# Recent Advances in Understanding Pain Mechanisms Provide Future Directions for Pain Management

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**Purpose/Objectives:** To review current knowledge of neurobiologic mechanisms that generate and maintain chronic pain and to explain how they might be applied in targeting treatment of chronic, inflammatory, and neuropathic pain syndromes.

**Data Sources:** Published research, literature review articles, and abstracts as well as national statistics.

**Data Synthesis:** Treatment for chronic pain associated with cancer and other syndromes remains suboptimal and falls significantly short of clinical needs. Data highlight the role that multiple neurobiologic mechanisms play in modulating and maintaining pain at various levels of the central and peripheral nervous systems. Novel agents have been developed that use a more targeted approach to treating chronic pain.

**Conclusions:** A growing body of evidence highlights the critical role that neurobiologic mechanisms play in the initiation and maintenance of chronic pain. A thorough understanding of these mechanisms ultimately may result in targeted treatment approaches that focus on the central and peripheral mechanisms involved in mediation of chronic, inflammatory, and neuropathic pain syndromes.

**Implications for Nursing:** A majority of patients undergoing active treatment for cancer experiences unrelieved pain. By gaining a better understanding of the mechanisms that generate and maintain chronic pain, oncology nurses can promote targeted pain management strategies that incorporate novel therapeutic agents.

## Key Points . . .

- Pain is an evolutionary warning system activated in response to potential or actual tissue damage, but it often becomes a chronic medical condition that offers no biologic advantage.
- A growing body of evidence suggests that pain is not a passive consequence of defined peripheral input but rather an active process that results from activation of complex mechanisms that interact at many different levels of the neuraxis.
- Neuronal plasticity, the processes by which the central nervous system responds to shifts in nociceptive pain thresholds and responsiveness, essentially characterizes the development of various chronic pain syndromes.
- Ultimately, effective pain treatments will depend on thoroughly elucidating the neurobiologic mechanisms that generate and maintain chronic pain and the development of therapeutic agents that target specific receptors, neurotransmitters, and sites involved in its mediation.

Pain represents a fundamental protective mechanism or warning system that is activated in response to potential or actual tissue damage. Although pain (and the capacity to experience it) commonly is considered an essential protective component in the evolutionary survival drive, it also can become a chronic medical condition that offers no biologic advantage.

Chronic pain represents one of the most disabling and costly afflictions in North America, Europe, and Australia (Harstall & Ospina, 2003). Recent data demonstrate that the prevalence of chronic pain in the general populations of developed countries ranges from 10%–55% (Harstall & Ospina). In the United States, approximately 9% of the adult population (American Pain Society, 2003) (approximately 20 million adults [U.S. Census Bureau, 2003]) suffers from noncancer-related chronic pain. Importantly, this 9% increases to an estimated 70%–90% when patients with advanced cancer are surveyed (Caraceni & Portenoy, 1999; Murray, Grant, Grant, & Kendall, 2003; Potter, Hami, Bryan, & Quigley, 2003). Overall, the economic burden of chronic pain in the United States is estimated to be as high as $100 billion (Nitu, Wallihan, Skljarevski, & Ramadan, 2003), of which almost two-thirds (i.e., $61 billion) can be attributed to lost time in work productivity (Stewart, Ricci, Chee, Morganstein, & Lipton, 2003).

Although various etiologic factors (e.g., cancer, joint syndromes, herpes zoster) play a critical role in the initiation of chronic pain, the complex interaction of multiple mechanisms at many different levels of the neuraxis produces actual pain symptoms (Woolf & Decosterd, 1999; Woolf & Max, 2001). A growing body of evidence suggests that pain is not a static or passive consequence of defined peripheral input but rather an active process that is generated partially in the peripheral

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