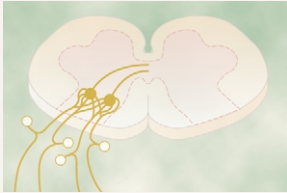


Somatic Sensations: II. Pain, Headache, and Thermal Sensations



Many, if not most, ailments of the body cause pain. Furthermore, the ability to diagnose different diseases depends to a great extent on a physician's knowledge of the different qualities of pain. For these reasons, the first part of this chapter is devoted mainly to pain and to the physiologic bases of some associated clinical phenomena.

Pain Is a Protective Mechanism. Pain occurs whenever any tissues are being damaged, and it causes the individual to react to remove the pain stimulus. Even such simple activities as sitting for a long time on the ischia can cause tissue destruction because of lack of blood flow to the skin where it is compressed by the weight of the body. When the skin becomes painful as a result of the ischemia, the person normally shifts weight subconsciously. But a person who has lost the pain sense, as after spinal cord injury, fails to feel the pain and, therefore, fails to shift. This soon results in total breakdown and desquamation of the skin at the areas of pressure.

Types of Pain and Their Qualities—Fast Pain and Slow Pain

Pain has been classified into two major types: *fast pain* and *slow pain*. Fast pain is felt within about 0.1 second after a pain stimulus is applied, whereas slow pain begins only after 1 second or more and then increases slowly over many seconds and sometimes even minutes. During the course of this chapter, we shall see that the conduction pathways for these two types of pain are different and that each of them has specific qualities.

Fast pain is also described by many alternative names, such as *sharp pain*, *pricking pain*, *acute pain*, and *electric pain*. This type of pain is felt when a needle is stuck into the skin, when the skin is cut with a knife, or when the skin is acutely burned. It is also felt when the skin is subjected to electric shock. Fast-sharp pain is not felt in most deeper tissues of the body.

Slow pain also goes by many names, such as *slow burning pain*, *aching pain*, *throbbing pain*, *nauseous pain*, and *chronic pain*. This type of pain is usually associated with *tissue destruction*. It can lead to prolonged, unbearable suffering. It can occur both in the skin and in almost any deep tissue or organ.

Pain Receptors and Their Stimulation

Pain Receptors Are Free Nerve Endings. The pain receptors in the skin and other tissues are all free nerve endings. They are widespread in the superficial layers of the *skin* as well as in certain internal tissues, such as the *periosteum*, the *arterial walls*, the *joint surfaces*, and the *falx* and *tentorium* in the cranial vault. Most other deep tissues are only sparsely supplied with pain endings; nevertheless, any widespread tissue damage can summate to cause the slow-chronic-aching type of pain in most of these areas.

Three Types of Stimuli Excite Pain Receptors—Mechanical, Thermal, and Chemical. Pain can be elicited by multiple types of stimuli. They are classified as *mechanical*, *thermal*, and *chemical pain stimuli*. In general, fast pain is elicited by the mechanical and thermal types of stimuli, whereas slow pain can be elicited by all three types.

Some of the chemicals that excite the chemical type of pain are *bradykinin*, *serotonin*, *histamine*, *potassium ions*, *acids*, *acetylcholine*, and *proteolytic enzymes*. In addition, *prostaglandins* and *substance P* enhance the sensitivity of pain endings but do not directly excite them. The chemical substances are especially important in stimulating the slow, suffering type of pain that occurs after tissue injury.

Nonadapting Nature of Pain Receptors. In contrast to most other sensory receptors of the body, pain receptors adapt very little and sometimes not at all. In fact, under some conditions, excitation of pain fibers becomes progressively greater, especially so for slow-aching-nauseous pain, as the pain stimulus continues. This increase in sensitivity of the pain receptors is called *hyperalgesia*. One can readily understand the importance of this failure of pain receptors to adapt, because it allows the pain to keep the person apprised of a tissue-damaging stimulus as long as it persists.

Rate of Tissue Damage as a Stimulus for Pain

The average person begins to perceive pain when the skin is heated above 45°C, as shown in Figure 48–1. This is also the temperature at which the tissues begin to be damaged by heat; indeed, the tissues are eventually destroyed if the temperature remains above this level indefinitely. Therefore, it is immediately apparent that pain resulting from heat is closely correlated with the *rate at which damage to the tissues is occurring* and not with the total damage that has already occurred.

The intensity of pain is also closely correlated with the *rate of tissue damage* from causes other than heat, such as bacterial infection, tissue ischemia, tissue contusion, and so forth.

Special Importance of Chemical Pain Stimuli During Tissue Damage. Extracts from damaged tissue cause intense pain when injected beneath the normal skin. Most of the chemicals listed earlier that excite the chemical pain receptors can be found in these extracts. One chemical that seems to be more painful than others is *bradykinin*. Many researchers have suggested that bradykinin might be the agent most responsible for causing pain following tissue damage. Also, the intensity of the pain felt correlates with the local increase in potassium ion concentration or the increase in proteolytic enzymes that directly attack the nerve endings and excite pain by making the nerve membranes more permeable to ions.

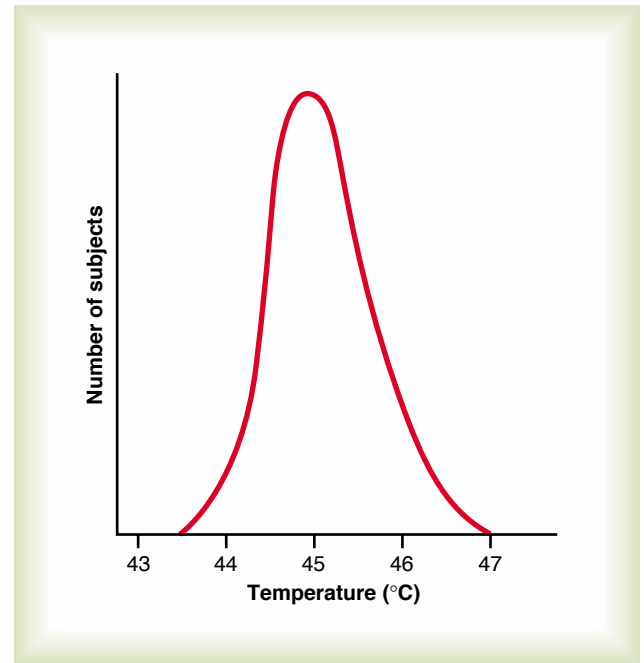


Figure 48–1

Distribution curve obtained from a large number of persons showing the minimal skin temperature that will cause pain. (Modified from Hardy DJ: Nature of pain. J Clin Epidemiol 4:22, 1956.)

Tissue Ischemia as a Cause of Pain. When blood flow to a tissue is blocked, the tissue often becomes very painful within a few minutes. The greater the rate of metabolism of the tissue, the more rapidly the pain appears. For instance, if a blood pressure cuff is placed around the upper arm and inflated until the arterial blood flow ceases, exercise of the forearm muscles sometimes can cause muscle pain within 15 to 20 seconds. In the absence of muscle exercise, the pain may not appear for 3 to 4 minutes even though the muscle blood flow remains zero.

One of the suggested causes of pain during ischemia is accumulation of large amounts of lactic acid in the tissues, formed as a consequence of anaerobic metabolism (metabolism without oxygen). It is also probable that other chemical agents, such as bradykinin and proteolytic enzymes, are formed in the tissues because of cell damage and that these, in addition to lactic acid, stimulate the pain nerve endings.

Muscle Spasm as a Cause of Pain. Muscle spasm is also a common cause of pain, and it is the basis of many clinical pain syndromes. This pain probably results partially from the direct effect of muscle spasm in stimulating mechanosensitive pain receptors, but it might also result from the indirect effect of muscle spasm to compress the blood vessels and cause ischemia. Also, the spasm increases the rate of metabolism in the muscle tissue, thus making the relative ischemia even greater, creating ideal conditions for the release of chemical pain-inducing substances.

Dual Pathways for Transmission of Pain Signals into the Central Nervous System

Even though all pain receptors are free nerve endings, these endings use two separate pathways for transmitting pain signals into the central nervous system. The two pathways mainly correspond to the two types of pain—a *fast-sharp pain pathway* and a *slow-chronic pain pathway*.

Peripheral Pain Fibers—“Fast” and “Slow” Fibers. The fast-sharp pain signals are elicited by either mechanical or thermal pain stimuli; they are transmitted in the peripheral nerves to the spinal cord by small type A δ fibers at velocities between 6 and 30 m/sec. Conversely, the slow-chronic type of pain is elicited mostly by chemical types of pain stimuli but sometimes by persisting mechanical or thermal stimuli. This slow-chronic pain is transmitted to the spinal cord by type C fibers at velocities between 0.5 and 2 m/sec.

Because of this double system of pain innervation, a sudden painful stimulus often gives a “double” pain sensation: a fast-sharp pain that is transmitted to the brain by the A δ fiber pathway, followed a second or so later by a slow pain that is transmitted by the C fiber pathway. The sharp pain appraises the person rapidly of a damaging influence and, therefore, plays an important role in making the person react immediately to remove himself or herself from the stimulus. The slow pain tends to become greater over time. This sensation eventually produces the intolerable suffering of long-continued pain and makes the person keep trying to relieve the cause of the pain.

On entering the spinal cord from the dorsal spinal roots, the pain fibers terminate on relay neurons in the dorsal horns. Here again, there are two systems for processing the pain signals on their way to the brain, as shown in Figures 48–2 and 48–3.

Dual Pain Pathways in the Cord and Brain Stem—The Neospinothalamic Tract and the Paleospinothalamic Tract

On entering the spinal cord, the pain signals take two pathways to the brain, through (1) the *neospinothalamic tract* and (2) the *paleospinothalamic tract*.

Neospinothalamic Tract for Fast Pain. The fast type A δ pain fibers transmit mainly mechanical and acute thermal pain. They terminate mainly in lamina I (lamina marginalis) of the dorsal horns, as shown in Figure 48–2, and there excite second-order neurons of the neospinothalamic tract. These give rise to long fibers that cross immediately to the opposite side of the cord through the anterior commissure and then turn upward, passing to the brain in the anterolateral columns.

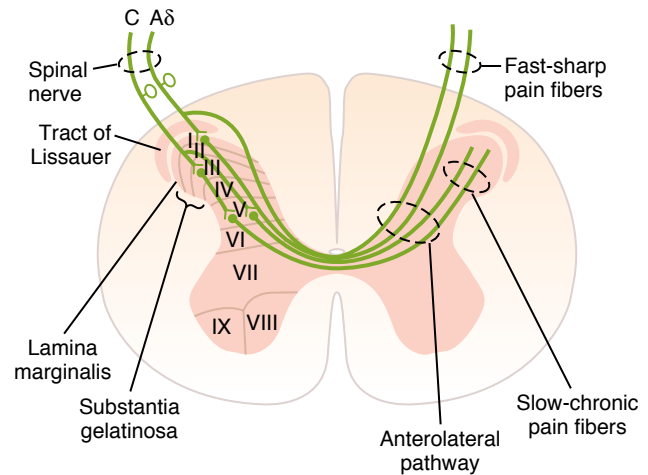


Figure 48–2

Transmission of both “fast-sharp” and “slow-chronic” pain signals into and through the spinal cord on their way to the brain.

To: Somatosensory areas

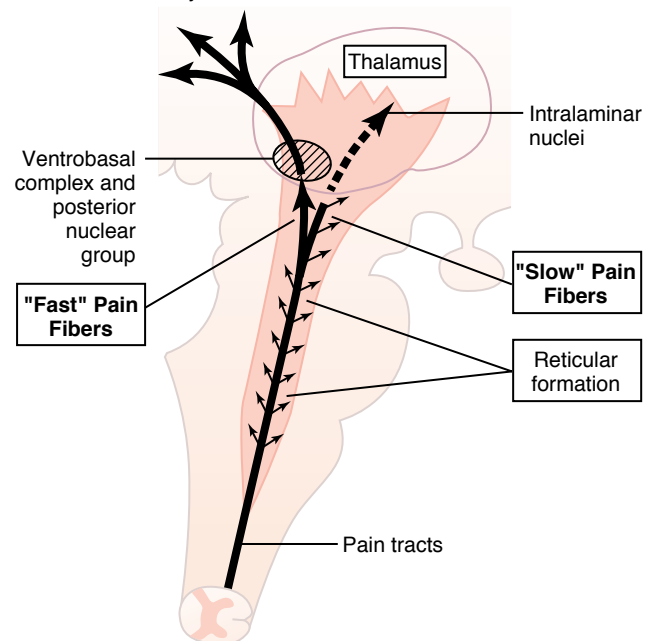


Figure 48–3

Transmission of pain signals into the brain stem, thalamus, and cerebral cortex by way of the *fast pricking pain pathway* and the *slow burning pain pathway*.

Termination of the Neospinothalamic Tract in the Brain Stem and Thalamus. A few fibers of the neospinothalamic tract terminate in the reticular areas of the brain stem, but most pass all the way to the thalamus without interruption, terminating in the *ventrobasal complex* along with the dorsal column–medial lemniscal tract for tactile sensations, as was discussed in Chapter 47. A few fibers also terminate in the posterior nuclear

group of the thalamus. From these thalamic areas, the signals are transmitted to other basal areas of the brain as well as to the somatosensory cortex.

Capability of the Nervous System to Localize Fast Pain in the Body. The fast-sharp type of pain can be localized much more exactly in the different parts of the body than can slow-chronic pain. However, when only pain receptors are stimulated, without the simultaneous stimulation of tactile receptors, even fast pain may be poorly localized, often only within 10 centimeters or so of the stimulated area. Yet when tactile receptors that excite the dorsal column–medial lemniscal system are simultaneously stimulated, the localization can be nearly exact.

Glutamate, the Probable Neurotransmitter of the Type A δ Fast Pain Fibers. It is believed that *glutamate* is the neurotransmitter substance secreted in the spinal cord at the type A δ pain nerve fiber endings. This is one of the most widely used excitatory transmitters in the central nervous system, usually having a duration of action lasting for only a few milliseconds.

Paleospinothalamic Pathway for Transmitting Slow-Chronic Pain. The paleospinothalamic pathway is a much older system and transmits pain mainly from the peripheral slow-chronic type C pain fibers, although it does transmit some signals from type A δ fibers as well. In this pathway, the peripheral fibers terminate in the spinal cord almost entirely in laminae II and III of the dorsal horns, which together are called the *substantia gelatinosa*, as shown by the lateral most dorsal root type C fiber in Figure 48–2. Most of the signals then pass through one or more additional short fiber neurons within the dorsal horns themselves before entering mainly lamina V, also in the dorsal horn. Here the last neurons in the series give rise to long axons that mostly join the fibers from the fast pain pathway, passing first through the anterior commissure to the opposite side of the cord, then upward to the brain in the anterolateral pathway.

Substance P, the Probable Slow-Chronic Neurotransmitter of Type C Nerve Endings. Research experiments suggest that type C pain fiber terminals entering the spinal cord secrete both glutamate transmitter and substance P transmitter. The glutamate transmitter acts instantaneously and lasts for only a few milliseconds. Substance P is released much more slowly, building up in concentration over a period of seconds or even minutes. In fact, it has been suggested that the “double” pain sensation one feels after a pinprick might result partly from the fact that the glutamate transmitter gives a faster pain sensation, whereas the substance P transmitter gives a more lagging sensation. Regardless of the yet unknown details, it seems clear that glutamate is the neurotransmitter most involved in transmitting fast pain into the central nervous system, and substance P is concerned with slow-chronic pain.

Projection of the Paleospinothalamic Pathway (Slow-Chronic Pain Signals) into the Brain Stem and Thalamus. The slow-chronic paleospinothalamic pathway terminates widely in the brain stem, in the large shaded area shown in Figure 48–3. Only one tenth to one fourth of the fibers pass all the way to the thalamus. Instead, most terminate in one of three areas: (1) the *reticular nuclei* of the medulla, pons, and mesencephalon; (2) the *tectal area* of the mesencephalon deep to the superior and inferior colliculi; or (3) the *periaqueductal gray region* surrounding the aqueduct of Sylvius. These lower regions of the brain appear to be important for feeling the suffering types of pain, because animals whose brains have been sectioned above the mesencephalon to block pain signals from reaching the cerebrum still evince undeniable evidence of suffering when any part of the body is traumatized. From the brain stem pain areas, multiple short-fiber neurons relay the pain signals upward into the intralaminar and ventrolateral nuclei of the thalamus and into certain portions of the hypothalamus and other basal regions of the brain.

Very Poor Capability of the Nervous System to Localize Precisely the Source of Pain Transmitted in the Slow-Chronic Pathway. Localization of pain transmitted by way of the paleospinothalamic pathway is poor. For instance, slow-chronic pain can usually be localized only to a major part of the body, such as to one arm or leg but not to a specific point on the arm or leg. This is in keeping with the multisynaptic, diffuse connectivity of this pathway. It explains why patients often have serious difficulty in localizing the source of some chronic types of pain.

Function of the Reticular Formation, Thalamus, and Cerebral Cortex in the Appreciation of Pain. Complete removal of the somatic sensory areas of the cerebral cortex does not destroy an animal’s ability to perceive pain. Therefore, it is likely that pain impulses entering the brain stem reticular formation, the thalamus, and other lower brain centers cause conscious perception of pain. This does not mean that the cerebral cortex has nothing to do with normal pain appreciation; electrical stimulation of cortical somatosensory areas does cause a human being to perceive mild pain from about 3 per cent of the points stimulated. However, it is believed that the cortex plays an especially important role in interpreting pain quality, even though pain perception might be principally the function of lower centers.

Special Capability of Pain Signals to Arouse Overall Brain Excitability. Electrical stimulation in the *reticular areas of the brain stem* and in the *intralaminar nuclei of the thalamus*, the areas where the slow-suffering type of pain terminates, has a strong arousal effect on nervous activity throughout the entire brain. In fact, these two areas constitute part of the brain’s principal “arousal system,” which is discussed in Chapter 59. This explains why it is almost impossible for a person to sleep when he or she is in severe pain.

Surgical Interruption of Pain Pathways. When a person has severe and intractable pain (sometimes resulting from rapidly spreading cancer), it is necessary to relieve the pain. To do this, the pain nervous pathways can be cut at any one of several points. If the pain is in the lower part of the body, a *cordotomy* in the thoracic region of the spinal cord often relieves the pain for a few weeks to a few months. To do this, the spinal cord on the side opposite to the pain is partially cut in its *anterolateral quadrant* to interrupt the anterolateral sensory pathway.

A cordotomy, however, is not always successful in relieving pain, for two reasons. First, many pain fibers from the upper part of the body do not cross to the opposite side of the spinal cord until they have reached the brain, so that the cordotomy does not transect these fibers. Second, pain frequently returns several months later, partly as a result of sensitization of other pathways that normally are too weak to be effectual (e.g., sparse pathways in the dorsolateral cord). Another experimental operative procedure to relieve pain has been to cauterize specific pain areas in the intralaminar nuclei in the thalamus, which often relieves suffering types of pain while leaving intact one's appreciation of "acute" pain, an important protective mechanism.

Pain Suppression ("Analgesia") System in the Brain and Spinal Cord

The degree to which a person reacts to pain varies tremendously. This results partly from a capability of the brain itself to suppress input of pain signals to the nervous system by activating a pain control system, called an *analgesia system*.

The analgesia system is shown in Figure 48-4. It consists of three major components: (1) The *periaqueductal gray* and *periventricular areas* of the mesencephalon and upper pons surround the aqueduct of Sylvius and portions of the third and fourth ventricles. Neurons from these areas send signals to (2) the *raphe magnus nucleus*, a thin midline nucleus located in the lower pons and upper medulla, and the *nucleus reticularis paragigantocellularis*, located laterally in the medulla. From these nuclei, second-order signals are transmitted down the dorsolateral columns in the spinal cord to (3) a *pain inhibitory complex located in the dorsal horns of the spinal cord*. At this point, the analgesia signals can block the pain before it is relayed to the brain.

Electrical stimulation either in the periaqueductal gray area or in the raphe magnus nucleus can suppress many strong pain signals entering by way of the dorsal spinal roots. Also, stimulation of areas at still higher levels of the brain that excite the periaqueductal gray area can also suppress pain. Some of these areas are (1) the *periventricular nuclei in the hypothalamus*, lying adjacent to the third ventricle, and (2) to a lesser extent, the *medial forebrain bundle*, also in the hypothalamus.

Several transmitter substances are involved in the analgesia system; especially involved are *enkephalin* and *serotonin*. Many nerve fibers derived from the

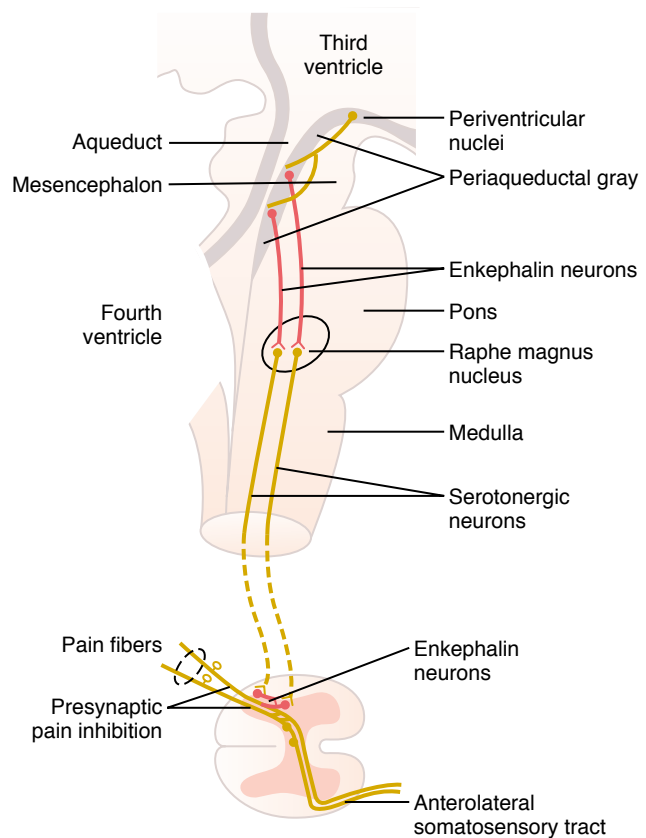


Figure 48-4

Analgesia system of the brain and spinal cord, showing (1) inhibition of incoming pain signals at the cord level and (2) presence of *enkephalin-secreting neurons* that suppress pain signals in both the cord and the brain stem.

periventricular nuclei and from the periaqueductal gray area secrete enkephalin at their endings. Thus, as shown in Figure 48-4, the endings of many fibers in the raphe magnus nucleus release enkephalin when stimulated.

Fibers originating in this area send signals to the dorsal horns of the spinal cord to secrete serotonin at their endings. The serotonin causes local cord neurons to secrete enkephalin as well. The enkephalin is believed to cause both *presynaptic* and *postsynaptic inhibition* of incoming type C and type A δ pain fibers where they synapse in the dorsal horns.

Thus, the analgesia system can block pain signals at the initial entry point to the spinal cord. In fact, it can also block many local cord reflexes that result from pain signals, especially withdrawal reflexes described in Chapter 54.

Brain's Opiate System—Endorphins and Enkephalins

More than 35 years ago it was discovered that injection of minute quantities of morphine either into the periventricular nucleus around the third ventricle or

into the periaqueductal gray area of the brain stem causes an extreme degree of analgesia. In subsequent studies, it has been found that morphine-like agents, mainly the opiates, also act at many other points in the analgesia system, including the dorsal horns of the spinal cord. Because most drugs that alter excitability of neurons do so by acting on synaptic receptors, it was assumed that the “morphine receptors” of the analgesia system must be receptors for some morphine-like neurotransmitter that is naturally secreted in the brain. Therefore, an extensive search was undertaken for the natural opiate of the brain. About a dozen such opiate-like substances have now been found at different points of the nervous system; all are breakdown products of three large protein molecules: *pro-opiomelanocortin*, *proenkephalin*, and *prodynorphin*. Among the more important of these opiate-like substances are β -endorphin, *met-enkephalin*, *leu-enkephalin*, and *dynorphin*.

The two enkephalins are found in the brain stem and spinal cord, in the portions of the analgesia system described earlier, and β -endorphin is present in both the hypothalamus and the pituitary gland. Dynorphin is found mainly in the same areas as the enkephalins, but in much lower quantities.

Thus, although the fine details of the brain’s opiate system are not understood, *activation of the analgesia system* by nervous signals entering the periaqueductal gray and periventricular areas, or *inactivation of pain pathways* by morphine-like drugs, can almost totally suppress many pain signals entering through the peripheral nerves.

Inhibition of Pain Transmission by Simultaneous Tactile Sensory Signals

Another important event in the saga of pain control was the discovery that stimulation of large type A β sensory fibers from peripheral tactile receptors can depress transmission of pain signals from the same body area. This presumably results from local lateral inhibition in the spinal cord. It explains why such simple maneuvers as rubbing the skin near painful areas is often effective in relieving pain. And it probably also explains why liniments are often useful for pain relief.

This mechanism and the simultaneous psychogenic excitation of the central analgesia system are probably also the basis of pain relief by *acupuncture*.

Treatment of Pain by Electrical Stimulation

Several clinical procedures have been developed for suppressing pain by electrical stimulation. Stimulating electrodes are placed on selected areas of the skin or, on occasion, implanted over the spinal cord, supposedly to stimulate the dorsal sensory columns.

In some patients, electrodes have been placed stereotactically in appropriate intralaminar nuclei of the thalamus or in the periventricular or periaqueductal area of the diencephalon. The patient can then personally control the degree of stimulation. Dramatic relief has

been reported in some instances. Also, pain relief has been reported to last for as long as 24 hours after only a few minutes of stimulation.

Referred Pain

Often a person feels pain in a part of the body that is fairly remote from the tissue causing the pain. This is called *referred pain*. For instance, pain in one of the visceral organs often is referred to an area on the body surface. Knowledge of the different types of referred pain is important in clinical diagnosis because in many visceral ailments the only clinical sign is referred pain.

Mechanism of Referred Pain. Figure 48–5 shows the probable mechanism by which most pain is referred. In the figure, branches of visceral pain fibers are shown to synapse in the spinal cord on the same second-order neurons (1 and 2) that receive pain signals from the skin. When the visceral pain fibers are stimulated, pain signals from the viscera are conducted through at least some of the same neurons that conduct pain signals from the skin, and the person has the feeling that the sensations originate in the skin itself.

Visceral Pain

In clinical diagnosis, pain from the different viscera of the abdomen and chest is one of the few criteria that can be used for diagnosing visceral inflammation, visceral infectious disease, and other visceral ailments. Often, the viscera have sensory receptors for no other modalities of sensation besides pain. Also, visceral pain differs from surface pain in several important aspects.

One of the most important differences between surface pain and visceral pain is that highly localized types of damage to the viscera seldom cause severe pain. For instance, a surgeon can cut the gut entirely in two in a patient who is awake without causing significant pain. Conversely, any stimulus that causes *diffuse stimulation of pain nerve endings* throughout a viscus causes pain that can be severe. For instance, ischemia

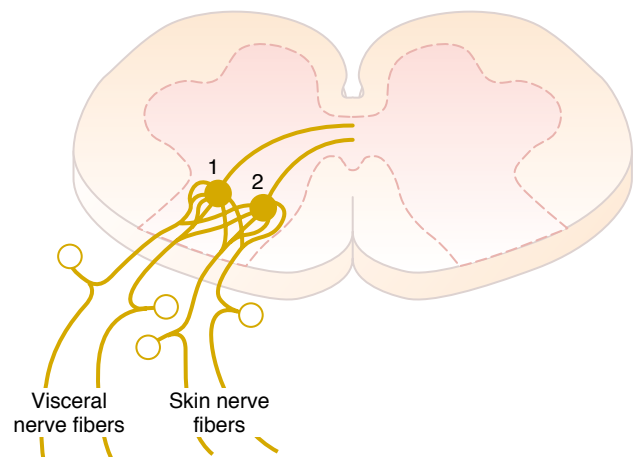


Figure 48–5

Mechanism of referred pain and referred hyperalgesia.

caused by occluding the blood supply to a large area of gut stimulates many diffuse pain fibers at the same time and can result in extreme pain.

Causes of True Visceral Pain

Any stimulus that excites pain nerve endings in diffuse areas of the viscera can cause visceral pain. Such stimuli include ischemia of visceral tissue, chemical damage to the surfaces of the viscera, spasm of the smooth muscle of a hollow viscus, excess distention of a hollow viscus, and stretching of the connective tissue surrounding or within the viscus. Essentially all visceral pain that originates in the thoracic and abdominal cavities is transmitted through small type C pain fibers and, therefore, can transmit only the chronic-aching-suffering type of pain.

Ischemia. Ischemia causes visceral pain in the same way that it does in other tissues, presumably because of the formation of acidic metabolic end products or tissue-degenerative products such as bradykinin, proteolytic enzymes, or others that stimulate pain nerve endings.

Chemical Stimuli. On occasion, damaging substances leak from the gastrointestinal tract into the peritoneal cavity. For instance, proteolytic acidic gastric juice often leaks through a ruptured gastric or duodenal ulcer. This juice causes widespread digestion of the visceral peritoneum, thus stimulating broad areas of pain fibers. The pain is usually excruciatingly severe.

Spasm of a Hollow Viscus. Spasm of a portion of the gut, the gallbladder, a bile duct, a ureter, or any other hollow viscus can cause pain, possibly by mechanical stimulation of the pain nerve endings. Or the spasm might cause diminished blood flow to the muscle, combined with the muscle's increased metabolic need for nutrients, thus causing severe pain.

Often pain from a spastic viscus occurs in the form of *cramps*, with the pain increasing to a high degree of severity and then subsiding. This process continues intermittently, once every few minutes. The intermittent cycles result from periods of contraction of smooth muscle. For instance, each time a peristaltic wave travels along an overly excitable spastic gut, a cramp occurs. The cramping type of pain frequently occurs in appendicitis, gastroenteritis, constipation, menstruation, parturition, gallbladder disease, or ureteral obstruction.

Overdistention of a Hollow Viscus. Extreme overfilling of a hollow viscus also can result in pain, presumably because of overstretch of the tissues themselves. Overdistention can also collapse the blood vessels that encircle the viscus or that pass into its wall, thus perhaps promoting ischemic pain.

Insensitive Viscera. A few visceral areas are almost completely insensitive to pain of any type. These include the parenchyma of the liver and the alveoli of the lungs. Yet the liver *capsule* is extremely sensitive to both direct trauma and stretch, and the *bile ducts* are also sensitive to pain. In the lungs, even though the alveoli are insensitive, both the *bronchi* and the *parietal pleura* are very sensitive to pain.

“Parietal Pain” Caused by Visceral Disease

When a disease affects a viscus, the disease process often spreads to the parietal peritoneum, pleura, or pericardium. These parietal surfaces, like the skin, are supplied with extensive pain innervation from the peripheral spinal nerves. Therefore, pain from the parietal wall overlying a viscus is frequently sharp. An example can emphasize the difference between this pain and true visceral pain: a knife incision through the *parietal* peritoneum is very painful, whereas a similar cut through the visceral peritoneum or through a gut wall is not very painful, if painful at all.

Localization of Visceral Pain—“Visceral” and the “Parietal” Pain Transmission Pathways

Pain from the different viscera is frequently difficult to localize, for a number of reasons. First, the patient's brain does not know from firsthand experience that the different internal organs exist; therefore, any pain that originates internally can be localized only generally. Second, sensations from the abdomen and thorax are transmitted through two pathways to the central nervous system—the *true visceral pathway* and the *parietal pathway*. True visceral pain is transmitted via pain sensory fibers within the autonomic nerve bundles, and the sensations are *referred* to surface areas of the body often far from the painful organ. Conversely, parietal sensations are conducted *directly* into local spinal nerves from the parietal peritoneum, pleura, or pericardium, and these sensations are usually *localized directly over the painful area*.

Localization of Referred Pain Transmitted via Visceral Pathways.

When visceral pain is referred to the surface of the body, the person generally localizes it in the dermatomal segment from which the visceral organ originated in the embryo, not necessarily where the visceral organ now lies. For instance, the heart originated in the neck and upper thorax, so that the heart's visceral pain fibers pass upward along the sympathetic sensory nerves and enter the spinal cord between segments C-3 and T-5. Therefore, as shown in Figure 48–6, pain from the heart is referred to the side of the neck, over the shoulder, over the pectoral muscles, down the arm, and into the sub-sternal area of the upper chest. These are the areas of the body surface that send their own somatosensory nerve fibers into the C-3 to T-5 cord segments. Most frequently, the pain is on the left side rather than on the right because the left side of the heart is much more frequently involved in coronary disease than the right.

The stomach originated approximately from the seventh to ninth thoracic segments of the embryo. Therefore, stomach pain is referred to the anterior epigastrium above the umbilicus, which is the surface area of the body subserved by the seventh through ninth thoracic segments. Figure 48–6 shows several other surface areas to which visceral pain is referred from other organs, representing in general the areas in the embryo from which the respective organs originated.

Parietal Pathway for Transmission of Abdominal and Thoracic Pain. Pain from the viscera is frequently localized to two surface areas of the body at the same time because of

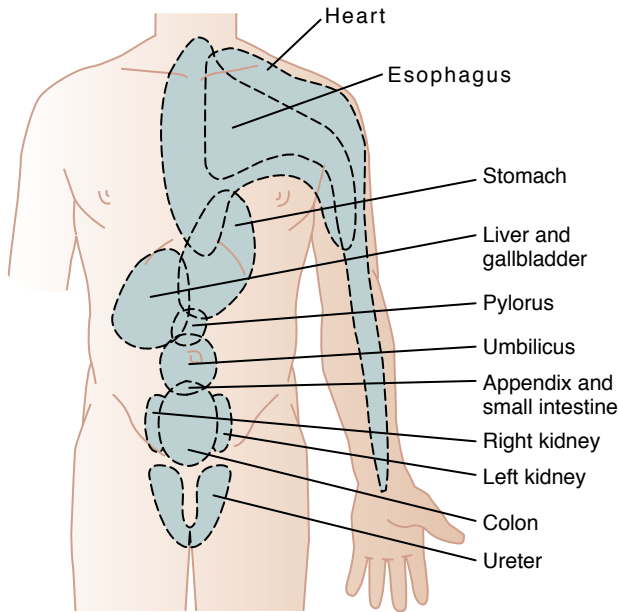


Figure 48-6

Surface areas of referred pain from different visceral organs.

the dual transmission of pain through the referred visceral pathway and the direct parietal pathway. Thus, Figure 48-7 shows dual transmission from an inflamed appendix. Pain impulses pass first from the appendix through visceral pain fibers located within sympathetic nerve bundles, and then into the spinal cord at about T-10 or T-11; this pain is referred to an area around the umbilicus and is of the aching, cramping type. Pain impulses also often originate in the parietal peritoneum where the inflamed appendix touches or is adherent to the abdominal wall. These cause pain of the sharp type directly over the irritated peritoneum in the right lower quadrant of the abdomen.

Some Clinical Abnormalities of Pain and Other Somatic Sensations

Hyperalgesia

A pain nervous pathway sometimes becomes excessively excitable; this gives rise to *hyperalgesia*, which means hypersensitivity to pain. Possible causes of hyperalgesia are (1) excessive sensitivity of the pain receptors themselves, which is called *primary hyperalgesia*, and (2) facilitation of sensory transmission, which is called *secondary hyperalgesia*.

An example of primary hyperalgesia is the extreme sensitivity of sunburned skin, which results from sensitization of the skin pain endings by local tissue products from the burn—perhaps histamine, perhaps prostaglandins, perhaps others. Secondary hyperalgesia frequently results from lesions in the spinal cord or the thalamus. Several of these lesions are discussed in subsequent sections.

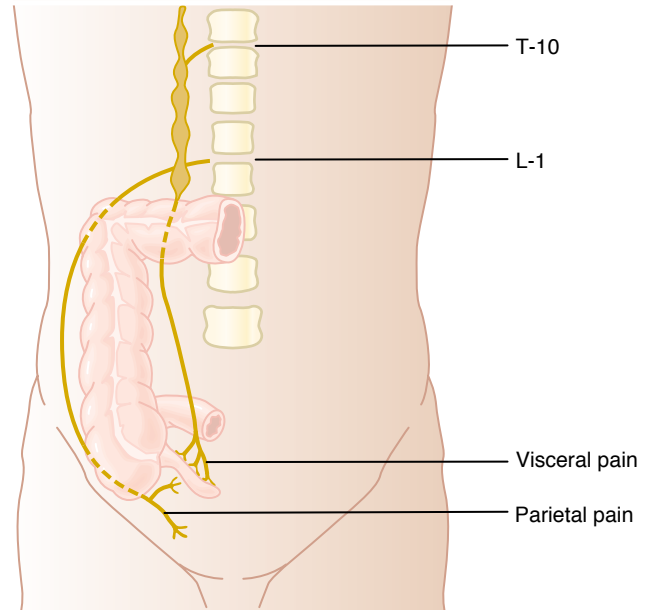


Figure 48-7

Visceral and parietal transmission of pain signals from the appendix.

Herpes Zoster (Shingles)

Occasionally *herpesvirus* infects a dorsal root ganglion. This causes severe pain in the dermatomal segment subserved by the ganglion, thus eliciting a segmental type of pain that circles halfway around the body. The disease is called *herpes zoster*, or “shingles,” because of a skin eruption that often ensues.

The cause of the pain is presumably infection of the pain neuronal cells in the dorsal root ganglion by the virus. In addition to causing pain, the virus is carried by neuronal cytoplasmic flow outward through the neuronal peripheral axons to their cutaneous origins. Here the virus causes a rash that vesiculates within a few days and then crusts over within another few days, all of this occurring within the dermatomal area served by the infected dorsal root.

Tic Douloureux

Lancinating pain occasionally occurs in some people over one side of the face in the sensory distribution area (or part of the area) of the fifth or ninth nerves; this phenomenon is called *tic douloureux* (or *trigeminal neuralgia* or *glossopharyngeal neuralgia*). The pain feels like sudden electrical shocks, and it may appear for only a few seconds at a time or may be almost continuous. Often it is set off by exceedingly sensitive trigger areas on the surface of the face, in the mouth, or inside the throat—almost always by a mechanoreceptive stimulus rather than a pain stimulus. For instance, when the patient swallows a bolus of food, as the food touches a tonsil, it might set off a severe lancinating pain in the mandibular portion of the fifth nerve.

The pain of tic douloureux can usually be blocked by surgically cutting the peripheral nerve from the hypersensitive area. The sensory portion of the fifth nerve is

often sectioned immediately inside the cranium, where the motor and sensory roots of the fifth nerve separate from each other, so that the motor portions, which are needed for many jaw movements, can be spared while the sensory elements are destroyed. This operation leaves the side of the face anesthetic, which in itself may be annoying. Furthermore, sometimes the operation is unsuccessful, indicating that the lesion that causes the pain might be in the sensory nucleus in the brain stem and not in the peripheral nerves.

Brown-Séquard Syndrome

If the spinal cord is transected entirely, all sensations and motor functions distal to the segment of transection are blocked, but if the spinal cord is transected on only one side, the *Brown-Séquard syndrome* occurs. The effects of such transection can be predicted from a knowledge of the cord fiber tracts shown in Figure 48–8. All motor functions are blocked on the side of the transection in all segments below the level of the transection. Yet only some of the modalities of sensation are lost on the transected side, and others are lost on the opposite side. The sensations of pain, heat, and cold—sensations served by the spinothalamic pathway—are lost *on the opposite side of the body* in all dermatomes two to six segments below the level of the transection. By contrast, the sensations that are transmitted only in the dorsal and dorsolateral columns—kinesthetic and position sensations, vibration sensation, discrete localization, and two-point discrimination—are lost *on the side of the transection* in all dermatomes below the level of the transection. Discrete “light touch” is impaired on the side of the transection because the principal pathway for the transmission of light touch, the dorsal column, is transected. That is, the fibers in this column do not cross to the opposite side until they reach the medulla of the brain. “Crude touch,” which is poorly localized, still persists because of partial transmission in the opposite spinothalamic tract.

Headache

Headaches are a type of pain referred to the surface of the head from deep head structures. Some headaches

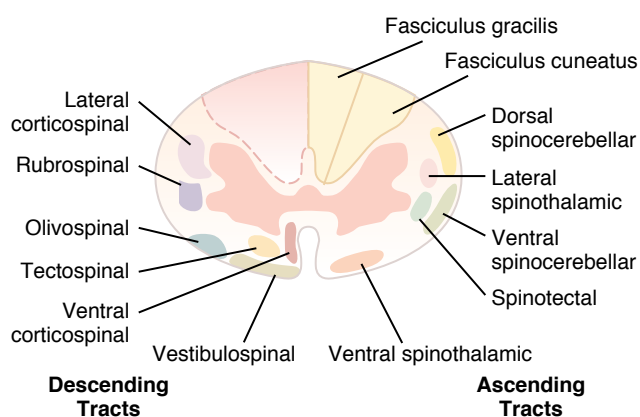


Figure 48–8

Cross section of the spinal cord, showing principal ascending tracts on the right and principal descending tracts on the left.

result from pain stimuli arising inside the cranium, but others result from pain arising outside the cranium, such as from the nasal sinuses.

Headache of Intracranial Origin

Pain-Sensitive Areas in Cranial Vault. The brain tissues themselves are almost totally insensitive to pain. Even cutting or electrically stimulating the sensory areas of the cerebral cortex only occasionally causes pain; instead, it causes prickly types of paresthesias on the area of the body represented by the portion of the sensory cortex stimulated. Therefore, it is likely that much or most of the pain of headache is not caused by damage within the brain itself.

Conversely, *tugging on the venous sinuses around the brain, damaging the tentorium, or stretching the dura at the base of the brain* can cause intense pain that is recognized as headache. Also, almost any type of traumatizing, crushing, or stretching stimulus to the *blood vessels of the meninges* can cause headache. An especially sensitive structure is the middle meningeal artery, and neurosurgeons are careful to anesthetize this artery specifically when performing brain operations under local anesthesia.

Areas of the Head to Which Intracranial Headache Is Referred.

Stimulation of pain receptors in the cerebral vault above the tentorium, including the upper surface of the tentorium itself, initiates pain impulses in the cerebral portion of the fifth nerve and, therefore, causes referred headache to the front half of the head in the surface areas supplied by this somatosensory portion of the fifth cranial nerve, as shown in Figure 48–9.

Conversely, pain impulses from beneath the tentorium enter the central nervous system mainly through the glossopharyngeal, vagal, and second cervical nerves, which also supply the scalp above, behind, and slightly below the ear. Subtentorial pain stimuli cause “occipital headache” referred to the posterior part of the head.

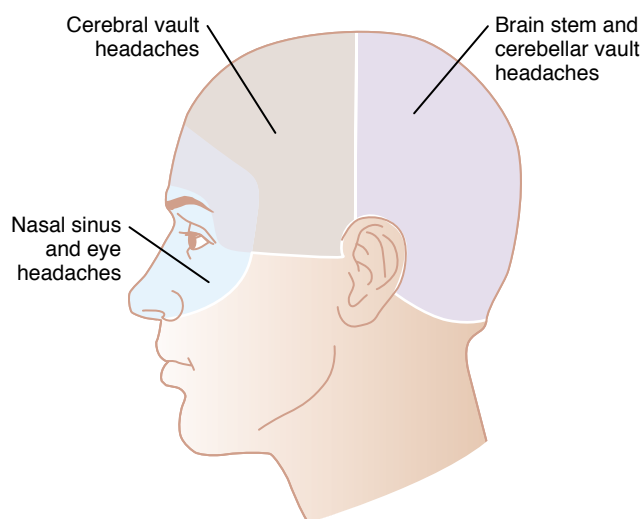


Figure 48–9

Areas of headache resulting from different causes.

Types of Intracranial Headache

Headache of Meningitis. One of the most severe headaches of all is that resulting from meningitis, which causes inflammation of all the meninges, including the sensitive areas of the dura and the sensitive areas around the venous sinuses. Such intense damage can cause extreme headache pain referred over the entire head.

Headache Caused by Low Cerebrospinal Fluid Pressure.

Removing as little as 20 milliliters of fluid from the spinal canal, particularly if the person remains in an upright position, often causes intense intracranial headache. Removing this quantity of fluid removes part of the flotation for the brain that is normally provided by the cerebrospinal fluid. The weight of the brain stretches and otherwise distorts the various dural surfaces and thereby elicits the pain that causes the headache.

Migraine Headache. Migraine headache is a special type of headache that is thought to result from abnormal vascular phenomena, although the exact mechanism is unknown. Migraine headaches often begin with various prodromal sensations, such as nausea, loss of vision in part of the field of vision, visual aura, and other types of sensory hallucinations. Ordinarily, the prodromal symptoms begin 30 minutes to 1 hour before the beginning of the headache. Any theory that explains migraine headache must also explain the prodromal symptoms.

One of the theories of the cause of migraine headaches is that prolonged emotion or tension causes reflex vasospasm of some of the arteries of the head, including arteries that supply the brain. The vasospasm theoretically produces ischemia of portions of the brain, and this is responsible for the prodromal symptoms. Then, as a result of the intense ischemia, something happens to the vascular walls, perhaps exhaustion of smooth muscle contraction, to allow the blood vessels to become flaccid and incapable of maintaining vascular tone for 24 to 48 hours. The blood pressure in the vessels causes them to dilate and pulsate intensely, and it is postulated that the excessive stretching of the walls of the arteries—including some extracranial arteries, such as the temporal artery—causes the actual pain of migraine headaches. Other theories of the cause of migraine headaches include spreading cortical depression, psychological abnormalities, and vasospasm caused by excess local potassium in the cerebral extracellular fluid.

There may be a genetic predisposition to migraine headaches, because a positive family history for migraine has been reported in 65 to 90 per cent of cases. Migraine headaches also occur about twice as frequently in women as in men.

Alcoholic Headache. As many people have experienced, a headache usually follows an alcoholic binge. It is most likely that alcohol, because it is toxic to tissues, directly irritates the meninges and causes the intracranial pain.

Headache Caused by Constipation. Constipation causes headache in many people. Because it has been shown that constipation headache can occur in people whose pain sensory tracts in the spinal cord have been cut, we know that this headache is not caused by nervous impulses from the colon. Therefore, it may result from

absorbed toxic products or from changes in the circulatory system resulting from loss of fluid into the gut.

Extracranial Types of Headache

Headache Resulting from Muscle Spasm. Emotional tension often causes many of the muscles of the head, especially those muscles attached to the scalp and the neck muscles attached to the occiput, to become spastic, and it is postulated that this is one of the common causes of headache. The pain of the spastic head muscles supposedly is referred to the overlying areas of the head and gives one the same type of headache as intracranial lesions do.

Headache Caused by Irritation of Nasal and Accessory Nasal Structures. The mucous membranes of the nose and nasal sinuses are sensitive to pain, but not intensely so. Nevertheless, infection or other irritative processes in widespread areas of the nasal structures often summate and cause headache that is referred behind the eyes or, in the case of frontal sinus infection, to the frontal surfaces of the forehead and scalp, as shown in Figure 48–9. Also, pain from the lower sinuses, such as from the maxillary sinuses, can be felt in the face.

Headache Caused by Eye Disorders. Difficulty in focusing one's eyes clearly may cause excessive contraction of the eye ciliary muscles in an attempt to gain clear vision. Even though these muscles are extremely small, it is believed that tonic contraction of them can cause retro-orbital headache. Also, excessive attempts to focus the eyes can result in reflex spasm in various facial and extraocular muscles, which is a possible cause of headache.

A second type of headache that originates in the eyes occurs when the eyes are exposed to excessive irradiation by light rays, especially ultraviolet light. Looking at the sun or the arc of an arc-welder for even a few seconds may result in headache that lasts from 24 to 48 hours. The headache sometimes results from “actinic” irritation of the conjunctivae, and the pain is referred to the surface of the head or retro-orbitally. However, focusing intense light from an arc or the sun on the retina can also burn the retina, and this could be the cause of the headache.

Thermal Sensations**Thermal Receptors and Their Excitation**

The human being can perceive different gradations of cold and heat, from *freezing cold* to *cold* to *cool* to *indifferent* to *warm* to *hot* to *burning hot*.

Thermal gradations are discriminated by at least three types of sensory receptors: cold receptors, warmth receptors, and pain receptors. The pain receptors are stimulated only by extreme degrees of heat or cold and, therefore, are responsible, along with the cold and warmth receptors, for “freezing cold” and “burning hot” sensations.

The cold and warmth receptors are located immediately under the skin at discrete separated *spots*. In

most areas of the body, there are 3 to 10 times as many cold spots as warmth spots, and the number in different areas of the body varies from 15 to 25 cold spots per square centimeter in the lips to 3 to 5 cold spots per square centimeter in the finger to less than 1 cold spot per square centimeter in some broad surface areas of the trunk.

Although the existence of distinctive warmth nerve endings is quite certain, based on psychological tests, they have not been identified histologically. They are presumed to be free nerve endings, because warmth signals are transmitted mainly over type C nerve fibers at transmission velocities of only 0.4 to 2 m/sec.

Conversely, a definitive cold receptor has been identified. It is a special, small type A δ myelinated nerve ending that branches a number of times, the tips of which protrude into the bottom surfaces of basal epidermal cells. Signals are transmitted from these receptors via type A δ nerve fibers at velocities of about 20 m/sec. Some cold sensations are believed to be transmitted in type C nerve fibers as well, which suggests that some free nerve endings also might function as cold receptors.

Stimulation of Thermal Receptors—Sensations of Cold, Cool, Indifferent, Warm, and Hot. Figure 48–10 shows the effects of different temperatures on the responses of four types of nerve fibers: (1) a pain fiber stimulated by cold, (2) a cold fiber, (3) a warmth fiber, and (4) a pain fiber stimulated by heat. Note especially that these fibers respond differently at different levels of temperature. For instance, in the *very* cold region, only the cold-pain fibers are stimulated (if the skin becomes even colder, so that it nearly freezes or actually does freeze, these fibers cannot be stimulated). As the temperature rises to +10° to 15°C, the cold-pain impulses cease, but the cold receptors begin to be stimulated, reaching peak stimulation at about 24°C and fading

out slightly above 40°C. Above about 30°C, the warmth receptors begin to be stimulated, but these also fade out at about 49°C. Finally, at around 45°C, the heat-pain fibers begin to be stimulated by heat and, paradoxically, some of the cold fibers begin to be stimulated again, possibly because of damage to the cold endings caused by the excessive heat.

One can understand from Figure 48–10 that a person determines the different gradations of thermal sensations by the relative degrees of stimulation of the different types of endings. One can also understand why extreme degrees of both cold and heat can be painful and why both these sensations, when intense enough, may give almost the same quality of sensation—that is, freezing cold and burning hot sensations feel almost alike.

Stimulatory Effects of Rising and Falling Temperature—Adaptation of Thermal Receptors. When a cold receptor is suddenly subjected to an abrupt fall in temperature, it becomes strongly stimulated at first, but this stimulation fades rapidly during the first few seconds and progressively more slowly during the next 30 minutes or more. In other words, the receptor “adapts” to a great extent, but never 100 per cent.

Thus, it is evident that the thermal senses respond markedly to *changes in temperature*, in addition to being able to respond to steady states of temperature. This means that when the temperature of the skin is actively falling, a person feels much colder than when the temperature remains cold at the same level. Conversely, if the temperature is actively rising, the person feels much warmer than he or she would at the same temperature if it were constant. The response to changes in temperature explains the extreme degree of heat one feels on first entering a tub of hot water and the extreme degree of cold felt on going from a heated room to the out-of-doors on a cold day.

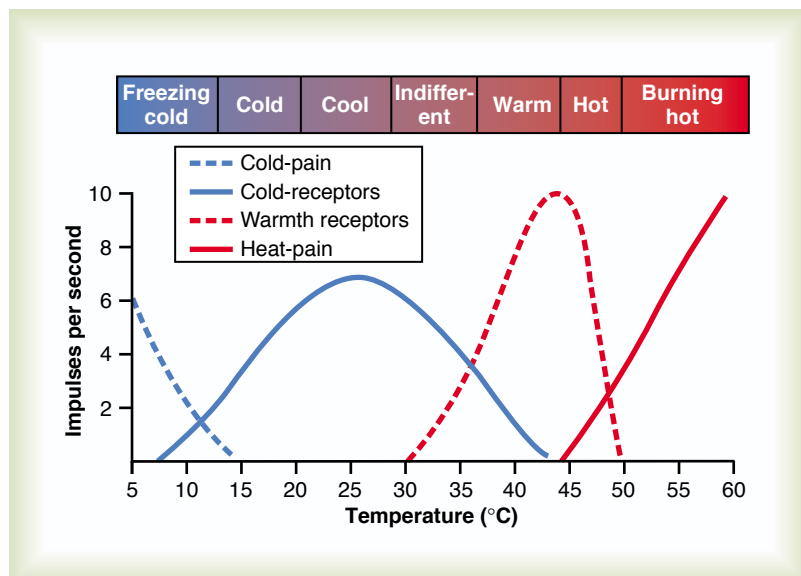


Figure 48–10

Discharge frequencies at different skin temperatures of a cold-pain fiber, a cold fiber, a warmth fiber, and a heat-pain fiber.

Mechanism of Stimulation of Thermal Receptors

It is believed that the cold and warmth receptors are stimulated by changes in their metabolic rates, and that these changes result from the fact that temperature alters the rate of intracellular chemical reactions more than twofold for each 10°C change. In other words, thermal detection probably results not from direct physical effects of heat or cold on the nerve endings but from chemical stimulation of the endings as modified by temperature.

Spatial Summation of Thermal Sensations. Because the number of cold or warm endings in any one surface area of the body is slight, it is difficult to judge gradations of temperature when small skin areas are stimulated. However, when a large skin area is stimulated all at once, the thermal signals from the entire area summate. For instance, rapid changes in temperature as little as 0.01°C can be detected if this change affects the entire surface of the body simultaneously. Conversely, temperature changes 100 times as great often will not be detected when the affected skin area is only 1 square centimeter in size.

Transmission of Thermal Signals in the Nervous System

In general, thermal signals are transmitted in pathways parallel to those for pain signals. On entering the spinal cord, the signals travel for a few segments upward or downward in the *tract of Lissauer* and then terminate mainly in laminae I, II, and III of the dorsal horns—the same as for pain. After a small amount of processing by one or more cord neurons, the signals enter long, ascending thermal fibers that cross to the opposite anterolateral sensory tract and terminate in both (1) the reticular areas of the brain stem and (2) the ventrobasal complex of the thalamus.

A few thermal signals are also relayed to the cerebral somatic sensory cortex from the ventrobasal complex. Occasionally a neuron in cortical somatic sensory area I has been found by microelectrode studies to be directly responsive to either cold or warm stimuli on a specific area of the skin. However, removal of the entire cortical postcentral gyrus in the human

being reduces but does not abolish the ability to distinguish gradations of temperature.

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