



## Neurobiology of Visceral Pain

### Definition

Pain arising from the internal organs of the body:

- Heart, great vessels, and perivascular structures (e.g., lymph nodes)
- Airway structures (pharynx, trachea, bronchi, lungs, pleura)
- Gastrointestinal tract (esophagus, stomach, small intestine, colon, rectum)
- Upper-abdominal structures (liver, gallbladder, biliary tree, pancreas, spleen)
- Urological structures (kidneys, ureters, urinary bladder, urethra)
- Reproductive organs (uterus, ovaries, vagina, testes, vas deferens, prostate)
- Omentum, visceral peritoneum

### Clinical Features of Visceral Pain

Key features associated with pain from the viscera include diffuse localization, an unreliable association with pathology, and referred sensations. Strong autonomic and emotional responses may be evoked with minimal sensation.

Referred pain has two components: (1) a localization of the site of pain generation to somatic tissues with nociceptive processing at the same spinal segments (e.g., chest and arm pain from cardiac ischemia) and (2) a sensitization of these segmental tissues (e.g., kidney stones may cause the muscles of the lateral torso to become tender to palpation).

These features are in contrast to cutaneous pain, which is well localized and features a graded stimulus-response relationship.

### Anatomy of Neurological Structures

Pathways for visceral sensation are diffusely organized both peripherally and centrally. Primary afferent nerve fibers innervating viscera project into the central nervous system via three pathways: (1) in the vagus nerve and its branches; (2) within and alongside sympathetic efferent fiber pathways (sympathetic chain and splanchnic branches, including greater, lesser, least, thoracic, and lumbar branches); and (3) in the pelvic nerve (with parasympathetic efferents) and its branches.

Passage through the peripheral ganglia occurs with potential synaptic contact (e.g., celiac, superior mesenteric, and hypogastric nerves). The gastrointestinal tract and peripheral ganglia form extensive neuronal plexuses that control autonomic functions. Their role in pain sensation is unknown.

Primary afferent cell bodies traveling to the central nervous system reside primarily in the nodose ganglion (vagal) and in the T2–L2 and S1–5 dorsal root ganglia (sympathetic-associated and pelvic-nerve-associated). There may be a role of vagal afferents in nociceptive sensation. Some, but not all, spinal afferents are unequivocally associated with pain sensation.

Visceral primary afferents have been demonstrated to enter the spinal cord and to arborize extensively, including within Lissauer's tract, to enter multiple spinal segments above and below the segment of entry. These afferents form synaptic contact with both superficial and deep dorsal horn neurons ipsilateral and contralateral to the side of entry. The result is extensive, diffuse central nervous system activation.

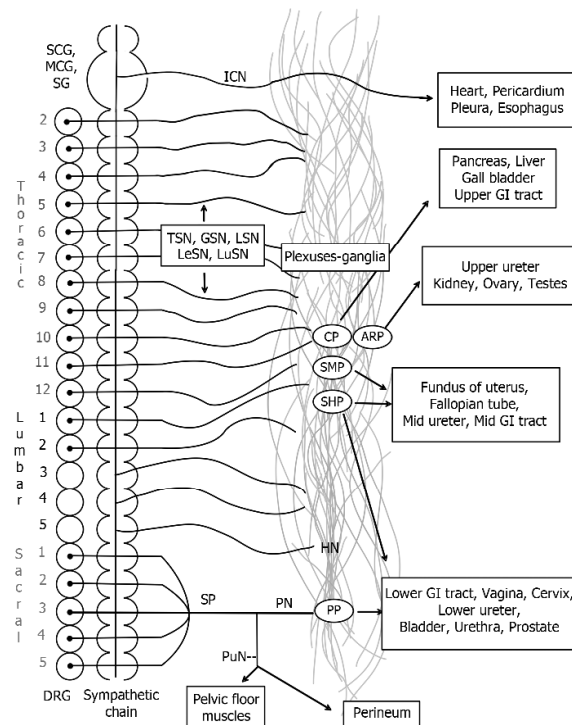


Figure 1. Spinal pathways for visceral sensation. Abbreviations: ARP: aortorenal plexus, CP: celiac plexus, DRG: dorsal root ganglia, HN: hypogastric nerve, ICN: inferior cardiac nerve, GSN: greater splanchnic nerve, LSN: lesser splanchnic nerve, LeSN: least splanchnic nerve, LuSN: lumbar splanchnic nerves, MCG: middle cervical ganglion, PN: pelvic nerve, PP: pelvic plexus, PuN: pudendal nerve, SCG: superior cervical ganglion, SG: stellate ganglion, SHP: superior hypogastric plexus, SMP: superior mesenteric plexus, SP: sacral plexus, TSN: thoracic splanchnic nerves. Adapted from a figure by E.C. Ness in Chin M, et al. (editors). Pain in Women. Oxford University Press; 2013.

Second-order processing of visceral stimuli occurs at spinal segments and brainstem sites receiving primary afferent input. Spinal dorsal horn neurons that respond to pain-generating visceral stimuli have received the most extensive study. Intraspinous nociceptive processing occurs, as well as relay to other central nervous system sites.

Visceral nociceptive information travels by both traditional spinothalamic pathways (the contralateral ventrolateral quadrant) as well as by ipsilateral and dorsal spinal pathways. Relay sites for ascending information have been identified at medullary, pontine, mesencephalic, and thalamic levels. Cortical processing of visceral information has been noted in the insular cortex, anterior cingulate cortex, and somatosensory cortex.

## Unreliable Nature of Visceral Sensation

Healthy visceral tissues evoke minimal sensations. Acutely inflamed tissues are more likely to produce painful sensations, but chronic inflammation has unreliable effects.

Electrophysiological studies have identified primary afferent nerve fibers that encode mechanical and/or chemical stimuli. Many, if not most, primary afferent nerve fibers are “silent” and unresponsive or minimally responsive to mechanical stimuli at baseline, but they become very mechanically sensitive and highly responsive to other stimuli in the presence of inflammation. Subsets of neurons respond only to high intensities of stimulation.

## References

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