Mechanisms of Pain Control
- Blocking ascending pathways
- Blocking descending pathways
- Release of β-endorphin

The concepts of the analgesic response to cutaneous receptor stimulation presented here were first proposed by Melzack and Wall and Castel.[8,23] These models essentially present three analgesic mechanisms:

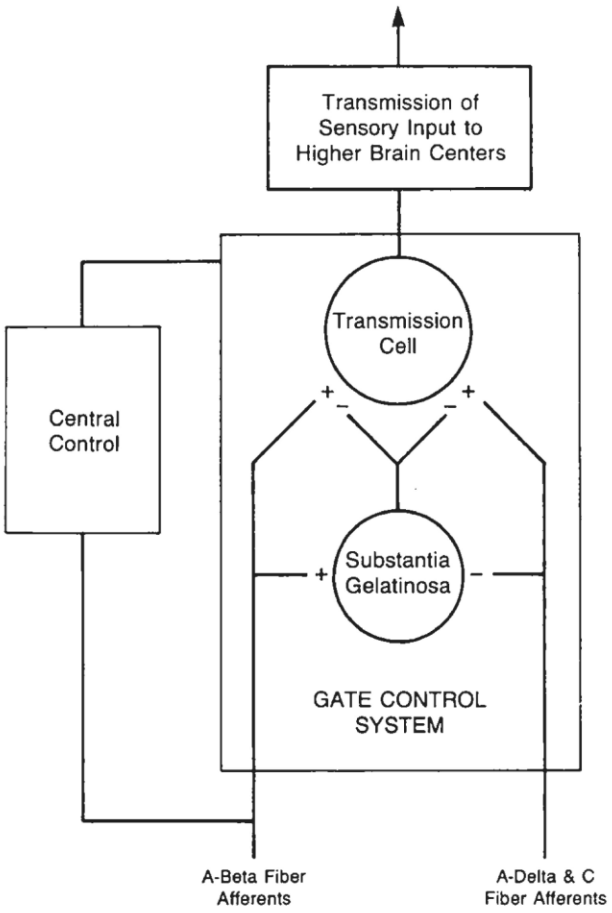
1. Stimulation from ascending A-beta afferents results in the blocking of impulses (pain messages) carried along A-delta and C afferent fibers.
2. Stimulation of descending pathways in the dorsolateral tract of the spinal cord by A-delta and C fiber afferent input results in a blocking of the impulses carried along the A-delta and C afferent fibers.
3. The stimulation of A-delta and C afferent fibers causes the release of endogenous opioids (β-endorphin), resulting in a prolonged activation of descending analgesic pathways.

These theories or models are not necessarily mutually exclusive. Recent evidence suggests that pain relief may result from combinations of dorsal horn and central nervous system activity.[2,10]

A decrease in input along nociceptive afferents also results in pain relief. Cooling afferent fibers decreases the rate at which they conduct impulses. Thus, a 20-minute application of cold is effective in relieving pain because of the decrease in activity, rather than an increase in activity along afferent pathways.

BLOCKING PAIN IMPULSES WITH ASCENDING A-BETA INPUT

Pain modulation caused by sensory stimulation and the resultant increase in the impulses in the large-diameter (A-beta) afferent fibers was proposed by the gate control theory of pain (Fig. 3-5).[23] Impulses ascending on these fibers stimulate the substantia



•**Figure 3-5** The gate control system. Increases A-beta input and stimulates the substantia gelatinosa that inhibits the flow of afferent input to sensory centers.

Treatment Tip
The modalities that are effective in "closing the gate" to ascending pain fibers should provide a significant amount of cutaneous input that would be transmitted to the spinal cord along A-beta fibers. The modalities of choice may include various types of heat or cold, electrical stimulating currents, counterirritants (analgesic balms), or massage.

gelatinosa as they enter the dorsal horn of the spinal cord. Stimulation of the substantia gelatinosa inhibits synaptic transmission in the large and small (A-delta and C) fiber afferent pathways. The "pain message" carried along the smaller-diameter fibers is not transmitted to the second-order neurons and never reaches sensory centers. The balance between the input from the small- and large-diameter afferents determines how much of the pain message is blocked or gated.

The concept of sensory stimulation for pain relief, as proposed by the gate control theory, has empirical support. Rubbing a contusion, applying moist heat, or massaging sore muscles decreases the perception of pain. The analgesic response to these treatments is attributed to the increased stimulation of large-diameter afferent fibers.

substantia gelatinosa (SG) Melzack and Wall proposed that the SG is responsible for closing the gate to painful stimuli.

The gate control theory also proposes that A-delta and C fiber impulses inhibit the substantia gelatinosa, facilitating the perception of pain. The sensation of pain does not diminish rapidly, because free nerve endings do not accommodate and the afferent impulses from them "open the gate" to further pain message transmission.

The discovery and isolation of endogenous opioids in the 1970s led to new theories of pain relief. Castel introduced an endogenous opioid analog to the gate control theory (Fig. 3-6).[8] This theory proposes that increased neural activity in A-alpha and A-beta primary afferent pathways triggers a release of enkephalin from **enkephalin interneurons** found in the dorsal horn. These neuroactive amines inhibit synaptic transmission in the A-delta and C fiber afferent pathways. The end result, as in the gate control theory, is that the pain message is blocked before it reaches sensory levels.

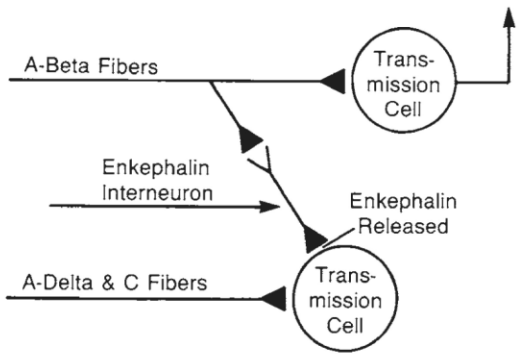
DESCENDING PAIN CONTROL MECHANISMS

The gate control theory proposed a second analgesic mechanism that involves descending efferent fibers.[23] The central control, originating in higher centers of the central nervous system, could affect the dorsal horn gating process. Impulses from the thalamus and brain stem (**central biasing**) are carried into the dorsal horn on efferent fibers in the dorsal or dorsal lateral paths (or tracts). Impulses from the higher centers act to close the gate and block transmission of the pain message at the dorsal horn synapse. Through this system, it was theorized, previous experiences, emotional influences, sensory perceptions, and other factors could influence the transmission of the pain message and the perception of pain.

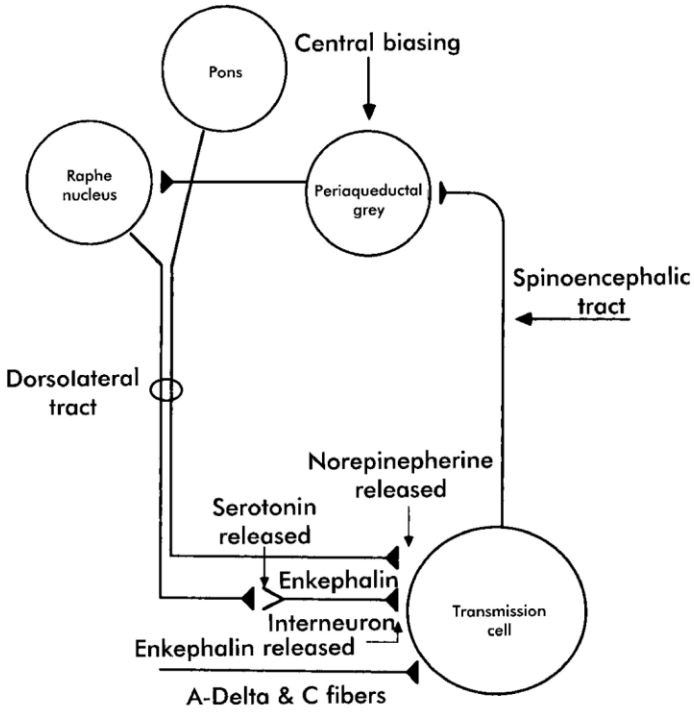
efferent Conduction of a nerve impulse away from an organ.

Castel offers an endogenous opioid model of descending influence over dorsal horn synapse activity (Fig. 3-7).[8] Stimulation of the **periaqueductal gray** region of the midbrain and the **raphe nucleus** in the pons and medulla by ascending neural input, especially from A-delta and C fiber afferents, and possibly central biasing, activates the descending mechanism. The periaqueductal gray stimulates the raphe nucleus. The raphe nucleus in turn sends impulses along serotonergic efferent fibers in the dorsal lateral tract, which synapse with enkephalin interneurons. The interneurons release

periaqueductal gray A midbrain structure that plays an important role in descending tracts that inhibit synaptic transmission of noxious input in the dorsal horn.



•**Figure 3-6** Presynaptic inhibition of dorsal horn synapse transmission owing to A-beta fiber stimulation at enkephalin interneurons.



•**Figure 3-7** Stimulation of the periaqueductal gray region of the midbrain and the raphe nucleus in the pons and medulla by ascending neural input, especially from A-delta and C fiber afferents, and possibly central biasing, activates the descending mechanism.

enkephalin into the dorsal horn, inhibiting the synaptic transmission of impulses to the second-order afferent neurons.

A second descending, norandrenergic pathway projecting from the pons to the dorsal horn has also been identified.[18] The significance of these parallel pathways is not fully understood. It is also not known if these norandrenergic fibers directly inhibit dorsal horn synapses or stimulate the enkephalin interneurons.

This model provides a physiologic explanation for the analgesic response to brief, intense stimulation. The analgesia following accupressure and the use of some transcutaneous electrical nerve simulators (TENS), such as point simulators, is attributed to this descending pain control mechanism.

enkephalinergic interneurons Neurons with short axons that release enkephalin. They are widespread in the central nervous system and are found in the substantia gelatinosa, nucleus raphae magnus, and periaqueductual gray matter.

Beta-Endorphin and Dynorphin

There is evidence that stimulation of the small-diameter afferents (A-delta and C) can stimulate the release of other endogenous opioids.[9,11,21,26,27,29,30] Beta-endorphin (BEP) and dynorphin are neuroactive peptides with potent analgesic effects. The term **endorphin** refers to an opiatelike substance produced by the body. The mechanisms regulating the release of BEP and dynorphin have not been fully elucidated. However, it is apparent that these large endogenous substances play a role in the analgesic response to some forms of stimuli used in the treatment of patients in pain.

β-endorphin A neurohormone derived from proopiomelanocortin (POMC).

One of the sources of BEP is the anterior pituitary. Here it shares the prohormone propiomelanocortin (POMC) with adrenocorticotropin (**ACTH**). Prolonged (20 to 40 min) small-diameter afferent fiber stimulation has been thought to trigger the release of BEP from the anterior pituitary gland. Electroacupuncture, and possibly TENS with long phase durations and low pulse rates (1 to 5 pulses/sec), will cause small-diameter afferent fiber depolarization necessary for BEP release.[30] The anterior pituitary gland may not, however, be a source of BEP in low pulse rate, long pulse width TENS-induced analgesia.[12] BEP does not readily cross the blood-brain barrier,

ACTH Adrenocorticotrophic hormone. This hormone stimulates the release of glucocorticoids (cortisol) from the adrenal glands.

suggesting that if BEP or other endogenous opioids are active analgesic agents within the central nervous system, they are released from areas within the brain.[4]

The neurons in the hypothalamus that send projections to the PAG and noradrenergic nuclei in the brain stem contain BEP. It is possible that BEP released from these neurons by stimulation of the hypothalamus is responsible for the analgesic response to the treatments (Fig. 3-8).[7]

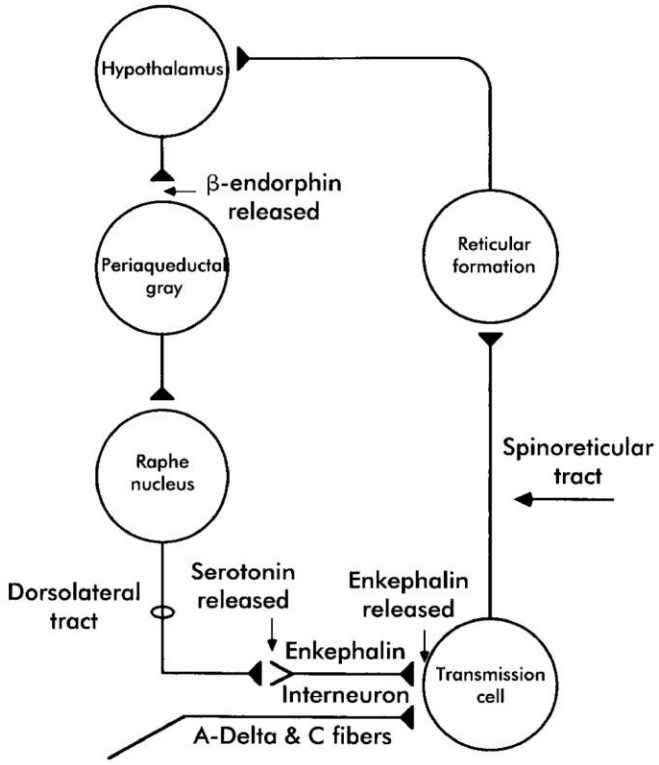
Dynorphin, a more recently isolated endogenous opioid, is found in the PAG, rostroventral medulla, and the dorsal horn.[18] It has been demonstrated that dynorphin is released during electroacupuncture.[16] Dynorphin may be responsible for suppressing the response to noxious mechanical stimulation.[18]

Summary of Pain Control Mechanisms

The body's pain control mechanisms are probably not mutually exclusive. Rather, analgesia is the result of overlapping processes. It is also important to realize that the theories presented are only models. They are useful in conceptualizing the perception of pain and pain relief. These models will help the therapist understand the effects of therapeutic modalities and form a sound rationale for modality application. As more research is conducted and as the mysteries of pain and neurophysiology are solved, new models will emerge. The therapist should adapt these models to fit new developments.

Cognitive Influences

Pain perception and the response to a painful experience may be influenced by a variety of cognitive processes, including anxiety, attention, depression, past pain experiences, and cultural influences. These individual aspects of pain expression are mediated by



•**Figure 3-8** The neurons in the hypothalamus that send projections to the periaqueductal gray and noradrenergic nuclei in the brain stem contain β-endorphin. It is possible that β-endorphin released from these neurons by stimulation of the hypothalamus is responsible for the analgesic response to the treatments.

higher centers in the cortex in ways that are not clearly understood. They may influence both the sensory discriminative and motivational affective dimensions of pain.

Many mental processes modulate the perception of pain through descending systems. Behavior modification, the excitement of the moment, happiness, positive feelings, **focusing** (directed attention toward specific stimuli), hypnosis, and suggestion may modulate pain perception. Past experiences, cultural background, personality, motivation to play, aggression, anger, and fear are all factors that could facilitate or inhibit pain perception. Strong central inhibition may mask severe injury for a period of time. At such times, evaluation of the injury is quite difficult.

Patients with chronic pain may become very depressed and experience a loss of fitness. They tend to be less active and may have altered appetites and sleep habits. They have a decreased will to work and exercise and often develop a reduced sex drive. They may turn to self-abusive patterns of behavior. Tricyclic drugs are often used to inhibit serotonin depletion for the patient with chronic pain.

Just as pain may be inhibited by central modulation, it may also arise from central origins. Phobias, fear, depression, anger, grief, and hostility are all capable of producing pain in the absence of local pathologic processes. In addition, pain memory, which is associated with old injuries, may result in pain perception and pain response that are out of proportion to a new, often minor, injury. Substance abuse can also alter and confound the perception of pain. Substance abuse may cause the chronic pain patient to become more depressed or may lead to depression and psychosomatic pain.

PAIN MANAGEMENT

How should the therapist approach pain? First, the source of the pain must be identified. Unidentified pain may hide a serious disorder, and treatment of such pain may delay the appropriate treatment of the disorder. Once a diagnosis has been made, many physical agents can provide pain relief. The therapist should match the therapeutic agent to each patient's situation. Casts and braces may prevent the application of ice or moist heat. However, TENS electrodes often can be positioned under a cast or brace for pain relief. Following acute injuries, ice may be the therapeutic agent of choice because of the effect of cold on the inflammatory process. There is not one "best" therapeutic agent for pain control. The therapist must select the therapeutic agent that is most appropriate for each patient, based on the knowledge of the modalities and professional judgment. In no situation should the therapist apply a therapeutic agent without first developing a clear rationale for the treatment.

In general, physical agents can be used to accomplish the following.

1. Stimulate large-diameter afferent fibers. This can be done with TENS, massage, and analgesic balms.
2. Decrease pain fiber transmission velocity with cold or ultrasound.
3. Stimulate small-diameter afferent fibers and descending pain control mechanisms with acupressure, deep massage, or TENS over acupuncture points or trigger points.[31]
4. Stimulate a release of BEP or other endogenous opioids through prolonged small-diameter fiber stimulation with TENS.[31]

Other useful pain control strategies include the following.

1. Encourage central biasing through cognitive processes, such as motivation, tension diversion, focusing, relaxation techniques, positive thinking, thought stopping, and self-control.
2. Minimize the tissue damage through the application of proper first aid and immobilization.
3. Maintain a line of communication with the patient. Let the patient know what to expect following an injury. Pain, swelling, dysfunction, and atrophy will occur following injury. The patient's anxiety over these events will increase his or her perception of pain. Often, a patient who has been told what to expect by someone he or she trusts will be less anxious and suffer less pain.