# AUTONOMIC NERVOUS SYSTEM

Kenneth Alonso, MD, FACP

# Central autonomic network

- Nucleus of the solitary tract receives visceral input from CN VII, IX, X.
- Relayed to forebrain via parabrachial nucleus
- Surrounds superior cerebellar peduncle in upper pons and provides input to hypothalamus, periacqueductal gray matter, amygdala, ventroposterior parvocellular nucleus of the thalamus, anterior insula and infralimbic area of the anterior cingulate cortex.
- The periacqueductal gray receives inputs from hypothalamus, nucleus of the solitary tract, and parabrachial nucleus
- Projects to medullary reticular formation.

# Central autonomic network

- Hypothalamus integrates autonomic and endocrine functions with behavior.
- Compares sensory information with set points.
- Medial forebrain bundle.
- Periventricular fiber system links hypothalamus to periacqueductal gray (sterotyped behavioral patterns).
- Axons from parvocelluar neurons (releasing hormones) as well as paraventricular and arcuate nuclei conveyed to median eminence for control of anterior pituitary
- Axons from the magnocellular neurons (oxytocin, vasopressin) which continue down the pituitary stalk also meet in the median eminence.

# Central autonomic pathways

- Central autonomic pathways descend beside the intermediate gray matter.
- They originate in part from the hypothalamus and in part from nuclear groups in the brainstem.
- They terminate in the intermediolateral cell columns that give rise to the preganglionic sympathetic and parasympathetic fibers of the peripheral autonomic system.
- The central sympathetic system is required for normal baroceptor reflex activity.
- The central parasympathetic pathway is required for bladder and bowel function.

# Adrenergic cell groups

- Noradrenergic neurons are located in one dorsal and one ventral column.
- The ventral column contains neurons associated with the nucleus ambiguus. T
- The dorsal column contains neurons from the dorsal motor vagal nucleus and the solitary tract nucleus. Both project to the hypothalamus and control cardiovascular and endocrine functions.
- The locus ceruleus in the periacqueductal gray matter provides major ascending output to the cortex as well as descending projections to the brain stem, cerebellum, and spinal cord.

# Adrenergic cell groups

- Neurons located more ventrolaterally in the periacqueductal gray as well as those along the ventrolateral margin of the pontine tegmentum mainly innervate the brain stem and spinal cord.
- Modulate pain perception.
- Adrenergic projections arise in the ventrolateral medulla near the nucleus ambiguus and project to the spinal cord (sympathetic preganglionic column providing tonic excitatory input to vasomotor neurons) as well as to the hypothalamus
- Modulate cardiovascular and endocrine responses

# Adrenergic cell groups

- Adrenergic projections arising in the nucleus of the solitary tract project to the parabrachial nucleus (gastrointestinal).
- Neuropeptide Y, somatostatin, enkephalins are also neurotransmitters found in adrenergic ganglia.

# Dopaminergic cell groups

- Dopaminergic neurons in the substantia nigra, the adjacent retrorubral field, and ventral tegmental area provide a major ascending pathway that terminates in the striatum, the frontal temporal cortex, and the limbic system (including the amygdala and lateral septum).
- Dopaminergic neurons from the locus ceruleus project to the ventral tegmental area
- Ventral tegmental area to habenula as well as parabrachial nucleus (adjacent to locus ceruleus)

# Dopaminergic cell groups

- Hypothalamic dopaminergic neurons in zona incerta provide long descending pathways to the autonomic areas of the lower brain stem and the spinal cord.
- Also project to thalamus.
- Those located along the wall of the 3$^{rd}$ ventricle are involved with endocrine control.
- Dopaminergic neurons also found in retina and olfactory bulb

# Serotonergic cell groups

- Most serotonergic neurons are located along the midline of the brain stem in the raphe nuclei.
- Neurons from the raphe magnus, pallidus, and obscuris nuclei in the caudal medulla project to the motor and autonomic systems in the spinal cord.
- Neurons from the raphe magnus nucleus at the level of the rostral medulla project to the spinal dorsal horn and is thought to modulate the perception of pain.
- Neurons in the raphe nucleus in the pons and midbrain project to nearly all of the forebrain.

# Cholinergic cell groups

- Cholinergic cell groups in the basal forebrain include the medial septum, diagonal band, and the nucleus basalis of Meynert.
- These topographiccaly innervate the entire cerebral cortex and hippocampus and amygdala.
- Pontine cholnergic cellgroups innervate the brain stem reticular formation as well as the thalamus.
- The pedunculopointine nucleus is located ventrolaterally near the superior serebellar peduncle
- Controls firing of glycinergic neurons in the lateral reticulospinal pathway.

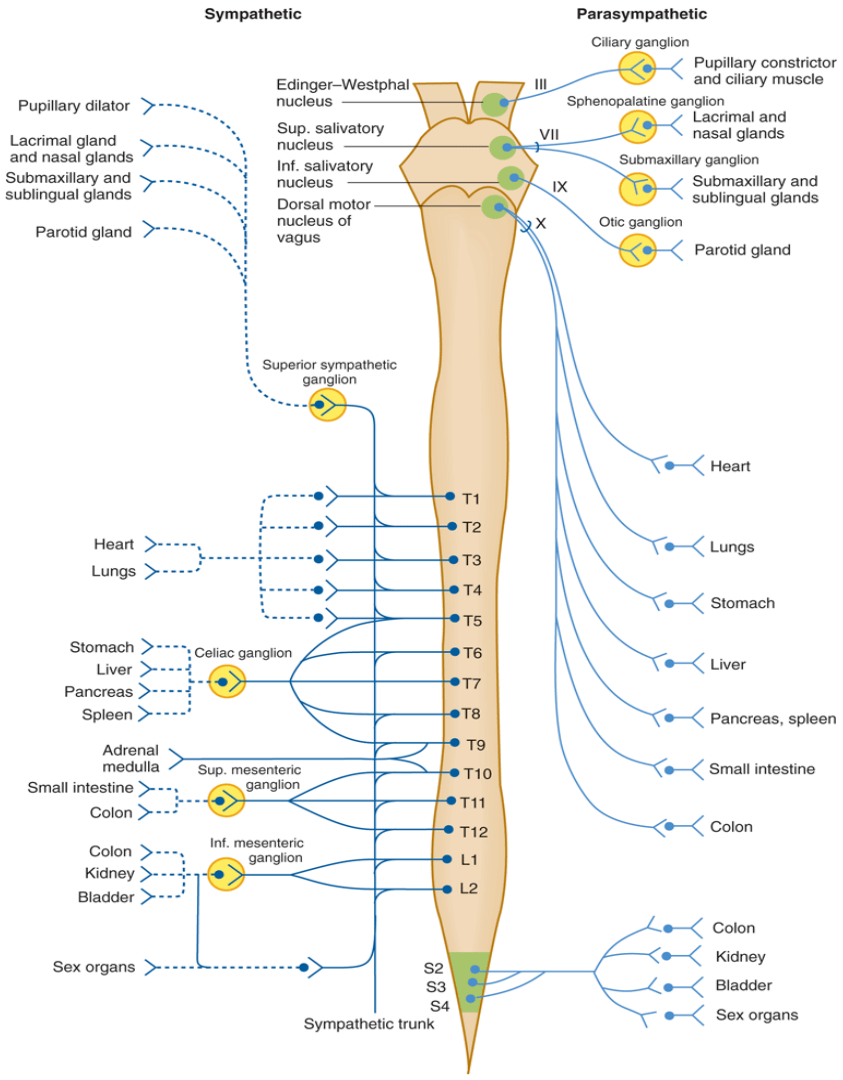
# Cholinergic cell groups

- The laterodorsal tegmental nucleus is a component of the periacqueductal gray matter just rostral to the locus ceruleus.
- VIP, substance P are neurotransmitters also found in cholinergic ganglia.

# Histaminergic cell groups

- All of the histaminergic cells in the brain are clustered in the tuberomammillary nucleus in the posterior lateral hypothalamus.
- One cluster is located ventrolaterally along the edge of the brain
- Another is located dorsomedially along the edge of the mammillary recess of the third ventricle.
- Histaminergic neurons innervate the entire neuraxis.

# Autonomic nervous system




Source: Waxman SG: *Clinical Neuroanatomy, 26th Edition*: http://www.accessmedicine.com



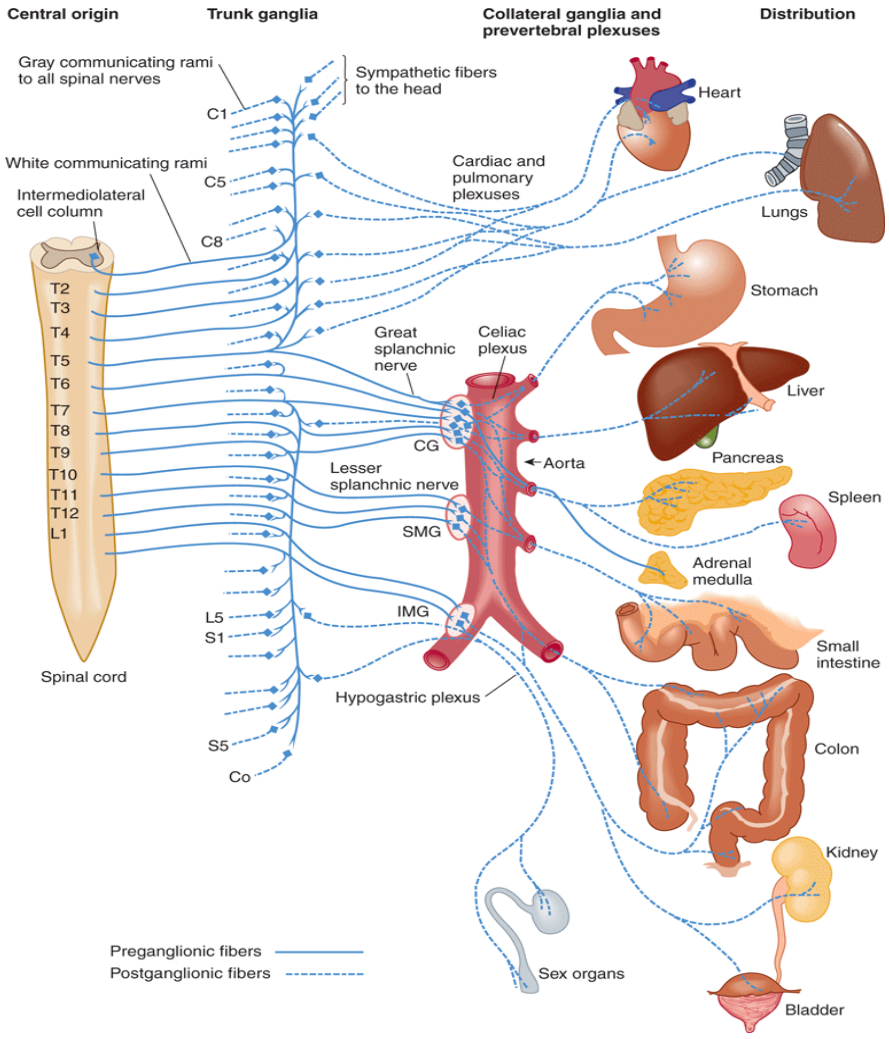
Overview of the sympathetic nervous system and of its sympathetic (thoracolumbar) and parasympathetic (craniosacral) divisions. Inf., inferior; Sup., superior.

Fig. 20-1 Accessed 07/01/2010

# Sympathetic innervation

- Head and Neck T1-4
- Heart T1-5
- Lungs T2-7
- Arms T5-7
- GI Tract
- Proximal to Ligament of Treitz T5-9
- Ligament of Treitz to splenic flexure T9-12
- Distal to splenic flexure T12-L2
- The spinal cord and sympathetic chain ganglia terminate at L2.
- All the sympathetic pre-ganglionic cell bodies are located in the lateral horn of the spinal cord segments T1 – L2.

# Sympathetic nervous system






Sympathetic division of the autonomic nervous system (left half). CG, celiac ganglion; IMG, inferior mesenteric ganglion; SMG, superior mesenteric ganglion.

Fig. 21-2 Accessed 07/01/2010

# Sympathetic nervous system

- Parietal portion innervates the body wall and limbs.
- Preganglionic and postganglionic fibers run with the spinal nerves.
- They leave the spinal nerve through the white communicating branch, synapse in the paravertebral ganglia and join to the spinal nerve again through the gray communicating branch.
- Vasomotor nerves regulate the diameter of the blood vessels.
- Sudomotor nerves regulate sweat glands.
- Piloarrector nerves regulate the arrector pili muscles in the skin.

# Sympathetic nervous system

- Visceral portion innervates organs.
- Preganglionic fibers leave the spinal nerve through white communicating branch and join the paravertebral ganglion.
- The preganglionic fibers synapse in the paravertebral ganglia and innervate the thoracic organs.
- The preganglionic fibers run through the paravertebral ganglia and synapse in the prevertebral or in the intramural ganglia of abdominal and pelvic organs.

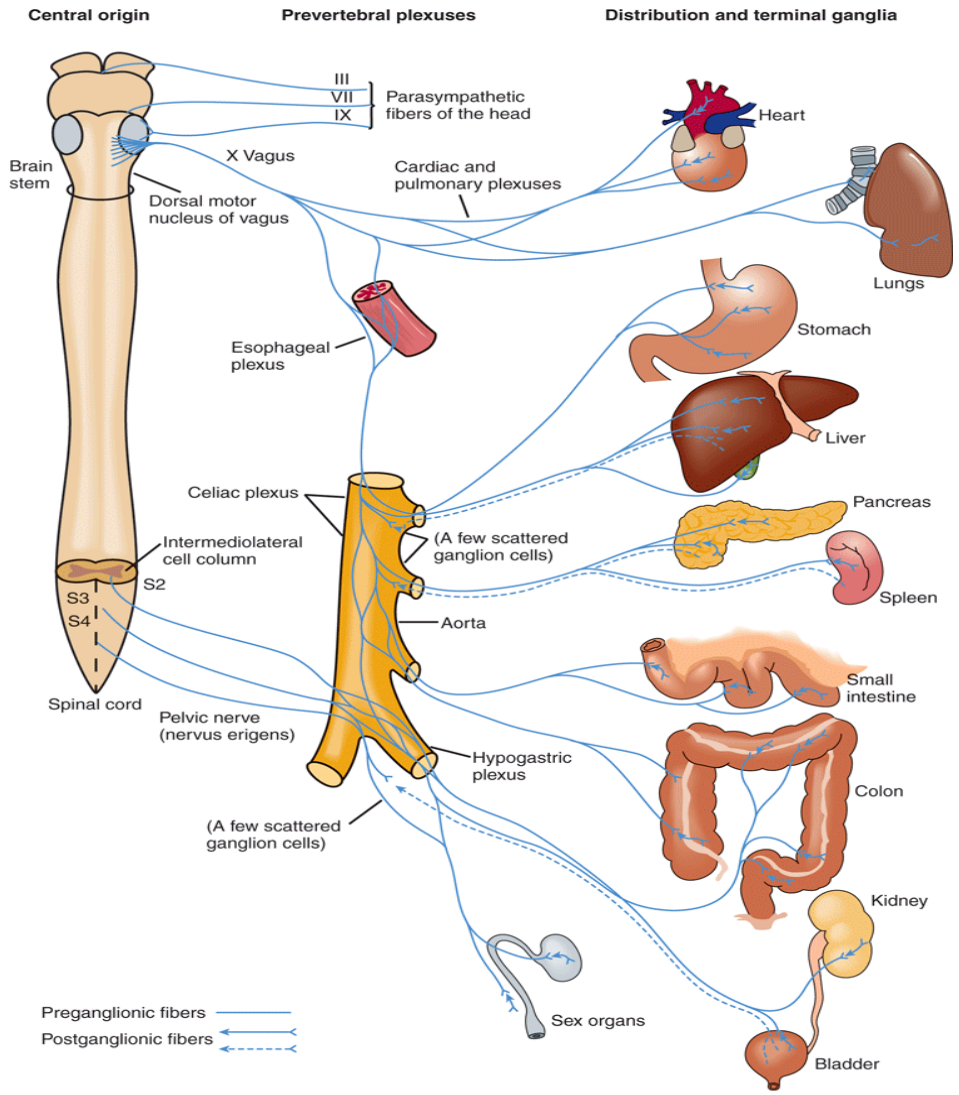
# Parasympathetic innervation

- Preganglionic cell bodies are located in the brain stem and in the lateral horn of the lower sacral spinal segments.
- There is no substantial parietal parasymphatetic innervation.
- Fibers innervate organs.

# Parasympathetic innervation

- Cranial parasympathetics control:
- Pupillary contraction (fibers with CN III)
- Innervate the small salivary glands (fibers with CN VII)
- Innervate the parotid gland (fibers with CN IX)
- Innervate the thoracic and abdominal organs (fibers with CN X).
- Sacral parasympathetics control micturition, defecation, erection.

# Parasympathetic nervous system





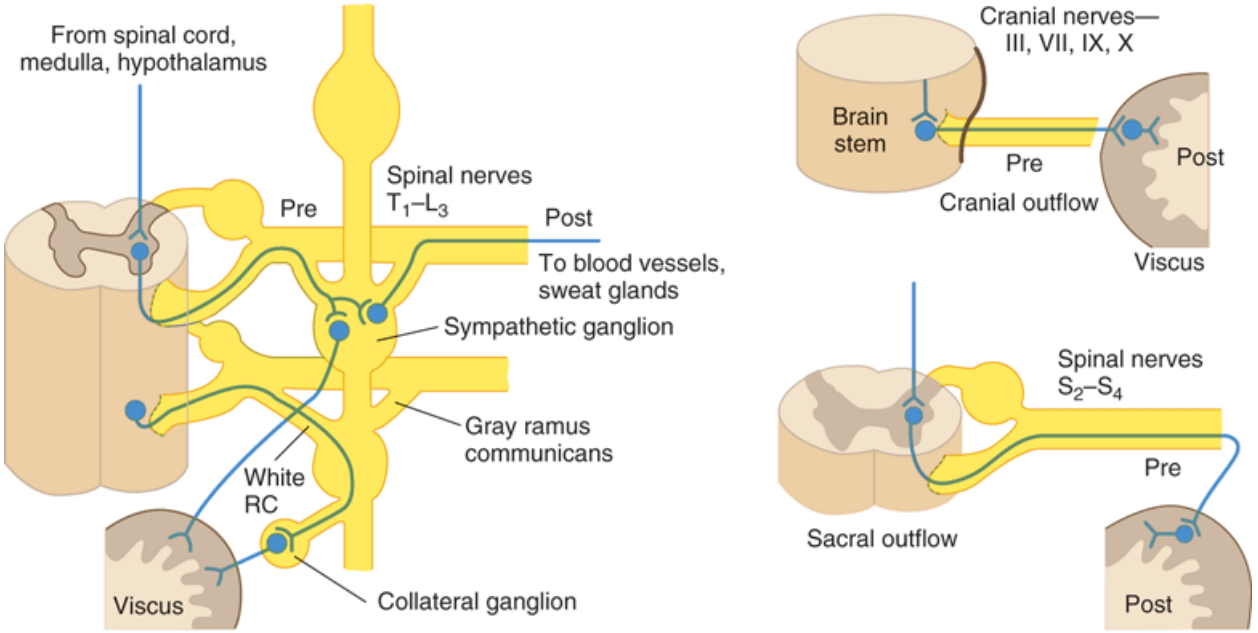

Parasympathetic division of the autonomic nervous system (only left half shown).

Fig. 20-5 Accessed 07/01/2010

# Parietal part segmental communication

- Every spinal nerve has a gray communicating branch and contains postganglionic fibers
- Only thoracic and upper lumbar segments have white communicating branches (pre-ganglionic fibers).
- Because post-ganglionic fibers cannot exist without pre-ganglionic fibers, segments above the thoracic and below the upper lumbar levels receive their efferents from thoracic and upper lumbar segments through the communicating parts of the paravertebral chain.

# Type of autonomic nervous system outflow






Pre, preganglionic neuron; Post, postganglionic neuron; CR, communicating ramus.

(Reproduced, with permission, from Ganong WF: *Review of Medical Physiology*, 22nd ed. McGraw-Hill, 2005.) Fig. 21-3 Accessed 07/01/2010

# Parietal innervation of the head

- Dorsal branches of the cervical spinal nerves (greater occipital nerve) and ventral branches of the cervical plexus (lesser occipital nerve, greater auricular nerve) innervate the occiput.
- The face is innervated by branches from the superior cervical ganglion through the external carotid plexus (and follow the external carotid artery).

# Visceral innervation of the head

- Branches from the external carotid plexus follow the artery and innervate the salivary glands:
- Facial plexus to submaxillary and submandibular glands
- Middle meningeal plexus to the parotid gland
- Sphenopalatine plexus to lacrimal, palatine, and nasal glands
- Branches from the internal carotid plexus follow the artery and innervate vessels of the brain, the pupillary dilator muscle,  the tarsal muscle of Müller, and the ciliary body.

# Autonomic nerves to the head

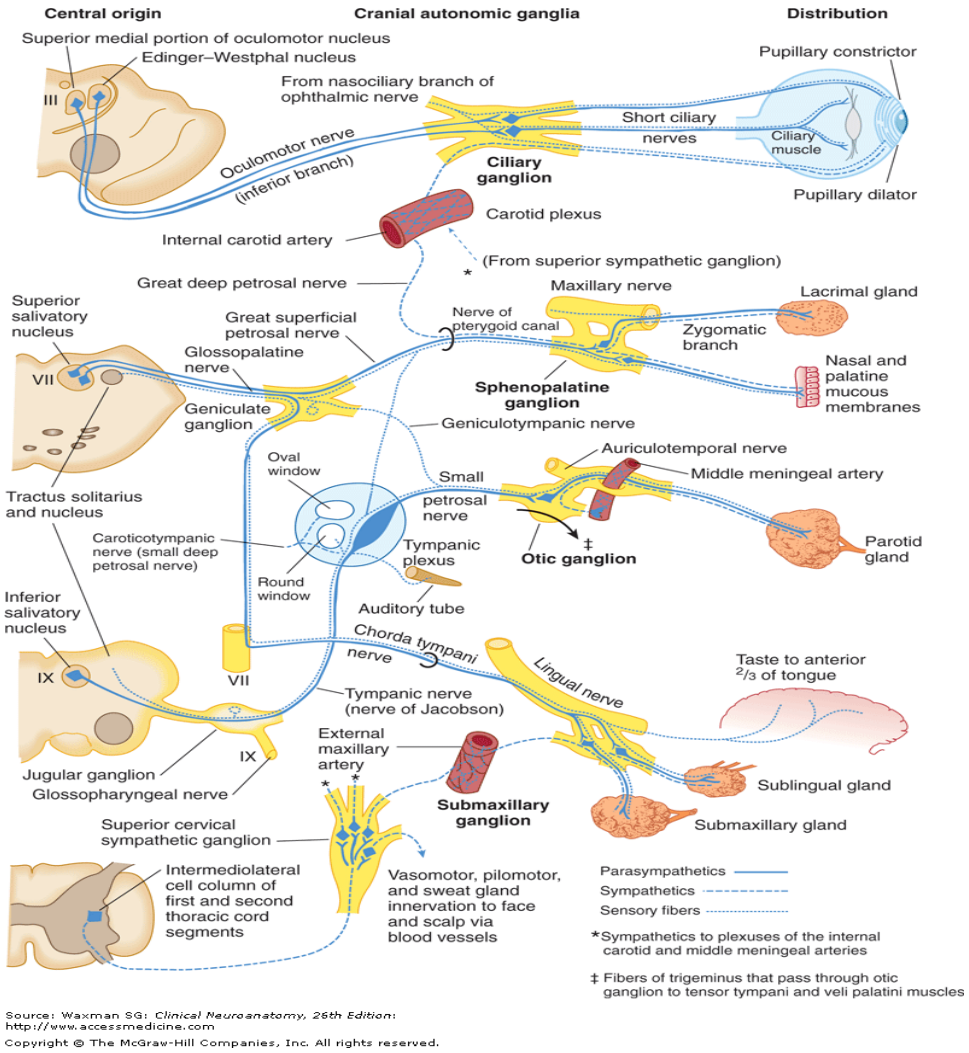


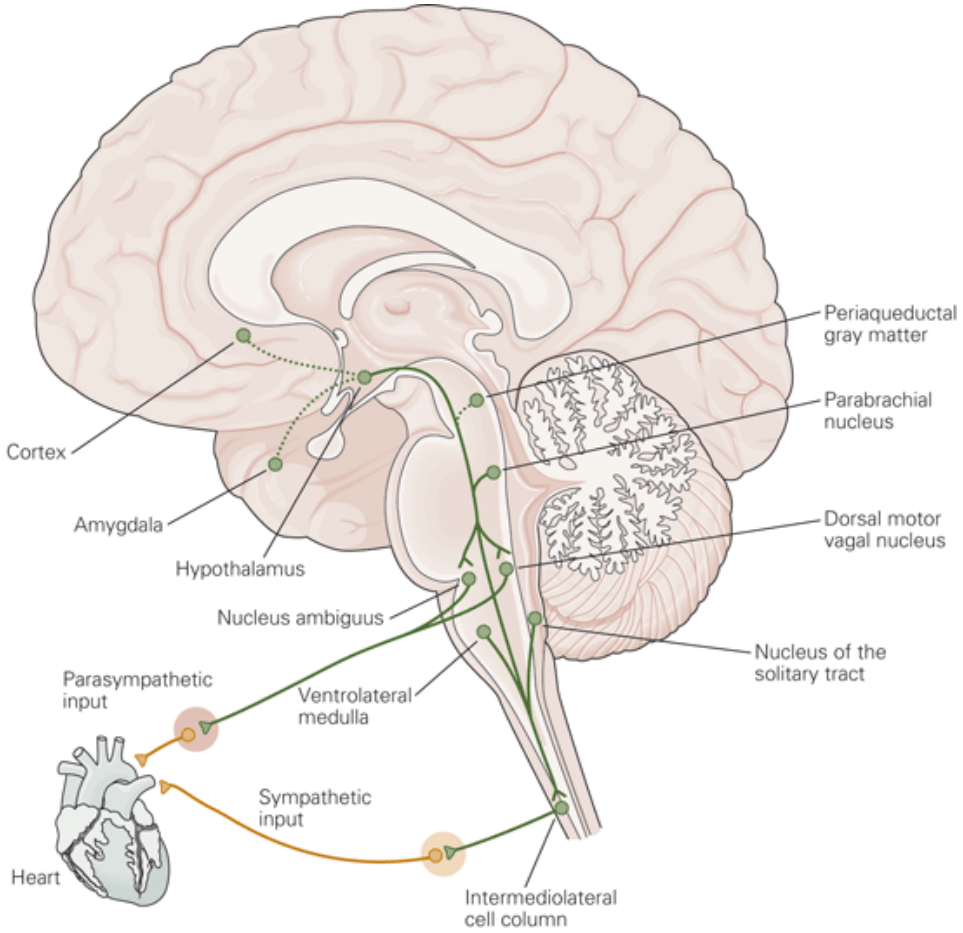



Fig. 20-4 Accessed 07/01/2010

# Innervation of thoracic organs

- Preganglionic cell bodies are in T1-T6 cord levels.
- Ganglion cells in the paravertebral chain (T1-T6 and cervical ganglia).
- Heart receives postganglionic fibers from the cervical and thoracic nerves (cardiac plexus).
- Lung is innervated by fibers from T2-T6 and from the superior cervical ganglion (pulmonary plexus).

# Descending autonomic pathways




Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

Direct projections (solid lines) to autonomic preganglionic neurons include the hypothalamic paraventricular nucleus, parabrachial nucleus, nucleus of the solitary tract, ventrolateral medulla, and medullary raphé. Indirect projections (dashed lines) include the cerebral cortex, amygdala, and periaqueductal grey matter.

(From Kandel ER, Schwartz JH, Jessell TM (editors): *Principles of Neural Science,* 4th ed. McGraw-Hill, 2000.) Fig. 17-6
Accessed 02/01/2010

# Heart function

- Postganglionic adrenergic fibers distributed to nodal and conducting tissues, left ventricular myocardium, coronary arteries
- Preganglionic parasympathetic supply arises in dorsal motor nucleus of the vagus.
- Fibers synapse within mural ganglia on the posterior wall of the atria and in the atrioventricular groove.
- Sympathetics also release neuropeptide Y (adjuvant inhibition of acetylcholine).
- Parasympathetics co-release VIP.
- Intramural ganglionic networks modulate parasympathetic function.

# Heart function

- Unipolar somas in the inferior ganglion of the vagus provide stretch sensitive endings close to the endocardium, particularly right atrium.
- Reflex slowing occurs by a central pathway to the dorsal vagal nucleus via the solitary nucleus.
- Unipolar somas in spinal dorsal root ganglia send peripheral processes to form chemosensitive nerve endings in the myocardium.
- Return is via central processes of these cells to reach the posterior gray horn via anterior nerve roots.

# Respiratory control system

- Controlled from the medulla.
- Dorsal respiratory nucleus (midlateral part of solitary nucleus) has inspiratory function.
- Phrenic motor neurons (contralateral) are activated by the dorsal respiratory nucleus.
- Receives excitatory projections from chemoreceptors in the medullary chemosensitive area and in the carotid body.

# Respiratory control system

- The chemosensitive area lies at the site of attachement of CN IX to the brainstem, where the choroid plexus extends through the lateral aperture of the 4$^{th}$ ventricle.
- At this juncture, the lateral reticular formation is exquisitely sensitive to $H^+$ concentration.
- Any increase stimulates the dorsal respiratory nucleus through direct synaptic contact.

# Respiratory control system

- The ventral respiratory nucleus is expiratory
- Functions as an oscillator, engaged in reciprocal inhibition with the inspiratory center.
- Abdominal wall motor neurons (contralateral) are activated by the ventral respiratory nucleus (forced expiration).
- The medial parabrachial nucleus (adjacent to the cerulean nucleus) has a pacemaker function.
- Stimulated by the amygdala.

# Respiratory control system

- Without training, breath-holding is possible for up to two minutes.
- With training, it may be possible to hold the breath for up to eleven minutes
- Physiological forces over-ride volitional control.
- With breath-holding and without training, it is possible to descend to 60 feet.
- The deepest free dive is 282 feet.

# Innervation of abdominal organs

- Pre-ganglionic cell bodies are in T5-L2 cord levels.
- Splanchnic nerves that travel from the sympathetic chain to abdominal structures carry preganglionic fibers.
- These fibers synapse on post-ganglionic cell bodies in the paravertebral ganglia which lie along the major vessels of abdomen or in the wall of the organ.
- Post-ganglionic fibers are distributed to all the organs along their blood vessels.

# Splanchnic nerves

- Greater splanchnic nerve (T5-T9) synapses in celiac plexus  and distributes primarily to supra-colic organs.
- Some pre-ganglionic fibers from greater splanchnic nerve go directly to they adrenal medulla where they synapse on cell bodies in the medulla for direct release of norepinephrine and epinephrine.
- Lesser splanchnic nerve (T10-T11) synapses in aortico-renal plexus and distributes to infra-colic organs, kidneys, adrenal glands.
- Least splanchnic nerve (T12) synapses in renal plexus and distributes to infra-colic organs, kidney, and adrenal glands.

# Splanchnic nerves

- Lumbar splanchnics (L1-L2) synapse in the inter-mesenteric plexus and distribute posteriorly to kidney, ureter, and gonads.
- Postganglionic fibers continue along aorta to pelvic structures as superior hypogastric plexus.
- Sacral splanchnics synapse in hypogastric and median sacral plexes and innervate pelvic organs.

# Enteric nervous system

- The enteric nervous system extends from the mid-region of the esophagus to the anal canal.
- The dorsal nucleus of the vagus provides the pre-ganglionic parasympathetic supply to the gut with the exception of distal colon and anus.
- That is derived from the pelvic-splanchnic nerves (S2-S4).
- Intramural ganglion cells are located in both intramural plexes.
- Acetylcholine is the principal excitatory transmitter with substance P
- GABA, nitric oxide, VIP inhibit.

# Enteric nervous system

- Postganglionic fibers of the myenteric plexus initiate peristaltic waves by simultaneously causing the gut to contract and by inhibiting neurons distally leading to relaxation.
- Parasympathetic ganglion cells in Meissner’s plexus (and in the pancreas) cause glandular secretion.
- Parasympathetic ganglion cells in the wall of the gall bladder causes expulsion of bile.

# Enteric nervous system

- Pre-ganglionic sympathetic nerves originate in the lateral horn cells.
- They terminate in the pre-vertebral splanchnic ganglia within the abdomen.
- Post-ganglionic fibers supply intestinal smooth muscle and blood vessels ($\beta_2$ receptors).
- Intrinsic visceral afferent neurons are bipolar.
- Some participate in local reflex arcs; others project to the splanchnic ganglia.

# Enteric nervous system

- Visceral afferents reaching the cortex have their unipolar somas in a nodose ganglion of the vagus and in posterior root ganglia at spinal levels.
- Nociceptive.

# Micturition cycle

- Axons from the micturition center in pons inhibit anterior horn motor neurons to the levator ani and other muscles of the pelvic floor.
- Pudendal nerve neurons, sensory to epithelium of trigone and urethra, discharge impulses to the posterior gray horn of S2-4.
- Secondary sensory neurons discharge to micturition center in pons.
- Sacral parasympathetics serving the bladder are simultaneously activated by the pontine micturition center and by neurons in the posterior horn at S2-4.

# Micturition cycle

- Detrussor responds to postganglionic stimulation by contracting to expel urine from the bladder.
- The external urethral sphincter, slave to Onuf's nucleus in the anterior horn, contracts to expel urine from the urethral canal.
- Levator ani contracts, resuming support role.
- Bladder refills.
- Compliant through tonic inhibitory $\beta_2$ action of the sympathetic system on the detrussor muscle and by $\alpha_2$ receptors on parasympathetic terminals.

# Micturition cycle

- When the bladder is half-full, vesical afferents from stretch receptors in the detrusor and mucous membrane of the trigone relay this information along spinoreticular fibers
- Activate the right lateral center of the pons, the periacqueductal gray, and the anterior cingulate cortex.
- Spinoreticular fibers in the Lateral center of the pons activate Onuf’s nucleus in the sacral cord, raising sphincter tone.

# Micturition cycle

- The inferior frontal gyrus inhibits the cingulate cortex, periacqueductal gray, and the preoptic area (voluntary control).
- The command for voluntary contraction of the pelvic floor is sent from the prefrontal cortex to the paracentral lobule.

# Sexual response

- Sympathetic fibers arise from T10-L2 and run with the splanchnic nerves.
- Synapse in the superior mesenteric plexus.
- Postganglionic fibers innervate the blood vessels and smooth muscle of the uterus and vagina in female and the ductus deferens, prostate and seminal vesicle in male.
- Sympathetic activity results in contraction of the vagina (in the woman) and ejaculation (in the man).

# Sexual response

- Parasympathetic tissues arise from S2-S4 and run with the pelvic nerves.
- Synapse in the hypogastric, uterovaginal (or prostatic) plexes.
- Postganglionic fibers innervate the erectile tissue of both sexes.
- Sympathetic activity results in erection of the erectile tissue in both sexes.
- Visceral afferent fibers run with sympathetic and sacral parasympathetic fibers.
- Cell bodies are located in the dorsal root ganglia of T10-L2 and S2-S4.

# Erection

- Psychic stimulation of the central parasympathetic pathway activates preganglionic neurons to pelvic ganglia supplying fibers to internal pudendal artery (muscarinic, VIP receptors).
- Cholinergic fibers also lead to nitrous oxide release.
- Glandular secretion (muscarinic receptors on acini of prostate and seminal vesicles).
- Psychic stimulation of the central sympatheticpathway activates pre-ganglionic neurons ($\alpha_1$ receptors).
- Bladder $\beta_2$ receptors prevent detrussor contraction.

# Erection

- Ejaculation through a reflex arc at S2-S4.
- Motor fibers in the pudendal nerve cause rhythmic contractions of the bulbospongiosus muscles.
- Detumescence.
- Central sympathetic fibers activate preganglionic neurons to pelvic sympathetic ganglia supplying fibers to $\alpha_1$ receptors on pudenal arterioles at entry into cavernous spaces.