01 - SECTION 1 Pain

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Cardinal Manifestations and Presentation of Diseases PART 2 Section 1 Pain James P. Rathmell, Howard L. Fields

Pain: Pathophysiology

and Management The province of medicine is to preserve and restore health and to relieve suffering. Understanding pain is essential to both goals. Because pain is universally understood as a signal of disease, it is the most common symptom that brings a patient to a physician’s attention. The function of the pain sensory system is to protect the body and maintain homeostasis. It does this by detecting, localizing, and identi fying potential or actual tissue-damaging processes. Because different diseases produce characteristic patterns of tissue damage, the quality, time course, and location of a patient’s pain lend important diagnostic clues. It is the physician’s responsibility to assess each patient promptly for any remediable cause underlying the pain and to provide rapid and effective pain relief whenever possible. THE PAIN SENSORY SYSTEM Pain is an unpleasant sensation localized to a part of the body. It is often described in terms of a penetrating or tissue-destructive pro cess (e.g., stabbing, burning, twisting, tearing, squeezing) and/or of a bodily or emotional reaction (e.g., terrifying, nauseating, sickening). Furthermore, any pain of moderate or higher intensity is accompanied by anxiety and the urge to escape or terminate the feeling. These prop erties illustrate the duality of pain: it is both sensation and emotion. When it is acute, pain is characteristically associated with behavioral arousal and a stress response consisting of increased blood pressure, heart rate, pupil diameter, and plasma cortisol levels. In addition, local muscle contraction (e.g., limb flexion, abdominal wall rigidity) is often present. ■ ■PERIPHERAL MECHANISMS The Primary Afferent Nociceptor A peripheral nerve consists of the axons of three different types of neurons: primary sensory afferents, motor neurons, and sympathetic postganglionic neurons (Fig. 14-1). The cell bodies of primary sensory afferents are in the dorsal root gan glia within the vertebral foramina. The primary afferent axon has two branches: one projects centrally into the spinal cord and the other projects peripherally to innervate tissues. Primary afferents are classified by their diameter, degree of myelination, and conduction veloc ity. The largest diameter afferent fibers, A-beta (Aβ), respond maximally to light touch and/or moving stimuli; they are present primarily in nerves that inner vate the skin. In normal individuals, the activity of these fibers does not produce pain. There are two other classes of primary afferent nerve fibers: the small diameter myelinated A-delta (Aδ) and the unmyelinated (C) axons (Fig. 14-1). These fibers are present in nerves to the skin and to deep somatic and visceral structures. Some tissues, such as the cornea, are innervated only by Aδ and C fiber afferents. Most Aδ and C fiber Aβ Aδ C Sympathetic preganglionic FIGURE 14-1 Components of a typical cutaneous nerve.

There are two distinct functional categories of axons: primary afferents with cell bodies in the dorsal root ganglion and sympathetic postganglionic fibers with cell bodies in the sympathetic ganglion. Primary afferents include those with large-diameter myelinated (Aβ), small-diameter myelinated (Aδ), and unmyelinated (C) axons. All sympathetic postganglionic fibers are unmyelinated.

afferents respond maximally to intense (painful) stimuli and produce the subjective experience of pain when they are activated; this defines them as primary afferent nociceptors (pain receptors). The ability to detect painful stimuli is completely abolished when conduction in Aδ and C fiber axons is blocked. Individual primary afferent nociceptors can respond to several dif ferent types of noxious stimuli. For example, most nociceptors respond to heat; intense cold; intense mechanical distortion, such as a pinch; changes in pH, particularly an acidic environment; and application of chemical irritants including adenosine triphosphate (ATP), serotonin, bradykinin (BK), and histamine. The transient receptor potential cat ion channel subfamily V member 1 (TRPV1), also known as the vanil loid receptor, mediates perception of some noxious stimuli, especially heat sensations, by nociceptive neurons; it is activated by heat, acidic pH, endogenous mediators, and capsaicin, a component of hot chili peppers. Sensitization When intense, repeated, or prolonged stimuli are applied to damaged or inflamed tissues, the threshold for activating primary afferent nociceptors is lowered, and the frequency of firing is higher for all stimulus intensities. Inflammatory mediators such as BK, nerve-growth factor, some prostaglandins (PGs), and leukotrienes contribute to this process, which is called sensitization. Sensitization occurs at the level of the peripheral nerve terminal (peripheral sensi tization) as well as at the level of the dorsal horn of the spinal cord (central sensitization). Peripheral sensitization occurs in damaged or inflamed tissues, when inflammatory mediators activate intracellu lar signal transduction in nociceptors, prompting an increase in the production, transport, and membrane insertion of chemically gated and voltage-gated ion channels. These changes increase the excit ability of nociceptor terminals and lower their threshold for activation by mechanical, thermal, and chemical stimuli. Central sensitization occurs when activity, generated by nociceptors during inflammation, enhances the excitability of nerve cells in the dorsal horn of the spinal cord. Following injury and resultant sensitization, normally innocuous stimuli can produce pain (termed allodynia). Sensitization is a clini cally important process that contributes to tenderness, soreness, and hyperalgesia (increased pain intensity in response to the same noxious stimulus; e.g., pinprick causes severe pain). A striking example of sen sitization is sunburned skin, in which severe pain can be produced by a gentle slap or a warm shower. Sensitization is of particular importance for pain and tenderness in deep tissues. Viscera are normally relatively insensitive to noxious mechanical and thermal stimuli, although hollow viscera do generate Dorsal root ganglion Peripheral nerve Spinal cord Sympathetic postganglionic

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