1. What is pain?
Some dictionaries define pain as “An unpleasant sensation, occurring in varying degrees of severity as a consequence of injury, disease, or emotional disorder.” The International Association for the Study of Pain defines pain as “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” Inherent to either of these definitions is the recognition that pain always has both a physical and emotional component. It is both a physiologic sensation and an emotional reaction to that sensation. In certain instances, pain may be experienced in the absence of obvious tissue injury; yet the pain is no less “real.” New information emphasizes how important it is to view the experience of pain as a complex neurobiological experience that is influenced by multiple factors occurring at multiple areas of the peripheral and central nervous system. Some of these factors are easily identifiable, while others are not as of yet.

2. What is suffering?
Suffering is the state of undergoing pain, distress, or hardship. Both physical and psychological issues are actively part of the suffering, and the pain itself may be only a small component. In some instances, pain may be an expression of suffering as has been described in somatoform disorders.

3. What is the difference between impairment and disability?
Impairment is any loss or abnormality of psychological, physiologic, or anatomic structure or function (e.g., impairment of vision). According to the World Health Organization (WHO) definition, disability results from impairment; it is any restriction or lack of ability to perform an activity in the manner or within the range considered normal for a human. In governmental terms, disability is sometimes called a functional limitation. Another definition of disability is a disadvantage (resulting from an impairment or functional limitation) that limits or prevents the fulfillment of a role that is normal for an individual (depending on age, sex, and social and cultural factors). This definition corresponds to the WHO classification of handicap. Importantly, the presence of an impairment (e.g., visual impairment) does not necessarily have to lead to disability—individuals with visual impairment such as myopia can be assisted with corrective lenses to limit any disability associated with myopia.

4. What is meant by “inferred pathophysiology”?
Even for well-recognized pain syndromes (e.g., migraine headache or painful diabetic neuropathy), we can rarely define with certainty the pathophysiologic mechanisms underlying a specific pain syndrome. This hinders our ability to specifically target and treat such mechanisms directly. However, a specific set of symptoms may lead us to believe that a pain syndrome is more likely due to nerve injury (neuropathic pain), lesions of muscle or bone (somatic nociceptive pain), or disease of the internal organs (visceral nociceptive pain). This “inferred pathophysiology” implies that we understand some of the basic mechanisms underlying a pain syndrome, and leads to the pathophysiologic classification of pain syndromes (see Chapter 2, Classification of Pain). However, this pathophysiologic classification is limited, because we can only infer, and rarely verify, the true mechanism.

5. What is the definition of nociception?
Nociception is the activation of a nociceptor by a perception of a potentially tissue-damaging (noxious) stimulus. It is the first step in the pain pathway.
6. **What is a nociceptor?**
A nociceptor is a specialized, neurologic receptor that is capable of differentiating between innocuous and noxious stimuli. In humans, nociceptors are the undifferentiated terminals of a-delta and c-fibers, which are the thinnest myelinated and unmyelinated fibers, respectively. A-delta fibers are also called high-threshold mechanoreceptors. They respond primarily to mechanical stimuli of noxious intensity.

7. **What is the difference between pain threshold and pain tolerance?**
Pain threshold refers to the lowest intensity at which a given stimulus (mechanical, thermal) is perceived as painful; it is relatively constant across subjects for a given stimulus. Similarly, barring disease states, mechanical pressure produces pain at approximately the same amount of pressure across subjects. Specific devices have been developed to specifically measure thermal and mechanical pain thresholds, for example.

In contrast, pain tolerance is the greatest level of pain that a person is able to endure. Tolerance varies much more widely across individuals and depends on a variety of medical and nonmedical factors. Clinically, pain tolerance is of much more importance than pain threshold. (More detailed discussions of threshold and tolerance are found in Chapter 6, Specific Pain Measurement Tools.)

8. **What is allosthenia?**
Allodynia refers to the state in which an innocuous (e.g., normally nonpainful) stimulus is perceived as painful. It is not normal! It is common in many neuropathic pain conditions, such as postherpetic neuralgia, diabetic neuropathy complex regional pain syndrome, and other peripheral neuropathies. In thermal allosthenia, the innocuous warm or cold sensation may be perceived as painful. With mechanical allosthenia, a very light touch, such as the clothes rubbing against the skin or bed sheets placed on the lower extremities, may be extremely painful, while firmer pressure is not.

When allosthenia occurs in a person experiencing a neuropathic painful disorder, the skin surface may appear normal. Allosthenia is also present in skin sensitized by a burn or inflammation (ankle sprain), but in these situations the affected skin is visibly abnormal.

9. **What is analgesia?**
Analgesia is the absence of pain in response to a normally noxious stimulus. Analgesia can be produced peripherally (at the site of tissue damage, receptor, or nerve) or centrally (in the spinal cord or brain). Different analgesic agents may target all or primarily one of these regions.

10. **What is the difference between analgesia and anesthesia?**
Anesthesia implies loss of many sensory modalities, leaving the area “insensate.” Analgesia refers specifically to the easing of painful sensation.

11. **What is meant by paresthesia?**
A paresthesia is any abnormal sensation. It may be spontaneous or evoked by a specific event. The most common paresthesia is the sense of “pins and needles” when a nerve in a limb is compressed (e.g., the limb “falls asleep”). Paresthesias are not always painful.

12. **What is a dysesthesia?**
A dysesthesia is a painful paresthesia. By definition, the sensation is unpleasant. Examples include the burning feet that may be felt in various peripheral neuropathies, or the spontaneous pain in certain types of diabetic neuropathy.

13. **What is hypoesthesia?**
Hypoesthesia is decreased sensitivity to stimulation. Essentially, it is an area of relative numbness and may be the consequence of any kind of nerve injury. Areas of hypoesthesia are often created intentionally (e.g., by local infiltrations of anesthetics).

14. **What is formication?**
Formication is a form of paresthesia in which the patient feels as though bugs are crawling on his or her body.

15. **What is anesthesia dolorosa?**
Anesthesia dolorosa is a syndrome in which pain is felt in an area that is otherwise numb or desensitized. It commonly occurs after partial nerve lesions and may be a complication of radiofrequency coagulation of the trigeminal nerve.
In a certain percentage of patients, the original trigeminal neuralgia pain is replaced by spontaneous pain in a now denervated area. The paradox is that an otherwise insensitive area is painful.

16. **What is meant by neuralgia?**

   Neuralgia is a clinically descriptive term, meaning intermittent pain in the distribution of a nerve or nerves. The condition described as “sciatica” may be due to the injury of the sciatic nerve, but is more commonly due to spinal nerve root compression (L5 or S1); pain is felt in the distribution of the sciatic nerve (radiating down the posterior aspect of leg). Trigeminal neuralgia, one of the most common primary neuralgias, is characterized by a jabbing pain in one or more of the distributions of the trigeminal nerve. Postherpetic neuralgia may occur after an outbreak of acute herpes zoster (shingles). Neuralgias are characteristically associated with an electrical, shock-like pain.

17. **What is hyperpathia?**

   Hyperpathia refers to a symptom in which nociceptive stimuli result in greater than expected or exaggerated levels of pain. The term hyperpathia also refers to an abnormally intense pain response to repetitive stimuli not sensitive to a simple stimulus, but over-responds to multiple stimuli. For example, a single pinprick may not be felt, but repetitive pinpricks produce intense pain. Hyperpathia is sometimes called summation dysesthesia.

18. **What are algogenic substances?**

   Algogenic substances, when released from injured tissues or injected subcutaneously, activate or sensitize nociceptors (algos = pain). Histamines, substance P, glutamate, potassium, and prostaglandins are a few examples of algogenic substances.

19. **What is meant by sensitization?**

   Sensitization is a state in which a peripheral receptor or a central neuron either responds to stimuli in a more intense fashion than it would under baseline conditions, or responds to a stimulus to which it is normally insensitive. Sensitization occurs both at the level of the nociceptor in the periphery and at the level of the second-order neuron in the spinal cord (see Chapter 3, Basic Mechanisms).

   In the periphery, tissue injury may convert a high-threshold mechanoreceptor (which normally would respond only to noxious mechanical stimuli) into a receptor that responds to gentle stimuli as though they were noxious. Centrally, the second-order neurons (those on which the primary afferents synapse) also may become hyper-excitabile. When spinal cord neurons are hyper-excitabile, they may fire spontaneously, giving rise to spontaneous pain. This is typically the case after deafferentation.

20. **What is a “lancinating” pain? What does its presence imply?**

   Lancinating literally means “cutting.” It is a sharp, stabbing pain that is often associated with neuropathic syndromes. The word is virtually never used by patients, but is frequently used by pain specialists who are writing about a patient’s complaint of “jabbing” pain.

21. **Define deafferentation.**

   Deafferentation implies the loss of normal input from primary sensory neurons. It may occur after any type of peripheral nerve injury. Deafferentation is particularly common in postherpetic neuralgia and in traumatic nerve injuries. The central neuron on which the primary afferent was to synapse may become hyper-excitable.

22. **Describe the gate control theory of pain.**

   The basic premises of the gate control theory of pain are that activity in large (nonnociceptive) fibers can inhibit the perception of activity in small (nociceptive) fibers, and that descending activity from the brain also can inhibit that perception. Given this construct, it is easy to understand why deafferentation may cause pain. If the large fibers are preferentially injured, the normal inhibition of pain perception does not occur.

23. **What is meant by “breakthrough” pain?**

   If a patient has acceptable baseline pain control on a stable analgesic regimen and suddenly develops an acute exacerbation of pain, this is referred to as breakthrough pain. It often occurs toward the end of a dosing interval, because of a drop in analgesic levels (end-of-dose breakthrough pain). “Incident” pain is a type of breakthrough pain that occurs either with a maneuver that would
normally exacerbate pain (weight bearing on an extremity with a bone metastasis) or with sudden disease exacerbation (hemorrhage, fracture, or expansion of a hollow viscus). Breakthrough pain can occur in an idiopathic fashion as well. The concept of breakthrough is generally accepted for cancer-related pain but is more controversial for non-cancer-related pain.

Recognizing the type(s) of breakthrough pain is important for treatment purposes. Pain consequent to decreasing analgesic levels may be controlled by increasing the dose or shortening the intervals between doses (if not otherwise contraindicated). Incident pain may be addressed by administering a dose of an appropriate analgesic before the exacerbating activity.

24. True or false: Central pain arises only when the original insult was central.
False. The term central pain is applied when the generator of the pain is believed to be in the spinal cord or the brain. The original insult may have been peripheral (nerve injury or postherpetic neuralgia), but the pain is sustained by central mechanisms. The basic process may be central sensitization. Central pain also may occur after central injuries, such as strokes or spinal cord injuries. The pain tends to be poorly localized and of a burning nature.

25. What is meant by referred pain?
Pain in an area removed from the site of tissue injury is called referred pain. The most common examples are pain in the shoulder from myocardial infarction, pain in the back from pancreatic disease, and pain in the right shoulder from gallbladder disease. The presumed mechanism is that afferent fibers from the site of tissue injury enter the spinal cord at a similar level to afferents from the point to which the pain is referred. This conjoint area in the spinal cord results in the mistaken perception that the pain arises from the referral site.

26. What is phantom pain?
Phantom pain is pain felt in a part of the body that has been surgically or otherwise removed. It is common for patients to have phantom sensation postoperatively; that is, after limb amputation, the patient feels as though the limb is still present. This sensation occurs in nearly all patients undergoing amputation. It usually subsides over days to weeks. A small percentage of patients develop true phantom limb pain, which may be extraordinarily persistent and resistant to conventional medical treatment.

27. What is meralgia paresthetica?
Meralgia paresthetica is a syndrome of tingling discomfort (dysesthesias) in an area of nerve injury, most commonly the lateral femoral cutaneous nerve. It is characterized by a patch of decreased sensation over the lateral thigh; this area is dysesthetic. Meralgia paresthetica may be due to more proximal nerve compression. A change in weight is commonly associated with the onset of meralgia paresthetica.

28. What is the difference between primary and secondary pain syndromes?
In primary pain syndromes, the pain itself is the disease. Examples include migraine, trigeminal neuralgia, and cluster headache. A secondary pain syndrome is due to an underlying (often structural) cause—for example, trigeminal neuralgia due to a tumor pressing on the cranial nerve. One of the major issues in any primary pain syndrome is to exclude an underlying destructive cause (tumor or infection).

29. What is palliative care?
The World Health Organization defines palliative care as “The active total care of patients, controlling pain and minimizing emotional, social, and spiritual problems at a time when disease is not responsive to active treatment.” In a broader sense, it is usually taken to mean the alleviation of symptoms when the primary disease cannot be controlled. The concept is now being extended to include symptom management at earlier stages of terminal diseases.

30. What is meant by the term addiction?
Addiction has been defined as a primary, chronic neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. Tolerance may or may not be present. Physical dependence may occur in a person experiencing addiction; however, physical dependence is not synonymous with addiction and may occur in people who do not suffer from addiction, as well as with nonanalgesic medications (discussed later).
31. **What is the definition of physical dependence?**
   Physical dependence is a state of adaptation that is manifested by a drug class–specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist. The term applies to non-opioid medications as well.

32. **What is the definition of drug tolerance?**
   Drug tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug’s effects (positive or negative) over time.

33. **What is the definition of pseudoaddiction?**
   The term pseudoaddiction refers to an iatrogenic syndrome of abnormal behavior developing as a direct consequence of inadequate pain management. Treatment strategies include establishing trust between the patient and the health care team and providing appropriate and timely analgesics to control the patient’s level of pain.

### KEY POINTS

1. The experience of pain by definition involves an emotional response; therefore assessment and treatment of pain must address *all* components of the painful experience.
2. The clinician should be familiar with the various types of abnormal sensations that can result in pain (e.g., allodynia) in order to optimally assess and treat painful conditions.
3. Treatment of both baseline pain and breakthrough pain are both important so that a patient can be as comfortable as possible.
4. Understanding the difference among addiction, pseudoaddiction, physical dependence, and tolerance is essential to effectively prescribing analgesics to patients with chronic pain.

### BIBLIOGRAPHY