

THE PAIN PROCESS

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Pain involves an incredibly complicated myriad of physiochemical responses leading to the perception of an unpleasant sensation arising from actual or potential tissue damage. While the full complexities of the pain process are beyond the scope of this discussion, an understanding of the terminology and basic neurophysiology involved is helpful in preventing and treating discomfort in our patients.

Pain can be classified as **physiologic**, which refers to the body's protective mechanism to avoid tissue injury, or **pathologic**, which arises from tissue injury and inflammation or damage to a portion of the nervous system. Pathologic pain can be further divided into categories such as **nociceptive** (peripheral tissue injury), **neuropathic** (damage to peripheral nerves or spinal cord), **visceral** (stimulation of pain receptors in the thoracic or abdominal viscera), and **somatic** (injury to tissues other than viscera, such as bones, joints, muscles and skin). It can also be defined temporally as **acute** (arising from a sudden stimulus such as surgery or trauma) or **chronic** (persisting beyond the time normally associated with tissue injury).

Nociception refers to the processing of a noxious stimulus resulting in the perception of pain by the brain. The components of nociception include transduction, transmission, modulation and perception. **Transduction** is the conversion of a noxious stimulus (mechanical, chemical or thermal) into electrical energy by a peripheral nociceptor (free afferent nerve ending). This is the first step in the pain process, and can be inhibited by NSAID's, opioids and local anesthetics. **Transmission** describes the propagation through the peripheral nervous system via first-order neurons. Nerve fibers involved include A-delta (fast) fibers responsible for the initial sharp pain, C (slow) fibers that cause the secondary dull, throbbing pain, and A-beta (tactile) fibers, which have a lower threshold of stimulation. Transmission can be reduced by local anesthetics and alpha-2 agonists. **Modulation** occurs when first-order neurons synapse with second-order neurons in the dorsal horn cells of the spinal cord. Excitatory neuropeptides (including, but not limited to, glutamate, aspartate and substance P) can facilitate and amplify the pain signals in ascending projection neurons. At the same time, endogenous (opioid, serotonergic and noradrenergic) descending analgesic systems serve to dampen the nociceptive response. Modulation can be influenced by local anesthetics, alpha-2 agonists, opioids, NSAID's, tricyclic antidepressants (TCA's) and NMDA receptor antagonists. **Perception** is the cerebral cortical response to nociceptive signals that are projected by third-order neurons to the brain. It can be inhibited by general anesthetics, opioids and alpha-2 agonists.

Hyper responsiveness (increased sensitivity) is a hallmark feature of both acute and chronic pathologic pain. This is a result of changes in the nervous system response (**neuroplasticity**) at peripheral and central locations. **Peripheral sensitization** occurs when tissue inflammation leads to the release of a complex array of chemical mediators, resulting in reduced nociceptor thresholds. This causes an increased response to painful stimuli (primary hyperalgesia). **Central sensitization** refers to an increase in the excitability of spinal neurons, mediated in part by the activation of NMDA receptors in dorsal horn neurons. The net effect is expanded receptor fields (pain in neighboring areas not subjected to injury, or secondary hyperalgesia) and painful responses to normally innocuous stimuli (mediated by A-beta fibers and referred to as allodynia). The combination of peripheral and central sensitization results in an increase in the magnitude and duration of pain.

Because the pain response is extremely complex and can involve multiple mechanisms in the same animal (inflammatory and neuropathic, acute and chronic), no one drug at one dose can be expected to be effectuated in every patient. Two important concepts should be kept in mind when treating pain. **Preemptive analgesia** involves initiating treatment before the nociceptive response

is triggered, in an effort to inhibit the development of peripheral and central sensitization.

Multimodal analgesia is the strategy of combining two or more analgesic drugs to achieve an additive or synergistic effect. This reduces the individual drug dosages (lowering the risk of side effects) and works best when each drug has a different mechanism of action (blocks a different portion of the nociceptive response).