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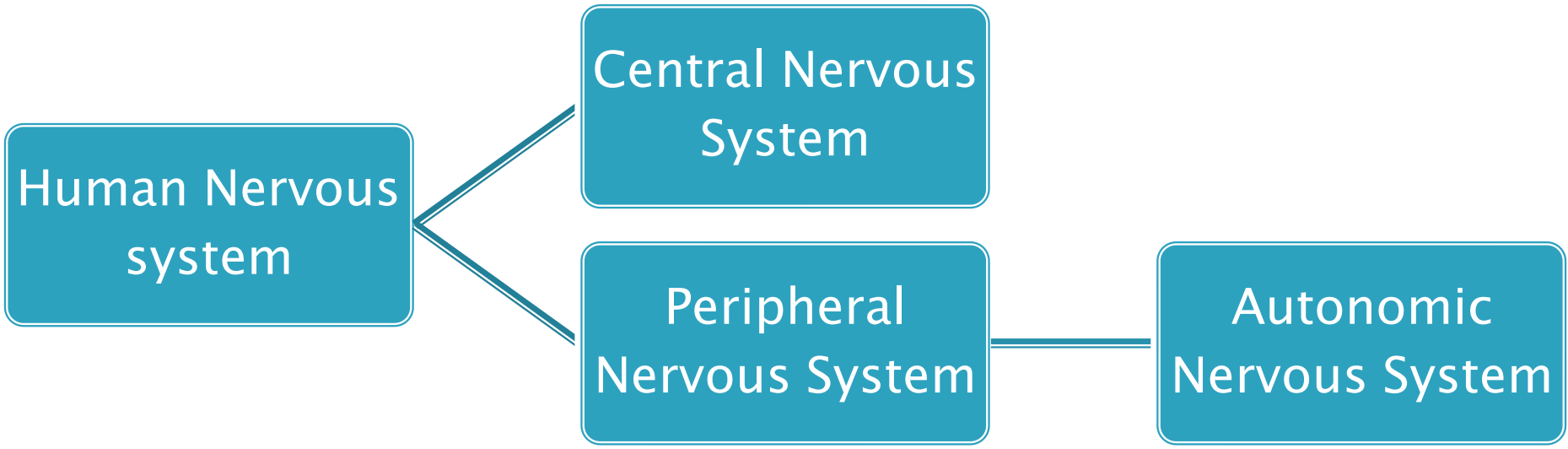
Designation: Professor
Department: Pharmacy
Subject: Pharmacology-I (BP 404T)
Unit: III
Topic: Organization and function of ANS

Divisions of human nervous system

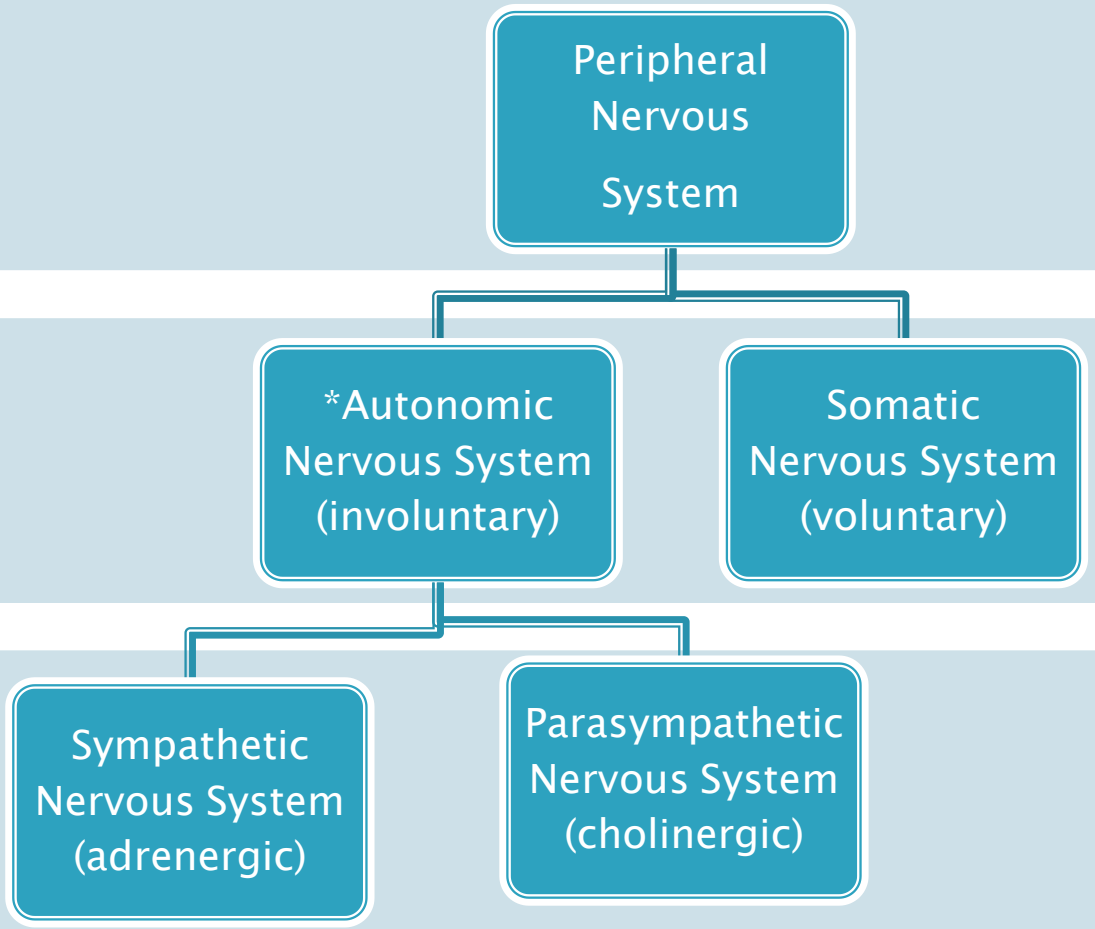


Nervous system

Includes neurons and ganglia outside of the brain and spinal cord

*Either "*fight and flight*" mode or "*rest and digest*"

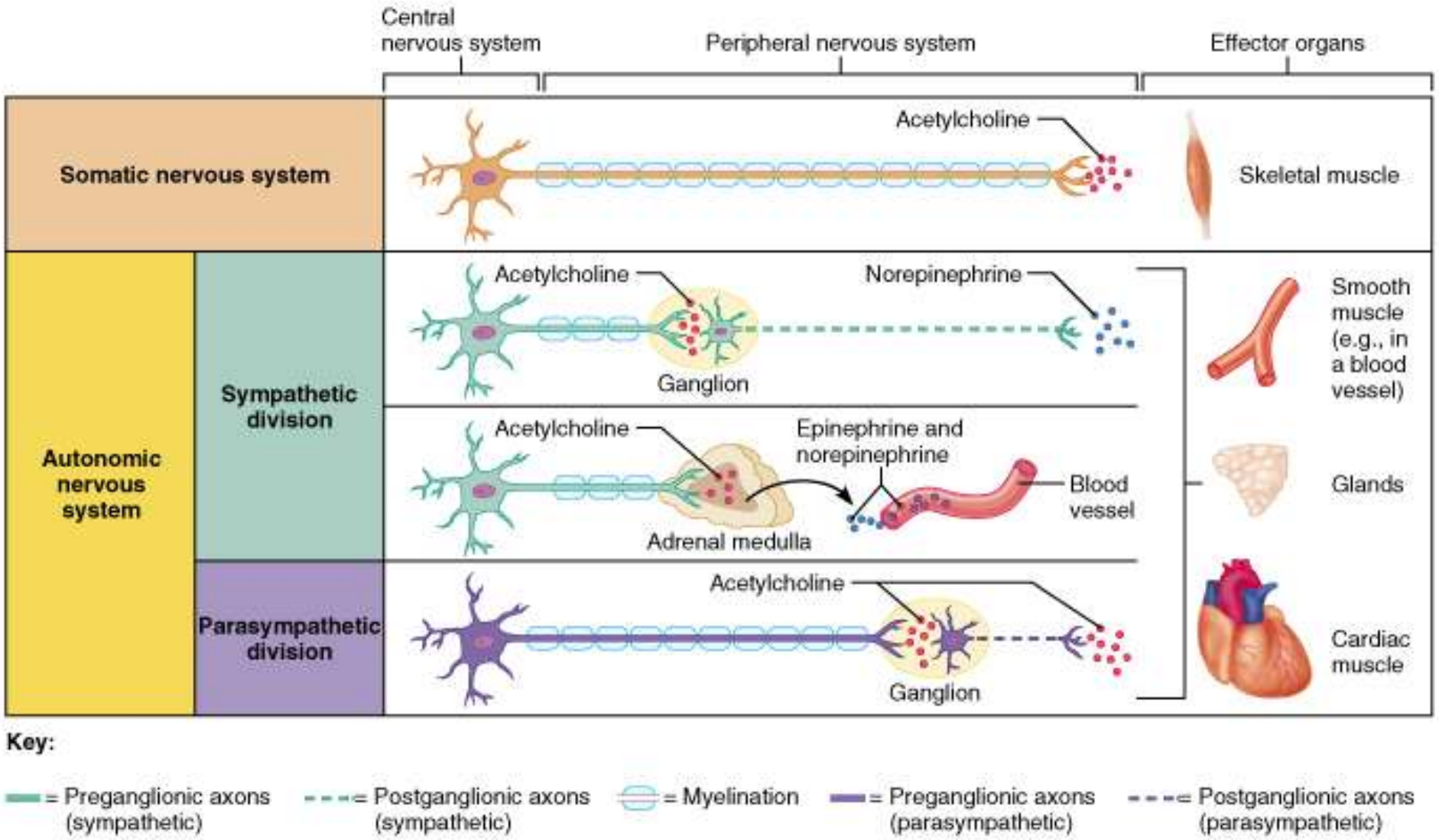
With neurotransmitters norepinephrine and acetylcholine

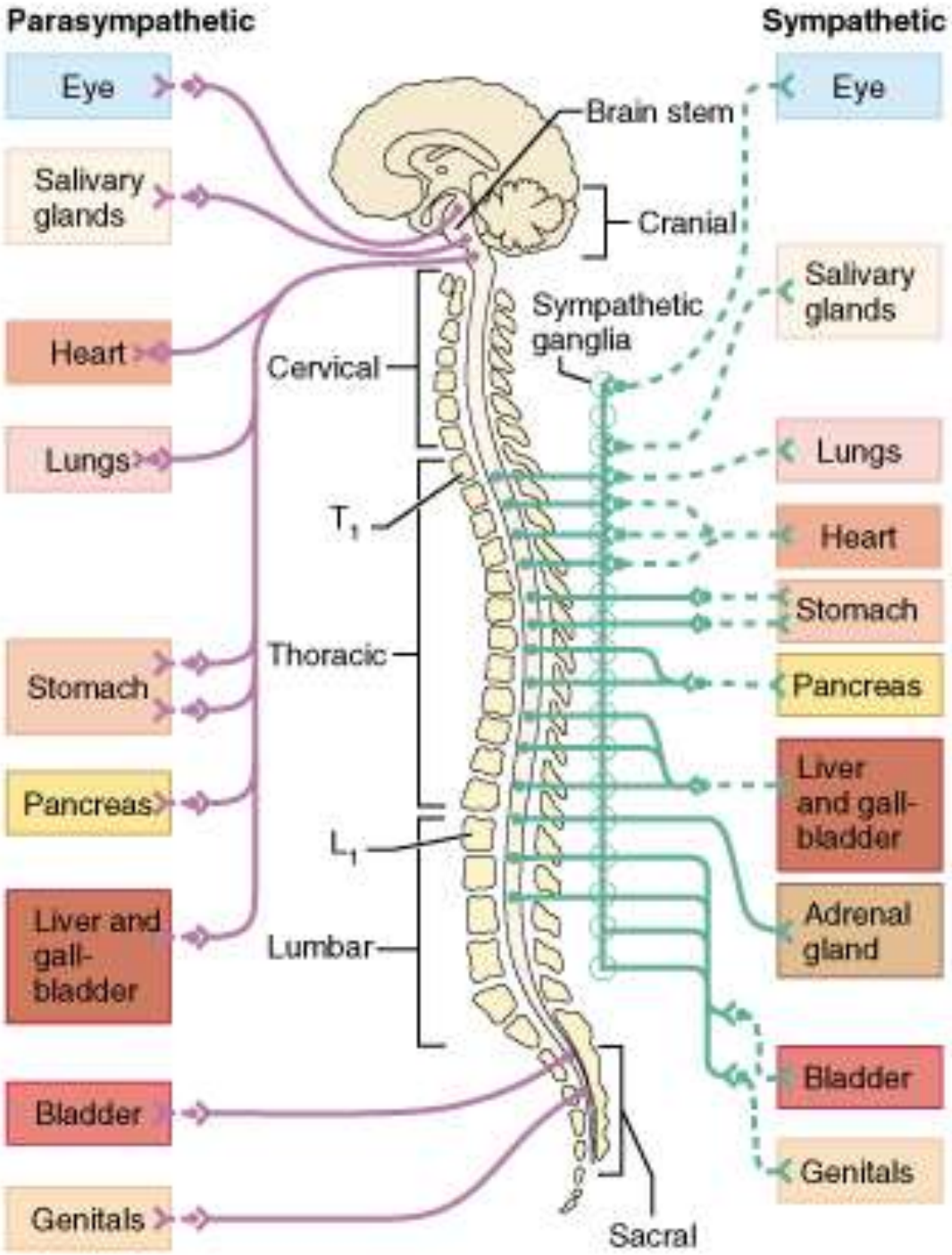


Sympathetic vs. Parasympathetic

Structural Differences:

	Symp.	Parasymp.
Point of CNS Origin	T1 → L2 (thoracolumbar)	Brainstem, S2 → S4 (craniosacral)
Site of Peripheral Ganglia	Paravertebral – in sympathetic chain	On or near target tissue
Length of preganglionic fiber	Short	Long
Length of postganglionic fiber	Long	Short


Central nervous system
Peripheral nervous system
Effector organs
Somatic nervous system
Acetylcholine
Skeletal muscle
Autonomic nervous system
Sympathetic division
Acetylcholine
Norepinephrine
Ganglion
Smooth muscle (e.g., in a blood vessel)
Acetylcholine
Epinephrine and norepinephrine
Blood vessel
Adrenal medulla
Glands
Parasympathetic division
Acetylcholine
Ganglion
Cardiac muscle
Key:
= Preganglionic axons (sympathetic)
= Postganglionic axons (sympathetic)
= Myelination
= Preganglionic axons (parasympathetic)
= Postganglionic axons (parasympathetic)


Parasympathetic
Sympathetic
Eye
Salivary glands
Heart
Lungs
Stomach
Pancreas
Liver and gall-bladder
Bladder
Genitals
Brain stem
Cranial
Cervical
Thoracic
Lumbar
Sacral
Sympathetic ganglia
T_1
L_1
Eye
Salivary glands
Lungs
Heart
Stomach
Pancreas
Liver and gall-bladder
Adrenal gland
Bladder
Genitals

Autonomic Nervous System

- Central Nervous System (CNS) – Brain and spinal cord
- Peripheral Nervous System (PNS) – Located outside the brain & spinal cord
  * Autonomic Nervous System (ANS) & the somatic
- The PNS receives stimuli from the CNS & initiates responses to the stimuli after it's interpreted by the brain

Autonomic Nervous System

- ANS acts on smooth muscles & glands
  - Controls & regulation of the heart, respiratory. system, GI tract, bladder, eyes & glands
  - Involuntary – person has little or no control
- Somatic – voluntary – person has control (skeletal muscle)

ANS

- ANS has 2 sets of neurons:

1. Afferent (sensory) – sends impulses to the CNS for interpretation
2. Efferent – receives impulses (info.) from the brain & transmits from the spinal cord to the effector organ cells
   - 2 branches – sympathetic & parasympathetic nervous system

Figure 20-2.
Sympathetic and Parasympathetic Effects on Body Tissues

BODY TISSUE/ORGAN	SYMPATHETIC RESPONSE*	PARASYMPATHETIC RESPONSE*
Eye 	Dilates pupils	Constricts pupils
Lungs 	Dilates bronchioles	Constricts bronchioles and increases secretions
Heart 	Increases heart rate	Decreases heart rate
Blood vessels 	Constricts blood vessels	Dilates blood vessels
Gastrointestinal 	Relaxes smooth muscles of gastrointestinal tract	Increases peristalsis
Bladder 	Relaxes bladder muscle	Constricts bladder
Uterus 	Relaxes uterine muscle	
Salivary gland 		Increases salivation

*The sympathetic and parasympathetic nervous systems have opposite responses on body tissues and organs.

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

ANS – Sympathetic nervous system (Adrenergic)

- Sympathetic Nervous System (adrenergic) Norepinephrine = neurotransmitter
- Drugs that mimic = adrenergic drugs, sympathomimetics, or adrenomemetics
  * Adrenergic agonists – Drugs initiate a response
- Drugs that block = adrenergic blockers, sympatholytics or adrenolytics
  * Adrenergic antagonists – prevent a response

Adrenergic receptors

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

ANS

- 4 types of adrenergic receptor organ cells:

1. Alpha-1 = vasoconstriction of blood vessels
   inc. blood return to heart, inc. circulation, inc. BP
2. Alpha-2 = inhibits release of norepinephrine
   dec. in vasoconstriction, dec. BP
3. Beta-1 = inc. in heart rate & force on contraction
4. Beta-2 = relaxation of smooth muscle in bronchi, uterus, peripheral blood vessels

Dopaminergic = dilate vessels, inc. in blood flow - only dopamine activates this receptor

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

ANS – Parasympathetic Nervous System (Cholinergic)

- Parasympathetic or Cholinergic Nervous System

  Acetylcholine = neurotransmitter

  – Drugs that mimic = cholinergic drugs, parasympathomimetics

  Cholinergic agonists – initiates a response

  – Drugs that block = anticholinergic, parasympatholytics

  Cholinergic antagonists – prevents a response

ANS

- Sympathomimetic pathway

Norepinephrine

From adrenergic fiber

Inc. heart rate

Pupil dilation

Adrenergic (sympathomimetic) agents

Fight or Flight

- Parasymathomimetic pathway

Acetylcholine

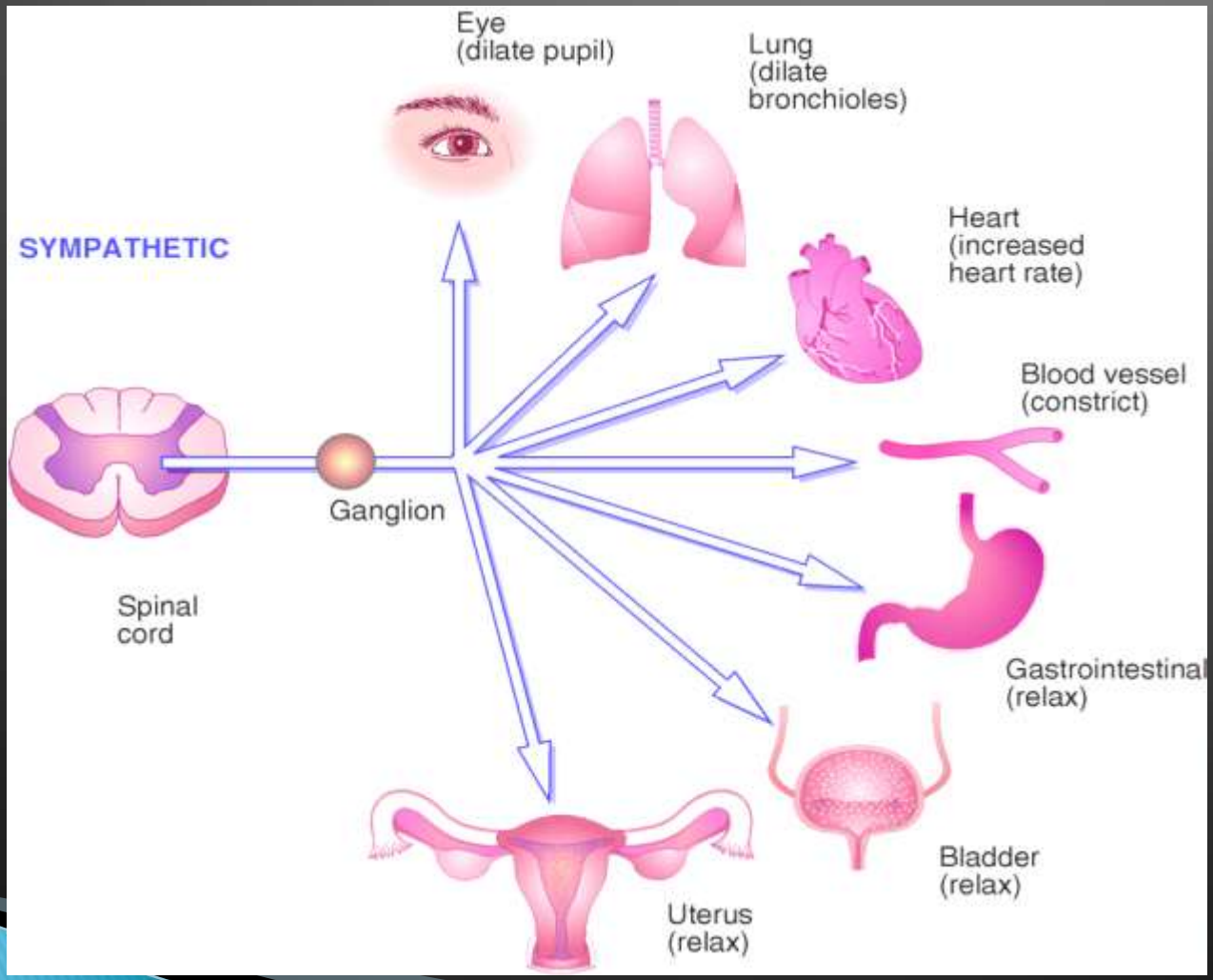
From cholinergic fibers

Dec. heart rate

pupil constriction

Cholinergic (parasympathomimetic agents)

SYMPATHETIC RESPONSES



Sympathomimetics / Adrenomimetics

- Stimulate adrenergic receptors: 3 categories

1. Direct-acting = directly stimulates receptors
   (epinephrine or norepinephrine)
2. Indirect-acting = stimulates release of norep. from terminal nerve endings (amphetamine)
3. Mixed-acting (indirect & direct) = stimulates receptor sites & release of norep. from nerve endings (Ephedrine)

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

Sympathomimetic Agents/ Adrenergics

- Action – Many of the adrenergic drugs stimulate more than one of the adrenergic receptor sites (alpha & Beta)
- Response = Inc. BP, pupil dilation, inc. HR, & bronchodilation
- Use = Cardiac stimulation, bronchodilator, decongestant
- Side effects = Hyperness in body

Sympathomimetics/Adrenergics

- Albuterol – Beta-2 agonist (bronchodilation)
  Use – bronchospasm, asthma, bronchitis
  SE – nervousness, restlessness
  CI – severe cardiac disease, HTN
- Epinephrine – stimulates alpha & beta
  Use – allergic reaction, cardiac arrest
  SE – nervousness, agitation
  CI – cardiac dysrhythmias

Adrenergic Agents

- Dopamine – alpha-1 & beta-1 stimulation

  Use – Hypotension, shock, inc. cardiac output, improve perfusion to vital organs

  SE – N & V, headache

  CI – V. Tach

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

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

Other adrenergics

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

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

Adrenergic Blockers (antagonists/sympatholytics)

- Block alpha & beta receptor sites (nonselective)
- direct or indirect acting on the release of norepinephrine and epinephrine
- Use – Cardiac arrthymias (HR), HTN (cardiac output), angina (O2 demand)
- SE – CHF, bronchospasm, bradycardia, wheezing

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

Nonselective vs Selective Beta blockers

- Nonselective have an equal inhibitory effect on B1 & B2 receptors –
  - Drugs have lots of interactions due to lots of alpha/beta receptor sites throughout body
  - use with caution on clients with cardiac failure or asthma
- Selective B1 helpful in asthma clients

Effects of beta blocking drugs

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

Adrenergic Blocking Agents

- Inderal (Propranolol) – Nonselective
  Use – angina, dysrhythmias, HTN, migraines
  SE – Many d/t nonselective
  CI – asthma, heart block > 1st degree
- Minipress (Prazosin) – A blocker
  Use – mild to mod. HTN
  SE – orthostatic hypotension
- Tenormin (Atenolol), Lopressor (Metoprolol)
  B1 (cardio) selective
  Use – mild to mod HTN, angina

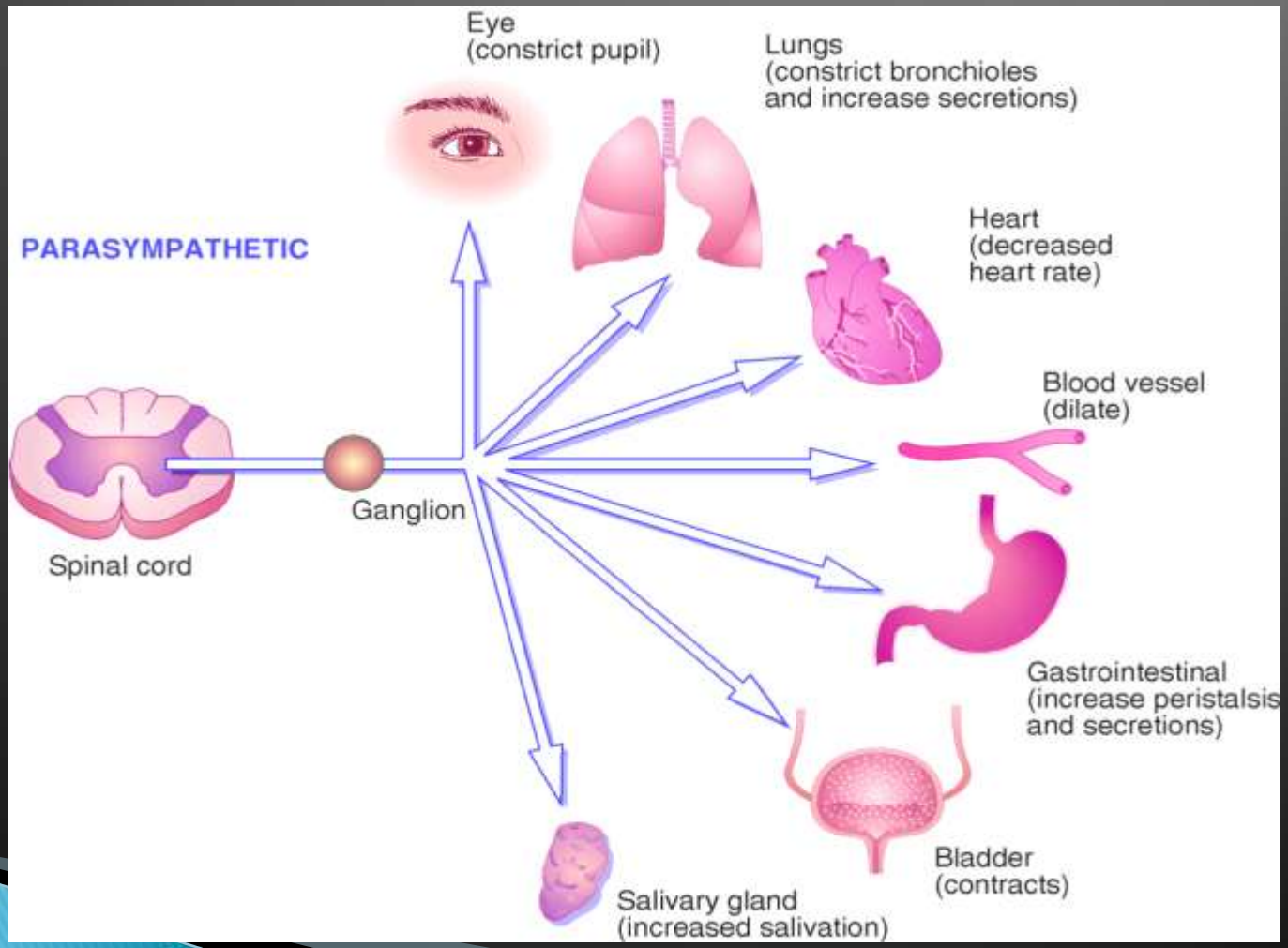
Indications for use

- 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

: Cholinergics and Anticholinergics

- Cholinergics stimulate the parasympathetic nervous system
- Mimic the neurotransmitter acetylcholine
- 2 types of cholinergic receptors
  1. muscarinic – stimulates smooth muscle & slows HR
  2. nicotinic – affect skeletal muscle
- Many = nonselective & affect both receptors
- Some affect only the muscarinic receptors and not the nicotinic receptors

Parasympathetic Responses



Cholinergic Agents

- Direct acting – act on the receptors to activate a tissue response
- Indirect acting – inhibit the action of the enzyme cholinesterase (acetylcholinesterase – ACH)
- Major uses = Stimulate bladder & GI tone, constrict pupils (miosis), neuro-muscular transmission

Drug Effects of Cholinergic Agents

"SLUDGE"

- Salivation
- Lacrimation
- Urinary incontinence
- Diarrhea
- Gastrointestinal cramps
- Emesis

Drug Effects of Cholinergic Agents

- At recommended doses, the cholinergics primarily affect the MUSCARINIC receptors.
- At high doses, cholinergics stimulate the NICOTINIC receptors.

Adrenergic Agents: Mechanism of Action

- Direct-acting (agonist)
  - Bind to cholinergic receptors, causing stimulation

Adrenergic Agents: Mechanism of Action

- Indirect-acting
  - Inhibit the enzyme “cholinesterase”

    Result: more ACh is available at the receptors

Indirect-Acting Cholinergic Agents (Cholinesterase Inhibitors)

- Reversible
  - Bind to cholinesterase for a period of minutes to hours
- Irreversible
  - Bind to cholinesterase and form a permanent covalent bond
  - The body must make new cholinesterase

Cholinergic Agents: Therapeutic Uses

Direct-Acting Agents

- Reduce intraocular pressure
- Useful for glaucoma and intraocular surgery

Examples: acetylcholine, carbachol, pilocarpine

Topical application due to poor oral absorption

Cholinergic Agents: Therapeutic Uses

Direct-Acting Agent—bethanechol

- Increases tone and motility of bladder and GI tract
- Relaxes sphincters in bladder and GI tract, allowing them to empty
- Helpful for postsurgical atony of the bladder and GI tract

Oral dose or SC injection

Cholinergic Agents: Therapeutic Uses

Indirect-Acting Agents

- Cause skeletal muscle contractions
- Used for diagnosis and treatment of myasthenia gravis
- Used to reverse neuromuscular blocking agents
- Used to reverse anticholinergic poisoning (antidote)

  Examples: physostigmine, pyridostigmine

Cholinergic Agents: Side Effects

Side effects are a result of overstimulation of the PSNS.

- Cardiovascular:
  - Bradycardia, hypotension, conduction abnormalities (AV block and cardiac arrest)
- CNS:
  - Headache, dizziness, convulsions
- Gastrointestinal:
  - Abdominal cramps, increased secretions, nausea, vomiting