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Overview of Pain: Classification and Concepts

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Pain is generally described as an unpleasant sensation. Pain, as a concept and symptom, is discussed and described throughout professional and lay medical literature. Pain is the reason for initial contact with any physician for the vast majority of medical problems, e.g., abdominal pain, chest pain, limb pain, low back pain. As such, pain *condition* classification is very sophisticated and advanced, as demonstrated by the IASP Chronic Pain Classification system (Merskey & Bogduk, 1994) and others (Derasari, 2000; Waldman, 2003).

The foundation for the history of physiological pain (mechanism) classification essentially started with Descartes (Melzack & Wall, 1965) in the 17th century but has not been framed in these terms until recently (Thienhaus & Cole, 1998, 2001). The history of pain condition classification is synonymous with the history of pain in humankind.

Only recently have physician neuroscientists and medical doctors begun to focus on pain mechanisms that are the foundation for understanding pain conditions and, therefore, for pain classification (Dallel & Voisin, 2001). This effort should proceed rapidly, because much information is already available. However, this progression is hindered by the difficulties of transferring scientific knowledge to medical practice.

The main reason to classify (i.e., label or name) clinical presentations of symptoms centered around pain is to facilitate communication between patient and doctor for better pain care outcomes. The goal of therapy is to reduce suffering and increase function, which is the overriding purpose for practicing pain management and is at the core of this textbook and of medicine itself (Fields & Martin, 2001).

THE PRESENT STATE OF PAIN THEORY AND THOUGHT

Pain is described in a myriad of ways:

- In temporal terms: chronic pain, subacute pain, and acute pain
- In characterizations: intermittent pain, intractable pain, lancinating pain, referred pain, burning pain, and dull pain
- In medical diagnoses: phantom pain, cancer pain, vascular pain, arthritic pain, nerve pain, muscle pain, fibromyalgia, myofascial pain, sympathetically maintained pain, and complex regional pain syndrome
- In mechanistic/etiologic terms: neuropathic and nociceptive pain
- In anatomic perceptional terms: headache, back pain, neck pain, facial pain, limb pain, abdominal pain, etc.
- In source or origin terms: central pain as originating in the spinal cord or brain, or peripheral pain
- In psychiatric/psychogenic terms: psychosomatic ("all-in-the-head") pain, etc.

Caudill (1995) analyzed pain from different angles to emphasize its complexity:

- Biologically — Serves as a signal that the body has been harmed.

- Psychologically — Is experienced as emotional suffering.
- Behaviorally — Alters the way a person moves and acts.
- Cognitively — Calls for thinking about its meaning, its cause, and possible remedies.
- Spiritually — Serves as a reminder of mortality.
- Culturally — Tests a people's fortitude or forces their submission.

DSM-IV-TR Pain Disorders

Pain Disorders are coded for their medical conditions in the *DSM-IV-TR* (American Psychiatric Association, 2000; First and Pincus, 2000) as follows:

307.80 Pain Disorder Associated with Psychological Factors
307.89 Pain Disorder Associated with Both Psychological Factors and a General Pain Condition

Elsewhere, the *DSM-IV-TR* (First & Pincus, 2000) attributes neural dysfunction to pain. Again, these are only descriptive categories and do not provide insight into underlying pain mechanism. Suffering, or the affective component, is not separated.

Pain Classification Characteristics

Pain has been classified by anatomic location, body system, duration, severity, frequency, and etiology (Cole, 2002). Merskey and Bogduk (1994) have done a prodigious job of compiling numerous pain conditions, basically all pain conditions mentioned in modern medical literature. Refer to Table 4.1 for a summary of the characteristics of this and other current systems of pain classification.

To add complexity, many factors, such as culture, personality, psychosocial stressors, nutritional status, and other disease states, can be involved to influence the degree of perceived pain and to confound understanding of the causal factors of the pain.

Healthcare professionals and the general public tend to think of location first for most pain classification systems. Waldman (2002, 2003) did so in listing and describing many locations for both common and uncommon pain conditions.

The simplest traditional categorization of pain has been "acute" and "chronic." Acute pain is usually just a result of the stimulation of a normally functioning pain detection system and serves to allow us to avoid or minimize tissue damage. Chronic pain merely means that pain is perceived over a long period of time, which is often arbitrarily set at 3 to 6 months.

However, while the chronology of pain has further subdivided pains basically into "acute" and "chronic," there is a mechanistic relationship, i.e., acute pain is simple nociceptive pain and chronic pain is a complex mix of pathologies along the neural pathways. Dr. Lippe (1998) has suggested the useful terms, *eudynia* (good pain) and *maldynia* (bad pain). As a generalization, many would describe eudynia as acute, and maldynia as chronic, although actual, individual cases tend to be more complex in both cases.

"Biopsychosocial" considerations are one step up from the "traditional" classification. The "pathogenetic"

TABLE 4.1
Pain Classification Systems

Categories	I	II	III	IV	V
Traditional	Acute	Subacute	Chronic		
Biopsychosocial	Acute	Recurrent acute	Cancer related	Chronic nonmalignant	
Pathogenetic	Primary	Secondary	TX. Effect (chemotherapy, tissue trauma, edema, etc.)		
ICD-9[a]	Disease process	Pain location	Secondary		
Dickerson (special case adapted by Brookoff, 2000, who elaborates the various subtypes)	Neuropathic	Inflammatory	Long-term		
IASP[b,c]	Region	System	Chronology	Intensity	Etiology

Note: The "traditional" classification scheme addresses chronology, location, and gross mechanisms.

[a] International Classification of Diseases, 9th edition.
[b] International Association for the Study of Pain.
[c] Merkey & Bogduk, 1994.

TX = therapy; Effect = therapy effect.

system grossly indicates the cause, primary or secondary, as major disease classifications. Inflammatory and long-term designations can involve both nociceptive and neuropathic pain. The IASP system provides a more detailed description of the pain, but fails to approach the cause, except generally in Etiology; the IASP definition of pain avoids linking pain to a specific stimulus.

The biopsychosocial model includes four categories: acute, recurrent acute, cancer-related, and chronic non-malignant pain. The first two categories deal with timing issues; the latter two categories speak to whether cancer is involved. Although useful in incorporating the issue of suffering, we suggest that these categories bear little relationship to mechanisms of pain. Except, perhaps, for vascular aches, identifying the location of the pain is not necessary to basic understanding. The basic pain mechanisms are the same — whether for arm, leg, abdominal, or ear pain. Further, we think that the mechanisms of pain and pain pathways are the same, whether or not cancer is involved.

The most advanced concepts are expressed by Craig (2002), who states that pain is just one manifestation of the mind–body homeostasis system. From the patient's point of view, the spectrum of pain control spans temporary treatments (usually pharmaceutical) in suppressing pain to permanent remission or cure of underlying pathology/disease.

Obviously, these are all very useful concepts; but, are still generally academic in nature and do not provide much practical help to a physician. Concepts of pain pathophysiology, and thus classification, are abundantly available in the scientific and medical literatures. There is a need to refine and clarify all of this information and apply it as simply as possible to the treatment of pain in the physician's office.

Pain and Suffering

Pain is an unpleasant sensation appreciated as suffering. Most of the present pain classification systems actually include suffering as an essential part of the pain condition described. If suffering is removed, then, theoretically, pain can occur without suffering and would then logically seldom come to medical attention.

Suffering, as a separate life experience, may remain in the psychopsychiatric realm and not be objectively measurable for some time. There is an implied linkage between pain and suffering, which we disconnect here.

PAIN IS A MICROSCOPIC EVENT

Certainly, the first step is to understand that nociceptive pain is not a psychological event; it is a microscopic physical, chemical, or thermal event.

Acute, noxious stimulation of nociceptive pain (detecting something at the pain nerve ending), which may also precede neuropathic pain (hypersensitive transmission pathways), occurs at microscopic pain nerve endings as a signal that something is wrong, physically, chemically, or thermally. The neurotransmitters across synapses and endogenous and exogenous neurotoxic substances are microscopic. The upstream normally functioning peripheral and central neurons are microscopic. Then, neuropathic pain is, by definition, pathology of neurons. Because neurons are microscopic, peripherally or centrally, neuropathic pain can be likewise nothing but a "microscopic" event.

The presence of macroscopic pathology may or may not explain local pain, nociceptively or neuropathically. Macroscopic pathology, in other words, is not necessary, and may even be unrelated, for pain to occur or pain to be perceived. However, many patients and clinicians seek macroscopic pathology as *the* explanation for pain and suffering, e.g., most low back pain patients think of a "slipped disc" first, even though at least 85% of low back pain is nonspecific and, indeed, microscopic.

Functional MRI (Coghill et al., 1994) or PET scans (Iadarola et al., 1995) can show characteristic areas of activation in response to noxious stimuli in both nociceptive and neuropathic pan states. While not yet used in daily clinical practice, this information illustrates that pain is measurable in that it cuases physiological brain phenomena akin to "perception." Suffering is likely to be manifested in different patterns, sometimes with the areas activated by pain, and someime without the coincidence of pain. Thus, there are some cases that theoretically could have pain without suffering. Lepers have no pain and no direct suffering (Brand, 1993).

PAIN MECHANISMS

It has been known in medical science for decades that evolutionally advanced somatic A-delta fibers and primitive sympathetic C-fibers transmit pain signals under specific circumstances. In addition to transmitting cold information, the A-delta fibers also transmit thermal and mechanical pain information relatively quickly and with precise locational information to the central nervous system. The C-fibers, on the other hand, transmit thermal and mechanical pain information relatively slowly and rather imprecisely to the central nervous system, i.e., warm pain and achy/burning pain are seen by the central nervous system as "through fogged glass."

Perception may be defined as the localization and quantification by the central nervous system of signals from the A-delta and C-fiber pain pathways. Present pain *condition* classification systems are helpful, but these classification systems are complex and do not seem to be organized to provide the practicing physician with handles

TABLE 4.2
Peripheral Nerve Fiber Types/Characteristics

Class\units	Stimuli/function	Perception	Conduction velocity (m/s)	Diameter (microns)	Myelinated
A-alpha fibers	Motor contraction Efferent transmission	None direct	30–85	12–22	Yes
A-beta fibers	Vibration, pressure Afferent transmission	Vibration, pressure	30–70	5–12	Yes
A-delta fibers*	Cold sensation, pain Fast pain, localized touch Afferent transmission	Cold sensation, pain Localized touch	5–30	1–5	Yes
C-fibers**	Hot sensation, pain Slow pain, generalized touch Afferent transmission	Hot sensation and pain Generalized touch	0.5–2.0	0.3–1.3	No

Note: Based on Haines, 1997; Cousins & Bridenbaugh, 1998; Ganong, 2003.

* Spinal laminas I and V.
** Spinal laminas I and II.
*** C-fibers can still be clumped and embedded in other nonconducting tissue.

that can help the physician more effectively treat those patients presenting with pain — particularly chronic pain. Medical doctors depend on knowledge of the pathophysiology, or at least a diagnosis, to decide on treatment. Thus, to maximize likelihood of a correct and effective treatment and a positive outcome, physicians need to understand where and what the pain mechanism is and how the pain is perceived.

A relatively recent trend has been to look at basic mechanisms of pain (Dallel & Voisin, 2001). By doing so, we are seeking to look one level deeper at the underlying mechanisms so treatment can be facilitated. Dallel and Voisin (2001) recognize the need for a clear roadmap: "Once pain-generating mechanisms are known, it becomes possible to establish the appropriate treatment of pain." We suggest that refining these concepts is a giant step in the right direction and propose to present a simple, clear pathophysiologically based classification model. We contend that pain treatment should primarily focus on reversing pathologic mechanisms that cause the pain in the first place.

Any one or combination of the microscopic mechanisms can contribute to pain: nerve pain ending/"sensor" stimulation, neural "wire" misfiring, and central nervous system/"perceptron" dysfunction (Woessner, 2002a).

RELEVANT NEUROANATOMY AND NEUROPHYSIOLOGY

It appears that the locational patterns of disease, including neuropathology, and the mixture of these mechanisms that are dynamic over time make understanding the basic neuroanatomy and neurophysiology important.

Nerves, or neurons, are long tubes of protoplasm (rather than a series of sausage links), which may, or may not, be surrounded by poorly conducting myelin (insulation). Nerves generally come in various sizes and characteristics and have numerous branches to other neurons. Neurons interact/communicate via numerous electrical (gap junction) and chemical synapses. There are motor (efferent) neurons, which primarily carry signals from the brain to muscles, and sensory (afferent) neurons, which primarily carry signals from the periphery to the brain.

The primary focus for investigation by pain practitioners should be the small sensory nerves, which carry unpleasant signals to the brain that may or may not be perceived by the brain. Descartes depicted a noxious stimulus causing information to flow along a pain pathway to the brain that is then perceived as pain in his famous illustration of a boy's foot touching the edge of a fire (as in Melzack & Wall, 1965). Characteristics of nerve fibers, including classification and conduction velocities, are listed in Table 4.2.

There are three types of fibers that carry pain signals to the brain — A-beta, A-delta, and C-fibers. The first two are evolutionarily modern fibers that are myelinated (insulated) and carry nerve impulses rapidly to the cortical regions of the brain (Haines, 1997).

Neural signals are conveyed by sodium and potassium ions moving out and into neurons via voltage-gated channels in specific patterns to form a relatively slow (see Table 4.2; not 186,000 mi/sec) moving wave of information to, from, and within the central nervous system. These voltage-gated channels are concentrated in "holes" in the myelin (nodes of Ranvier) of the somatic nerves (A fibers),

but are more evenly distributed in the more primitive, unmyelinated nerve fibers (C-fibers).

In the absence of neural wire damage, there is a continuum across various numbers of synapses (switching stations) from the source or place of stimulation to the site of perception. At the distal end of sensory nerves, there are various types of nerve endings. When it comes to pain nerves, those endings are so-called "free" nerve endings. At the proximal end are the perceptor areas of the brain (Haines, 1997).

The A-beta fibers are probably reserved for deep, lancinating pain; certainly these carry vibratory signals. The A-delta fibers are somatic, myelinated fibers that have primary connections to the cortical regions of the brain. These fibers convey sharp, lancinating, easily localized pain signals; these pain sensations usually pass quickly unless constant or recurrent stimulation occurs.

Then, a more generalized, burning/aching pain sensation is perceived in the brain. This latter pain takes longer to pass. The C-fibers are relatively primitive and are not covered by myelin and conduct rather slowly to the subcortical part of the brain (Haines, 1997). Thus, when one experiences a paper cut, one quickly appreciates a "zing" followed by a "burning" pain. You know exactly where the "zing" comes from (A-delta pain pathways), but the brain "sees" the burning pain through "fogged glass" (C-fiber pain pathways).

Now that we know generally how these small nerves work, we need to know where these nerve endings and small pain nerves reside. Our standard anatomy books often do not depict or describe these networks of nerves. Dr. Fishman (2000), an insightful pain doctor, has described in his book entitled *The War on Pain* that these nerve fibers cover and line most of the tissue plane surfaces throughout the body.

HOW PAIN IS MEASURED

If pain is separated from suffering, it is easy to understand that pain is then measurable physiologically. As indicated in Table 4.2, neurophysiologists have assigned identifiable physiological functions to different nerve types. As with large-fiber functional testing, the small fibers, i.e., the A-delta and C-fibers, can be tested electrically and thermally. Measurement of small pain fiber function by preferred frequency transmission measurements (= current perception threshold [CPT]) has been clinically available for more than ten years. Thermal testing is as old as neurology itself; the basic physical examination includes qualitative testing with the handle of a reflex hammer as is for comparative cold sensation and heated for comparative warm sensation. In the laboratory, neuroscientists have been able to quantify thermal nerve, i.e., A-delta and C-fiber, function for decades. Machines are available now to test the function of pain nerve pathways in clinical settings. Testing pain nerves thus provides valuable information for diagnosis, and more effective treatment (Woessner, 2002b).

Imaging of pain perception has also been accomplished with transcranial magnetic stimulation (Gale, 2004), positron emission tomography (PET) (Iadarola, et al., 1995), single photon emission computed tomography (SPECT), functional magnetic resonance imaging (fMRI) (Coghill, et al., 1999) and near infrared spectroscopy techniques (NIRS) (Cope, 2000). "Research in diagnostic imaging of neuronal activity is … endemic at many academic medical centers. … The ability to map transmission of pain and other disorders not only to block but to alter and reprogram neurotransmission is now a very active and ever-changing research area (Cope, 2000)."

An interesting question arises from this research: Can a human being perceive pain without suffering? My clinical experience indicates that this is exactly so. Most clinicians, indeed, do understand that patients suffer for a variety of reasons. Thus, what medicine really needs is Suffering Relief Specialists rather than Pain Medicine Specialists per se. With the proper mindset, a pain specialist should be able to tackle the broader, and sometimes separate, issue of suffering. Thus, measuring and understanding physiological pain and comparing the results to perceived pain allow the clinician to more precisely treat "pain patients."

PROPOSED PHYSIOLOGICAL PAIN MODEL

This physiological pain model (Woessner, 2002a) focuses on underlying causative mechanisms, as opposed to the pain condition classification systems listed in Table 4.1. To review terms, nociceptive pain is merely normal functioning of the neural sensor/wire/perception system. This system serves useful purposes in alerting the brain to bodily injury. Neuropathic and central pain, however, is a manifestation of true dysfunction and can be the "disease" itself.

If we consider a bundle of axons, neuropraxia, axonotmesis, and neurotmesis represent points along a complex continuum of damage to axons and nerves. The three possibilities for individual axons are normal function, hyperfunction (hyperesthesia, hyperalgesia, hyperpathia, and allodynia), and hypofunction (hypoesthesia, hypoalgesia, and conduction block). Hyperfunction can also be thought of as sensitization or irritation. The ultimate hypofunction is axon death without regrowth. Free nerve endings can also be sensitized or irritated, which is considered here to be in the neuropathic category.

Understanding neurophysiology of pain pathways is helpful. Further, we propose that all pain can be understood by considering problems of stimulation of sensors, conduction along nerves, and/or perception in the spinal cord and brain. The perception then may involve feedback, either positive or negative (i.e., release or not of native painkiller, e.g., endorphins). If negative, the result

is, by and large, a dysfunction that conceptually could stand alone.

Haines (1997) describes an electronic schematic of the nerve cell membrane and forms the basis of concepts discussed below. A key concept is that the neural pain system follows basic electrochemical principles.

The analogy of the neural net in complex electrical circuitry seems to be an accurate one. The pain sensors (free nerve endings) are relatively simple. The wires (peripheral nerves) are even simpler. The central nervous system is incredibly complex. We are discovering that the spinal cord is not just a transmission device; complex interactions can occur here also. Finally, the complexity of the brain is difficult to imagine with millions of neurons and billions of synapses (Haines, 1997).

Stimulation of the sensors is nociceptive or eudynia. Malfunction of the wires and perceptron is neuropathic. Note that neuropathic pain is divided into central and peripheral parts of the pain nervous system because, while relatively little is known about either, these two parts of the pain pathways are clearly distinguished from each other.

Essentially no pain condition is unifactorial. For the actual pain conditions that the practicing physician encounters, it is useful to assess the pain using a conceptual framework. This approach is useful as a tool in assessing an individual patient's pain and deciding on treatment within the conceptual pain model.

STIMULATION OF PAIN SENSORS (NOCICEPTION)

Normal stimulation of pain sensors is the "good" pain described in *The Gift Nobody Wants* (Brand, 1993). It is termed "eudynia" in that the free nerve endings of pain pathways are working perfectly and normally — giving good information to the body and brain that tissue is being damaged — or is about to be damaged — and that the body needs to do something about it. Impact on mechano(noci)ceptors, heat or cold stimulation of thermo(noci)ceptors or caustic chemicals on chemo(noci)ceptors start the process of perception of pain. In other words, this type of pain is based on mechanical, thermal, and/or chemical stimulation of normally functioning pain nerves; nerves that detect pain as a signal indicating impending or active tissue damage.

MISFIRING OF WIRES (NEUROGENIC OR NEUROPATHIC PAIN)

During the normal transmission of neural signals to the central nervous system, any damage to the neural pathway itself may manifest itself analogously to "static" in radio transmissions. This neural "static" alters the neural signal and is then perceived as pain. Nerves can be damaged just as any soft tissue, in which these nerves occur, can be damaged. Neuropathic pain, therefore, is a result of damaged and malfunctioning wires/nerve fibers. One can also conceive of similar damage to nerve fibers in the central nervous system. As long as those fibers are not the end of the pathway, the phenomenon is the same. Damaged nerve fibers follow a course of anatomic and physiologic change involving irritation (hyperactivity) and dysfunction/death (hypoactivity) (Iadarola et al., 1995). Upon nerve death, of course, signals can no longer be transmitted along the neural pathway.

Mechanisms of hypersensitive or pain neuropathology include "rapid repriming" of sodium channels or "electrical bursting in pain signaling neurons." These sodium channels are specific to the "spinal sensory neurons" (Waxman, 2001, p. 382). Waxman et al. (2001) provide significant detail of this mechanism without indicating the nerve type; we assume that a similar mechanism works for both the A-delta and C-fiber pain nerves and, at least, is related to local microscopic mechanical and chemical occurrences.

DYSFUNCTION OF PERCEPTION (CENTRAL PAIN)

The most complex, and very difficult to study, part of the pain pathway(s) is in the central nervous system and occurs at the end of the neural pathway, where these signals are interpreted. Perception and consequences can occur in the dorsal horn. If central neurons malfunction in any part of the pain perception pathway, one possible consequence is that the brain perceives "pain." The environment of the central nervous system can also play a part. This complex system can be considered together to be a *perceptron* (Woessner, 2002a). This word has been chosen to convey the true complexity and computer-like nature of these central nervous system phenomena. If the "perception" is the cause of the perceived pain, this pain pathology can also be called central neurogenic pain.

ANTINOCICEPTIVE DYSFUNCTION

The human body possesses antipain (antinociception) systems including endorphins, enkephalins, etc. that are utilized as natural pain killers and neural feedback modulation to reduce perception of pain and the quantity of pain signals arriving at the "perception." In normal function, the human body releases these painkillers to modulate or mollify pain. At the very least, if these chemicals are not released or do not arrive at the affected receptors, the perceptrons will appreciate pain or greater pain, in the presence of pain signals (Craig, 2002).

Pain experts have also recognized that pain is nociceptive and/or neuropathic (Abrams, 2000), which are

commonly thought to be equivalent to "acute" and "chronic," respectively. The difficulty is that most acute and chronic pain conditions are a combination of both nociceptive and neuropathic pain, which can and do change over time. An acutely damaged nerve can result in acute neuropathic pain, and chronic arthritis can result in a chronic recurrent nociceptive pain.

Antinociceptive dysfunction (Brookoff, 2000) occurs in the perceptron (brain and/or spinal cord) and can worsen both nociceptive and neuropathic pains; antinociceptive pain, in other words, is dysfunction of the natural pain modulation system (Heinricher, 2002). Then, externally delivered painkillers are antinociceptive, as well.

Then, there are natural pain modulations that can malfunction resulting in more pain (hyperalgesia) or even pain without a noxious stimulus (allodynia). In this physiological manner, pain can be better understood. Each possible mechanism is dynamic in anatomical location, along pain pathways, and over time; each mechanism is individual and unique according to the underlying pain condition.

COMPLEX PAIN FROM A MIXTURE OF MECHANISMS

Over time and with the presence of widespread and/or severe causal factors, more than one aspect of the pain perception system may be malfunctioning at the same time. For example, it is common for patients to develop pain in a limb due to trauma that injures small pain fibers in addition to the other soft tissue. One can have stump pain along with phantom pain, possibly not coincidentally. Central sensitization can develop over time in a patient with ongoing peripheral disease. Dysfunctional efferent reflexes or reactions can change the physical and chemical environment of pain sensors, which then causes nociceptive pain as in complex regional pain syndrome (CRPS).

REFERRED PAIN AND NONTENDER SYNDROMES

Likewise, clinicians should be aware of pain perceived in body areas that are not tender on palpation. In other words, referred pain is pain that is perceived separately from the true pain generator and was first discussed in publications by Sturge (1883), Ross (1887), and others (Bonica and Loesser, 2001; Coda & Bonica, 2001). Local acute pain is relatively easy to understand, and physicians usually appreciate radicular pain, which is one type of referred pain. The concept of referred pain can be difficult for clinicians and patients alike.

Physicians strive to achieve the best possible understanding of pain conditions and try to find an acceptable label or diagnosis, even for conditions and presentations that are uncommon and/or difficult to understand. As the patient's presentation becomes more complex and as pain conditions become more chronic, physiologically legitimate presentations may not be understood.

Understanding referred pain requires specialized and diverse knowledge along with wide clinical experience. Suggesting that complaints are "non-anatomic" or "non-physiologic" may very well be a clear indication of the diagnostician's ignorance rather than a negative reflection on the motives of the patient. Individual variations in the presenting pain patterns complicate interpretation. Even well-known and classic pain patterns may be difficult to diagnose in the face of complex disease and multiple causes of pain. There are other complex, and poorly understood, pain conditions defined below.

Referred Pain Mechanisms

Kosek and Hansson (2003) have specifically found that "referred pain is most likely a consequence of misinterpretation of the origin of input from the stimulated focal pain area, due to excitation of neurons somewhere along the neuraxis with projected fields in the referred pain area … [this] suggests that the divergence of the input is not reciprocally arranged."

The best-known referred pain patterns may originate from viscera and myofascial trigger points. Each type is presented below. Other pain syndromes, with different names, however, also fall within this general category with the broad definition given above, where the pain is perceived at a site separate from the pathology.

Ombregt et al. (2003) have provided more precise principles limiting and defining referred pain:

1. Radicular pain is directly related to spinal segments.
2. The perceived pain site and causative pathology are usually on same side of midline.
3. The main pain is usually felt deeply.
4. The referred pain is referred distally within a dermatome, but not necessarily throughout that dermatome.
5. Referred pain may be contiguous with or may be separated from pathology.

The author proposes a sixth principle (Woessner, 2003): that the site of perceived pain is not tender, whereas the site of pathology is tender. Central pain phenomena do not necessarily fit completely within these general principles, but it is still useful to understand the similarities.

Selzer and Spencer (1969) suggest five underlying mechanisms involved with referred pain:

1. "Convergence-Projection" describes one neuron receiving impulses from two sources; i.e., peripheral neurons, resulting in the central path-

ways not being able to distinguish between the sources (Ruch, 1960).
2. "Peripheral Branching of Primary Afferent Nociceptors" involves the fact that single neurons are very long narrow tubes that may have various branches that come from different peripheral sources, again making it impossible for central pain pathways to distinguish the source.
3. "Convergence-Facilitation" is ephatic transmission that occurs where nerves from two different body areas are in close proximity and results in signals from the viscera being transmitted along an associated spinothalamic tract to be perceived in the brain as coming from various skin areas (originally proposed by Ruch, 1960).
4. "Sympathetic Nervous System Activity," which is suggested to restrict blood flow to an area causing pain in that area or by releasing substances that sensitize nerve endings in the area of perceived pain such that hyperesthesia or allodynia occurs. Except as illustrated elsewhere, this possibility does not make much sense.
5. "Convergence or Image Projection at the Supraspinal Level" describes ephaptic transmission in central locations rather than at the dorsal root, or some similar mechanism to be perceived as being pain in one area while the stimulation comes from another.

There are, of course, other possibilities and/or contributing factors to referred pain:

1. Note that when nerve root pathology affects only the nerve root surface pain nerves, we expect local pain to be perceived and local tenderness to be elicited. For more severe pathology that extends physically as pressure and chemically to the pain nerve inside the nerve root, we expect that the brain would perceive the pain more distal to nontender locations in the feet or hands, understood as "radicular" pain. This mechanism is likely for all non-central syndromes considered here.
2. Mistransmission or ephatic transmission solely in the central nerve system, as in the phantom pain phenomenon discussed in the labeled section below.
3. The embryologic relationship of the internal organs to spinal levels, which is then directly related to sympathetic chain levels. The importance of the embryologic levels must reflect organization in the central nervous system. In addition, the main nerve fiber type of the sympathetic nerve system is the C-fiber, the primitive, unmyelinated pain fiber, emphasizing that ontogeny follows phylogeny.
4. Along these pathways, neuropathic pain can also be referred and, in some cases, may indicate that the nerve is "trying" to normalize, to heal. Certainly, dead neurons do not transmit pain signals or any other impulse.
5. Central pain syndromes could very easily fit into the same category as phantom pain. Deafferention pain syndrome is consistent with "total body amputation" from the head/brain and represents a pain syndrome without nerve impulses of any sort coming from the periphery. In other words, the pathology or dysfunction is in the neurons of the central nervous system, but not necessarily just in the brain.
6. Wide dynamic range (WDR) neurons and interneurons of the spinal cord represent neuropathic dysfunction that could by specific, complex mechanisms end with the perception of pain where there is no pathology; the pathology, in this case, is in the spinal cord.
7. Sympathetic chain pathology is the same as the spinal cord pathology. We may eventually identify WDR neurons of the sympathetic chains; we will probably come up with a different name.
8. Patchy brain modulation of pain, i.e., antinociception, could well leave the brain appreciating pain where there is no pain with or without a reason, i.e., nerve impulses of any kind coming from elsewhere.

Certainly, more than one or all of these phenomena could occur together to form the various widespread and complex pain problems that a physician must manage and try to cure.

Embryology and Referred Pain

Various authors (Marcus, 1998; Ombregt et al., 2003) discuss the embryologic basis for referred pain. Certainly, the referred pain mechanisms must have a relationship to nerve pathways and networks. These pathways and networks are geometrically and positionally related to where the precursor structures occurred in early ontogenic stages and how these structures migrate during growth and maturation. Thus, referred pain patterns have an evolutionarily ancient (phylogenic) and developmentally individual relationship (ontogenic) to dermatomes, myotomes, sclerotomes, viscerotomes, etc. Central pathway and network pathology can probably be understood in the same way.

Factors Causing Referred Pain

Ombregt et al. (2003) described factors that predispose to referred pain. Stronger central and/or proximal deep (vs. superficial) stimuli more likely cause the perception of pain beyond the pathology. Sclerotomal referred pain is more likely than myotomal referred pain, and much more likely than bone pain. This order of occurrence may be generally inversely related to intensity and pain-related dysfunction.

Marcus (1998) adds and states differently that "tenacious" pain stimulation is more likely to be referred; superficial pain is more likely to be localizable (less likely referred), deep (excluding bone) is more likely referred; soft tissue referred pain is less localizable, i.e., more likely referred; and distal pathology is more localizable than proximal.

Viscerotomes

Visceral referred pain is probably the most widely recognized, while still being the least understood of all the referred pain patterns. Head (1893) noted disturbances of sensation arising from visceral disorders. Cousins (1987) refers to these patterns as "viscerotomes." Lingappa and Farey (2000), in fact, describe "referred pain" as "the phenomenon in which injury to internal organs causes pain that localizes, in part, to surface structures or other organs clearly distinct from the site of primary injury. Typically, the pain is referred to other structures that have the same embryonic origin" (pp. 798). There are established patterns of referred pain from internal organs. Drewes et al. (2003) have provided a detailed description of the various referred visceral pain distributes, providing basic information to understand the complexities of viscerotomes.

Ephatic transmission is analogous to electrical shorting out. Via these shorts, "many different afferent sensory nociceptive neurons synapse with the same ascending fibers in the spinal cord," which causes the brain to mistake the origin of the pain signals; in other words, the pain feels like it is coming for some typical locations on the skin or nearby subcutaneous tissues and possibly deeper structures, rather than the actual internal organ from which the pain signals are coming (Lingappa & Farey, 2000, pp. 798–799). These scientists also suggest that the brain generally will have more recent memory of surface/subcutaneous pain and will "ignore" deep pain until an inciting event occurs.

With A-delta pain fiber involvement, a skin injury is easily locatable. Visceral pain is difficult for the human brain to locate, because the pain is "referred" to the skin, and involves sympathetic C-fibers, which subserve poorly localized pain.

Angina pectoris is well known to cause left arm pain, alerting to the possibility of impending myocardial infarction. Abdominal pain that becomes rapidly generalized implies perforation and leakage of fluid into the peritoneal cavity, irritating parietal peritoneum. Biliary pain can radiate to the right inferior scapula. Pancreatic and abdominal aneurismal pain may radiate to the back. Ureteral colic classically is referred to the groin and thigh (Haist & Robbins, 2002).

The areas of the body to which visceral pain is referred are described in narrative rather in schematics. Note that we expect that each patient will display variations on these generalizations. Word descriptions may actually represent reality better than the various published schematics because each viscerotome schematic is different and inconsistent, with individuals and populations being unique and different to some degree.

Common Pain Radiation Patterns

Lungs: Pain is referred in a collar-like band completely around the neck from about C6 to T3 levels.

Diaphragm: Pain is referred in a pattern similar to the lungs and shoulder.

Heart: Pain can be referred to around the mouth, but is more commonly referred over the left chest and contiguously down the anterior left arm and directly to the mid-back between the scapulae from T4 to T7.

Gallbladder: Pain is referred to superior and lateral right shoulder, offset superior similar in size and circular shape to the superficial distribution of the axillary nerve.

Liver: Pain is referred in a similar pattern to the heart, but only on the right hemi-body.

Stomach: Pain is referred just to the right of midline in the epigastric area and to the mid-back, just below the referred angina from T7 to T9.

Ovaries: Pain is referred to the skin area immediately over the ovaries anteriorly and directly posteriorly, but more lateral.

Appendix: Pain is referred to the umbilicus and then to McBurney's point in the right hypogastric area when parietal peritoneum becomes inflamed.

Kidneys: Pain is referred to the skin area somewhat below the kidneys, posteriorly only, and medial to the posterior referred ovarian pain; there is also an area half way down the right lateral thigh, the right chest just to the right of the lower sternum.

Ureters: Pain is referred to an anterior band across the pelvis, including the groin and the genitals, but not extending to the back.

Bladder: Pain is referred to a continuous area encompassing the sacrum from S2 down to the upper medial thighs.

Radicular Pain

Radicular pain originates at the nerve root, cervical, thoracic, lumbar, or sacral, and typically radiates or is referred along a dermatome. Dermatomal pain suggests nerve root involvement from a herniated disc or other physical or chemical irritation at the nerve root exiting from the spinal canal.

Consistent with the definition, there can be various pathologies at the nerve roots, which include (1) nerve root compression from a herniated disc, (2) foraminal stenosis from bone spurs or arthritis irritating the nerve root, (3) nerve root pressure from mass lesions, (4) chemical changes at the nerve roots secondary to diabetes, (5) scarring from previous spinal surgery or chronic disc pathology, and (6) all other nerve root injuries. The radiating component is technically "referred pain." This type of "referred pain" is not a nociceptive process; it is neuropathic, even if momentary. Pain with such a specific distribution seems unlikely to even be central.

Thinking of the distribution of pain nerves in the cross section of a nerve root is instructive. If the pathology is minor, the pain on this surface of the nerve root is most affecting, and thus local pain is appreciate. With more compression the pain nerve pathways/axons deeper in the nerve root are affected and "fool" the brain into thinking that the painis located more distal toward the limb involved.

Overlapping Distributions

The nerves that innervate dermatomes interdigitate at the borders to some extent, making the boundary edges fuzzy. In addition, the sensory distributions, which characterize and define dermatomes, may not be identical to the pain patterns. Therefore, exact determinations of pain perception distributions are not "cut and dried."

Referred Muscular Pain

Referred muscle pain in voluntary muscles is most often accompanied by secondary hyperalgesia and hypotrophic changes. A schematic of these referral distributions is shown in *Bonica's Management of Pain* (Coda & Bonica, 2001).

"Myotomal" pain involves problems with the fascial tissue planes that surround muscle groups. While "myotomal" may not be the correct description, when muscles were injected with hypertonic saline, which is an experimental substance known to produce pain, mapped patterns of referred pain emerged (Coda & Bonica, 2001). While we would expect that these would be the same referred pain patterns as myofascial trigger points, gross inspections reveal no clear congruence or overlap.

Sclerotomes

Pain referred from tendinous and/or ligamentous interfaces with bone surfaces has no specific, well-recognized name (Hackett, 1958). Sclerotomes are pain referral patterns from sites of enthesopathy, i.e., pathology of the collagenous attachments (tendons, ligaments, cartilage, etc.) to bones generated by inflammation.

Dural Pain Patterns

Bogduk (2003) has recognized that the spinal dura is innervated. Cailliet (1988) has further shown that the dura is innervated by sympathetic C-fibers. Ombregt et al. (2003) and Butler (1991) have postulated that certain pain perception patterns occur when the pain nerves on the dura are stimulated.

Certainly, these diffuse patterns do not even vaguely resemble dermatomal distributions. They are much more widespread than the limited zones of referred trigger point pain. For instance, dural nerves stimulated by scar tissue in the lumbar region may result in perceived pain and discomfort throughout the legs.

Kernig's and Brudzinski's signs, i.e., the meningeal signs (Gerard & Kleinfield, 1993), are reminiscent of this same phenomenon. By definition, these are consistent with meningeal irritation, i.e., dural irritation, where A-delta and C-fiber pain nerve endings occur, anteriorly and laterally (Cailliet, 1988).

Thermatomes

There are thermal patterns of pain, which are probably related to the distribution of sympathetic C-fibers nerves and with sympathetic chain pathway components, without shorting, crossing over, emphatically to the A-delta fiber pathways.

Hooshmand (2000) has coined the word *thermatomes* to describe referred pain patterns related to the circulatory distribution of sympathetic C-fiber nerves. These relatively amorphous distributions are consistent with the observation that these C-fiber nerve pathways end up seeing pain "through fogged glass."

If we think of the possible evolutionary origin of the sympathetic chains, which in lower animals transmit all efferent and afferent nerve impulses, those pathways should be able to reestablish transmission pathways in compensation, much like collateral circulation.

Facial Referral Patterns

Innervation of the face and anterior neck is not completely appreciated by healthcare professionals.

Guyton & Hall (2000, pp. 558–560) show that:

Nasal sinus and eye aches radiate to a wide area around the eyes from below the nose and up to mid-fore.
Cerebral vault aches occur frontally to parietally at the ear.
Brainstem and cerebellar vault aches occur from the ear through the entire occiput.

Phantom Pain

Phantom sensations and pain are well-described phenomena, which means that the brain perceives the existence of a body part, from which no nerve impulses could possibly be emanating.

In a sense, phantom pain is the ultimate "referred pain." Perceived pain location is obviously not where the pain is originating because there cannot be peripheral pain nerve stimulation. Stump and neuroma pains are separate pain phenomena and are not referred pain, and therefore, these pains are not phantom pain. There is surprising confusion about these, i.e., stump and neuroma pains versus phantom pain.

Referred Pain Due to Healing Pain Nerves

Healing nerves and tissue cause pain by the following:

1. Inflammation is part of the healing process; the natural chemicals involved are caustic to pain nerve endings. The treatment dilemma here is if you stop the pain with anti-inflammatory medications, do you not also stop the healing?
2. Consequent muscle spasms occur. Spasm or cramping muscles change, usually decrease circulation; ischemia causes pain by causing a caustic microenvironment around nerve endings. In addition, the spasm/cramping muscles are causing pressure on the A-delta and C-fibers that occur in the myofascial tissue planes.
3. Improper healing of any tissue can reasonably contort it and cause pain and dysfunction; such nociceptive pain is caused by pressure on and/or caustic chemical environment around the nerve endings; neuropathic pain would come from the changed neuroanatomy, thus changed neurophysiology, and also from the changes in the chemical microenvironment.

HOW, IN THE END, DOES PAIN AND REFERRED PAIN CLASSIFICATION HELP?

For nociceptive pain, the primary goal is to resolve ("cure") or remove the stimulant, i.e., the causative pathology, while covering up the pain. For neuropathic pain, the goal is to stop the irritation and promote rebuilding the damaged nerves or normalization of their function. For central pain, the goal is to employ techniques to change the central nervous system neural environment. For antinociceptive pain, the goal is to normalize pain perception and reestablish natural painkiller production and function.

The ultimate approach for effectively treating pain is individualizing and balancing the various approaches for optimal results in complex chronic pain cases. By understanding the underlying mechanisms, physicians clearly have a better chance of effectively serving their patients with better pain relief. Suffering is probably the most difficult part of pain to quantify and treat. However, it is expected that suffering will improve as we improve our abilities to treat pain.

SUMMARY

Pain classification depends on the understanding of pain mechanisms. The more we know about these mechanisms, the more likely we are to apply the appropriate terms to the pain conditions that we see in our clinics. We cannot abandon the time-honored names that we are using.

Basically, there are two categories, i.e., nociceptive and neuropathic pain. Eudynia and maldynia, respectively, may actually be more useful terms because the accepted terminology may be limited by the historical processes involved in pain (condition) classification. Accurate consideration of these basic concepts should be applied to every pain condition encountered by the practitioner in order to plan appropriate treatment of the pain.

Referred pain is neuropathologic, i.e., not nociceptive. Referred pain is important because it may have diagnostic value. Referred pain adds another layer of complexity to the process of making a diagnosis. Making the diagnosis by artfully and systematically combining the findings obtained from the clinical history and physical examination allows the clinician to formulate a coherent treatment plan.

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