

- Synthetic catecholamine that acts on beta 1 and 2 receptors
- Stimulates heart, dilates blood vessels in skeletal muscle and causes bronchodilation
- No alpha stimulation
- Used in heart blocks (when pacemaker not available) and as a bronchodilator

NEOSYNEPHRINE (PHENYLEPHRINE)

- Pure alpha
- Decreases CO and renal perfusion
- No B1 or B2 effects
- Longer lasting than epinephrine
- Can cause a reflex bradycardia
- Useful as a mydriatic

TOXICITY OF ADRENERGICS IN CRITICALLY ILL PATIENTS

- Affects renal perfusion
- Can induce cardiac dysrhythmias
- Increases myocardial oxygen consumption
- May decrease perfusion of liver
- Tissue necrosis with extravasation

TOXICITY

- Do not give epinephrine and Isuprel at same time or within 4 hours of each other. Could result in serious dysrhythmias.

ANTI-ADRENERGICS

- Sympatholytic
- Block or decrease the effects of sympathetic nerve stimulation, endogenous catecholamines and adrenergic drugs

ANTIADRENERGIC S—MECHANISMS OF ACTION AND EFFECTS

- Can occur by blocking alpha 1 receptors postsynaptically
- Or by stimulation presynaptic alpha 2 receptors. Results in return of norepineprhine to presynaptic site. Activates alpha 2 resulting in negative feedback. Decreases release of additional norepinephrine.

ALPHA-ADRENERGIC AGONISTS AND BLOCKING AGENTS

- Alpha 2 agonists inhibit release of norepinephrine in brain; thus, decrease effects on entire body
- Results in decrease of BP
- Also affects pancreatic islet cells, thus some suppression of insulin secretion

ALPHA 1 ADRENERGIC BLOCKING AGENTS

- Act on skin, mucosa, intestines, lungs and kidneys to prevent vasoconstriction
- Effects: dilation of arterioles and veins, decreased blood pressure, pupillary constriction, and increased motility of GI tract

ALPHA 1 ADRENERGIC BLOCKING AGENTS

- May activate reflexes that oppose fall in BP such as fluid retention and increased heart rate
- Can prevent alpha medicated contraction of smooth muscle in nonvascular tissues
- Thus, useful in treating BPH as inhibit contraction of muscles in prostate and bladder

ALPHA 1 ANTAGONISTS

- Minipress (prazosin)—prototype.
- Hytrin (terazosin) and Cardura (doxazosin)—both are longer acting than Minipress.

ALPHA 1 ANTAGONISTS CONT.

- Flomax (tamsulosin). Used in BPH. Produces smooth muscle relaxation of prostate gland and bladder neck. Minimal orthostatic hypotension.
- Priscoline (tolaxoline) used for vasospastic disorders. Pulmonary hypertension in newborns. Can be given sub Q, IM or IV.

ALPHA 2 AGONISTS

- Catapres (clonidine). PO or patch.
- Tenex (guanfacine)
- Aldomet (methyldopa). Can give IV. Caution in renal and hepatic impairment.

BETA ADRENERGIC BLOCKING MEDICATIONS

- Prevent receptors from responding to sympathetic nerve impulses, catecholamines and beta adrenergic drugs.

EFFECTS OF BETA BLOCKING DRUGS

- Decreased heart rate
- Decreased force of contraction
- Decreased CO
- Slow cardiac conduction
- Decreased automaticity of ectopic pacemakers

EFFECTS OF BETA BLOCKING DRUGS

- Decreased renin secretion from kidneys
- Decreased BP
- Bronchoconstriction
- Less effective metabolism of glucose. May result in more pronounced hypoglycemia and early s/s of hypoglycemia may be blocker (tachycardia)

EFFECTS OF BETA BLOCKING AGENTS

- Decreased production of aqueous humor in eye
- May increase VLDL and decrease HDL
- Diminished portal pressure in clients with cirrhosis

INDICATIONS FOR USE

- Alpha 1 blocking agents are used for tx of hypertension, BPH, in vasospastic disorders, and in persistent pulmonary hypertension in the newborn
- May be useful in treating pheochromocytoma
- May be used in Raynaud's or frostbite to enhance blood flow

REGITINE (PHENTOLAMINE)

- Used for extravasation of potent vasoconstrictors (dopamine, norepinephrine) into subcutaneous tissues.

INDICATIONS FOR USE

- Alpha 2 agonists are used for hypertension—Catapres
- Epidural route for severe pain in cancer
- Investigationally for anger management, alcohol withdrawal, postmenopausal hot flashes, ADHD, in opioid withdrawal and as adjunct in anesthesia

BETA BLOCKING MEDICATIONS

- Mainly for cardiovascular disorders (angina, dysrhythmias, hypertension, MI and glaucoma)
- In angina, beta blockers decrease myocardial oxygen consumption by decreasing rate, BP and contractility. Slow conduction both in SA node and AV node.

BETA BLOCKERS

- Possibly work by inhibition of renin, decreasing cardiac output and by decreasing sympathetic stimulation
- May worsen condition of heart failure as are negative inotropes
- May reduce risk of "sudden death"

BETA BLOCKERS

- Decrease remodeling seen in heart failure
- In glaucoma, reduce intraocular pressur by binding to beta-adrenergic receptors in ciliary body, thus decrease formation of aqueous humor

BETA BLOCKERS

- Inderal (propranolol) is prototype
- Useful in treatment of hypertension, dysrhythmias, angina pectoris, MI
- Useful in pheochromocytoma in conjunction with alpha blockers (counter catecholamine release)
- migraines

BETA BLOCKERS

- In cirrhosis, Inderal may decrease the incidence of bleeding esophageal varices
- Used to be contraindicated in heart failure, now are standard
- Known to reduce sudden death
- Often given with ACEIs
- Indications include: htn, angina, prevention of MI

RECEPTOR SELECTIVITY

- Acetutolol, atenolol, betaxolol, esmolol, and metoprolol are relatively cardioselective
- These agents lose cardioselection at higher doses as most organs have both beta 1 and beta 2 receptors
- Byetta is new agent that is cardioselective

Non-Receptor selectivity

- Carteolol, levobunolol, metipranolol, nadolol, propranolol, sotalol and timolol are all non-selective
- Can cause bronchoconstriction, peripheral vasoconstriction and interference with glycogenolysis.

COMBINATION SELECTIVITY

- Labetalol and carvedilol (Coreg) block alpha 1 receptors to cause vasodilation and beta 1 and beta 2 receptors which affect heart and lungs
- Both alpha and beta properties contribute to antihypertensive effects
- May cause less bradycardia but more postural hypotension
- Less reflex tachycardia

INTRINSIC SYMPATHOMIMETIC ACTIVITY

- Have chemical structure similar to that of catecholamines
- Block some beta receptors and stimulate others
- Cause less bradycardia
- Agents include: Sectral (acebutolol), Cartrol (carteolol), Levatol (penbutolol) and Visken (pindolol)

SPECIFIC CONDITIONS-ALPHA AGONISTS AND ANTAGONISTS

- In tx for BPH, patient should be evaluated for prostate cancer
- With alpha 2 agonists, sudden cessation can cause rebound BP elevation
- With alpha 1 blockers, first dose syncope may occurr from hypotension. Give low starting dose and at hs. May also cause reflex tachycardia and fluid retention.

SPECIFIC CONDTIONS-BETA BLOCKERS

- With significant bradycardia, may need med with ISA such as pindolol and penbutolol
- Patient with asthma, cardioselectivity is preferred
- For MI, start as soon as patient is hemodynamically stable

SPECIAL CONDITIONS—BETA BLOCKERS

- Should be discontinued gradually. Long term blockade results in increase receptor sensitivity to epinephrine and norepinephrine. Can result in severe hypertension. Taper 1-2 weeks.

ETHNIC CONSIDERATIONS

- Monotherapy in African Americans is less effective than in Caucasians.
- Trandate (labetalol) with both alpha and beta effects has been shown to be more effective in this population than Inderal, Toprol or timolol.

THANK YOU….!