

The Depth and Breadth of Pain

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ABSTRACT

No poison can kill a positive thinker and no medicine can cure a negative thinker. Pain is a complex perceptual experience. Pain is a major public health problem. Beat back pain without surgery and conquer pain without painkillers. Delays have dangerous ends. Knee braces invite injury. Chronic pain affects one in three people in the United States. There are more Americans suffering from chronic pain than with diabetes, heart disease, and cancer combined. Chronic pain is caused by degeneration, illnesses, injuries, surgeries, and treatment side effects. Pain is a major public health problem and is the most common reason why Americans use complementary and integrative health practices. Recent imaging evidence suggests a possible hypothalamic origin for a headache attack, but further research is needed. A migraine is associated with a modest increase in the risk of ischemic stroke. The etiology for this association remains unclear. They interact with opioid receptors on nerve cells in the brain and nervous system to produce pleasurable effects and relieve pain. Codeine is a naturally occurring opioid that is a weak analgesic compared to morphine. It should be used only for mild-to-moderate pain. The ideal treatment of any pain is to remove the cause. Some conditions are so painful that rapid and effective analgesia is essential (e.g., post-operative state, burns, trauma, cancer, and sickle cell crisis). Analgesic mediators are the first line of treatment in these cases and all practitioners should be familiar with their use.

Key words: Cyclooxygenase (COX)-2, codeine, granuloma, fentanyl, L-carnitine, morphine, multiple sclerosis (MS), methadone, neurotransmitters, nonsteroidal anti-inflammatory agents (NSAIDs), prostaglandins, sciatic pain, sufentanil,

INTRODUCTION

Pain, defined as a symptom, sign, or a syndrome, has been researched extensively compared to any other area in neurophysiology.^[1] No difference in pain prevalence was found between patients undergoing anticancer treatment and those in an advanced or terminal phase of the disease.^[2] Factors influencing the development of chronic pain in cancer survivors who have completed treatment include peripheral neuropathy due to chemotherapy, radiation-induced brachial

plexopathy, chronic pelvic pain secondary to radiation, and postsurgical pain.^[3] Controversies exist about the definition and epidemiology of breakthrough cancer pain among the new fentanyl products.^[4] Background new drug treatments, clinical trials, and standards of quality for the assessment of evidence justify an update of evidence-based recommendations for the pharmacological treatment of neuropathic pain.^[5] In 1986, the World Health Organization (WHO) proposed a strategy for cancer pain treatment based on a sequential three-step analgesic ladder from non-opioids

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to weak opioids to strong opioids.^[6] It manifests itself in a variety of forms involving, in turn, a multiplicity of responses and therapeutic strategies.^[7] Diabetic patients often suffer from muscle cramps. L-carnitine supplementation in diabetic patients reduced muscle cramps.^[8] The use of both over-the-counter and prescription nonsteroidal medications is frequently recommended in a typical neurosurgical practice.^[9] Bone cancer pain is a devastating manifestation of metastatic cancer.^[10] Prostaglandins are lipid mediators produced by cyclooxygenases (COX) from arachidonic acid, which serve pivotal functions in inflammation and pain.^[11]

The pathophysiology of pain in multiple sclerosis (MS) is poorly understood, but there are multiple schools of thought. Different mechanisms are associated with causation of this pain e.g. acute pain due to inflammation; chronic or intermittent neuropathic pain related to central nervous system (CNS) lesions; pain secondary to spasticity, spasms and muscle cramps from higher motor neuron lesions; and musculoskeletal pain from adopting maladaptive body positions and general physical deconditioning.^[12] Multiple sclerosis (MS) is primarily a chronic inflammatory disorder of the brain and spinal cord, characterized by episodes of neurological dysfunction due to widespread microglial activation associated with extensive and chronic neurodegeneration.^[13,14] Central pain is an important symptom in MS (around 30%) and causes much suffering.^[15] The clinical, electrophysiological and neuropathological characteristics of five patients with CIDP and pain as the main presenting symptom, and their course with treatment.^[16] CIDP is an immune-mediated treatable polyneuropathy, which the prevalence is reported between 1 and 7.7/100,000.^[17,18] Muscle injuries undergo the healing phases of degeneration, inflammation, regeneration, and fibrosis.^[19] Neuropathic pain should not be considered a disease by itself but considered as a clinical condition common to different pathologies.^[20,21]

HISTORY

Low back pain has been with humans since at least the Bronze Age. The oldest known surgical treatise - the Edwin Smith Papyrus, dating to about 1500 BCE - describes a diagnostic test and treatment for a vertebral sprain. Hippocrates (c. 460 BCE–c. 370 BCE) was the first to use a term for sciatic pain and low back pain; Galen (active mid to late second century CE) described the concept in some detail. Through the Medieval period, folk medicine practitioners provided treatments for back pain based on the belief that it was caused by spirits.^[22]

American neurosurgeon Harvey Williams Cushing increased the acceptance of surgical treatments for low back pain.^[24] In the 1920s and 1930s, new theories of the cause arose, with physicians proposing a combination of nervous system and psychological disorders such as nerve weakness (neurasthenia) and female hysteria.^[23] Muscular rheumatism

(now called fibromyalgia) was also cited with increasing frequency.^[24] Emerging technologies such as X-rays gave physicians new diagnostic tools, revealing the intervertebral disc as a source for back pain in some cases. In 1938, orthopedic surgeon Joseph S. Barr reported on cases of disc-related sciatica improved or cured with back surgery.^[22]

Powerful cognitive processes shape the way that we perceive pain. This perception is determined by our expectations and the situation in which we find ourselves. Clinicians need this knowledge to develop techniques for personalized treatment of chronic pain and to prevent pain from spiraling out of control.^[25] Chronic pain affects one in three people in the United States. There are more Americans suffering from chronic pain than with diabetes, heart disease, and cancer combined. With chronic pain, one's nervous system is sometimes altered, making it more sensitive to pain.^[26]

SIGNIFICANT GAP IN RESEARCH

A problem in the management of pain is the lack of distinction between acute and chronic pain syndromes. The search results in complex clinician-patient relationships that usually include many drug trials, particularly sedatives, with adverse consequences (e.g., irritability and depressed mood) related to long-term use. Treatment failures provoke angry responses and depression from both the patient and the clinician, and the pain syndrome is exacerbated. The longer the existence of the pain disorder, the more important becomes the psychological factors of anxiety and depression. As with all other conditions, it is counterproductive to speculate about whether the pain is “real.” It is real to the patient, and acceptance of the problem must precede a mutual endeavor to alleviate the disturbance.

Components of the chronic pain syndrome consist of anatomic images, chronic anxiety and depression, anger, and changed lifestyle. Usually, the anatomic problem is irreversible since it has already been subjected to many interventions with increasingly unsatisfactory results. Chronic anxiety and depression produce heightened irritability and overreaction to stimuli. Anxiety and depression are seldom discussed, almost as if there is a tacit agreement not to deal with these issues.

Changes in lifestyle involve some of the pain behaviors. Demands for attention and efforts to control the behavior of others revolve around the central issue of the control of other people (including clinicians). Cultural factors frequently play a role in the behavior of the patient and how the significant people around the patient cope with the problem. Some cultures encourage demonstrative behavior, while others value the stoic role.

Another secondary gain that frequently maintains the patient in the sick role in financial compensation or other benefits.^[27]

MAJOR ADVANCES AND DISCOVERIES

Conventional care often fails to manage chronic pain effectively, and other approaches to relieve or reduce pain and increase functional ability are needed. Research studies have shown that some complementary health modalities may reduce pain associated with some conditions.^[28] Wide variation in coverage of non-pharmacological treatments for low back pain may be driven by the absence of best practices, the administrative complexities of developing and revising coverage policies, and payers' economic incentives.^[29] Lamotrigine, daily aspirin, and flunarizine have evidence for efficacy in prevention of a migraine with aura, and magnesium, ketamine, furosemide, and single-pulse transcranial magnetic stimulation have evidence for use as acute treatments.^[30] Opioid drugs that include the illicit drug heroin as well as prescription pain relievers oxycodone, hydrocodone, codeine, morphine, fentanyl, and others. They interact with opioid receptors on nerve cells in the brain and nervous system to produce pleasurable effects and relieve pain.^[31] Opioids are a class of drugs that include the illicit drug heroin as well as prescription pain relievers' oxycodone, hydrocodone, codeine, morphine, fentanyl, and others. They interact with opioid receptors on nerve cells in the brain and nervous system to produce pleasurable effects and relieve pain.^[32]

Although pain is an unpleasant experience, it may indirectly promote healing because it encourages protection of the damaged site. Pus consists of dead phagocytes, dead cells, cell debris, fibrin, inflammatory exudate, and living and dead microbes. It is contained within a membrane of new blood capillaries, phagocytes, and fibroblasts. The most common causative pyogenic (pus forming) microbes are *Staphylococcus aureus* and *Streptococcus pyogenes*. Small amounts of pus from boils and larger amounts form abscesses. *S. aureus* produces the enzyme coagulase, which converts fibrinogen to fibrin, localizing the pus. *S. pyogenes* produces toxins that break down tissue, causing spreading infection. Healing, following pus formation, is by the second intention. Superficial abscesses tend to rupture and discharge pus through the skin. Healing is usually complete unless tissue damage is extensive. Deep-seated abscesses rupture with complete discharge of pus on to the surface, followed by healing. Rupture and limited discharge of pus on to the surface, followed by the development of a chronic abscess with an infected open channel or sinus.

Acute inflammation occurs when the cause has been successfully overcome. Damaged cells and residual fibrin are removed, being replaced with new healthy tissue, and repair is complete, with or without scar formations. Acute inflammation may become chronic if resolution is not complete, for example, if live microbes remain at the site, as in some

deep-seated abscesses, wound infections, and bone infections. Chronic inflammation process is very similar to those of acute inflammation, but because the process is of longer duration, considerably more tissue is likely to be destroyed. The inflammatory cells are mainly lymphocytes instead of neutrophils, and fibroblasts are activated, leading to the laying down of collagen and fibrosis. If the body defenses are unable to clear the infection, they may try to wall it off instead, forming nodules called granulomas, within which are collections of defensive cells. The development of the granuloma and its subsequent degeneration and necrosis is the hallmark of infection caused by *Mycobacterium tuberculosis*.^[33]

WHERE THE RESEARCH GO NEXT?

It is subjective, and the clinician must rely on the patient's perception and description of pain. Alleviation of pain depends on the specific type of pain, nociceptive, or neuropathic pain. For example, with mild-to-moderate arthritic pain (nociceptive pain), no opioid analgesics such as nonsteroidal anti-inflammatory agents (NSAIDs) are often effective. Neuropathic pain can be treated with opioids (some situations require higher doses) but responds best to anticonvulsants, tricyclic antidepressants, or serotonin/norepinephrine reuptake inhibitors. However, for severe or chronic malignant or non-malignant pain, opioids are considered part of the treatment plan in select patients. Opioids are natural, semi-synthetic, or synthetic compounds that produce morphine-like effects. These agents are divided into chemical classes based on their chemical structure. Clinically, this is helpful in identifying opioids that have a greater chance of cross-sensitivity in a patient with an allergy to a particular opioid. All opioids act by binding to specific opioid receptors in the central nervous system (CNS) to produce effects that mimic the action of endogenous peptide neurotransmitters (e.g., endorphins, enkephalin, and dynorphins). Although the opioids have a broad range of effects, their primary use is to relieve intense pain, whether that pain results from surgery, injury, or chronic disease.

Morphine and other opioids exert their major effects by interacting stereospecifically with opioid receptors on the membranes of certain cells in the CNS and other anatomic structures such as gastrointestinal (GI) tract and the urinary bladder. Morphine also appears to inhibit the release of many excitatory transmitters from nerve terminals carrying nociceptive (painful) stimuli.

Management of the pain is one of the clinical medicines greatest challenges. Pain is defined as an unpleasant sensation that can be either acute or chronic and is consequence of complex neurochemical processes in the peripheral and central nervous systems (CNS). Opioids is natural semi synthetic or synthetic compounds that produce morphine like effects.^[34] Aspirin and other

related compounds constitute a class of drugs known as NSAIDs. NSAIDs have three desirable pharmacological effects - anti-inflammatory, analgesic, and antipyretic. All NSAIDs and COX-2 agents appear equally effective in the treatment of pain disorders.^[35] Prostaglandins are lipid mediators produced by COX from arachidonic acid, which serve pivotal functions in inflammation and pain. While the development of selective inhibitors of inducible COX-2 (so-called coxibs) has greatly reduced GI side effects, the recent disappointment about a potential cardiovascular toxicity of COX-2-selective inhibitors has boosted interest in alternative targets.^[36]

CURRENT DEBATE

Recent data suggest that 53–70% of patients with cancer-related pain require an alternative route for opioid administration, months, and hours before death.^[37] Bone cancer pain is a devastating manifestation of metastatic cancer. Unfortunately, current therapies can be ineffective, and when they are effective, the duration of the patient’s survival typically exceeds the duration of pain relief. Current and future therapies include external beam radiation, osteoclast-targeted inhibiting agents, anti-inflammatory drugs, transient receptor potential vanilloid type 1 antagonists, and antibody therapies that target nerve growth factor or tumor angiogenesis.^[38] Skeletal muscle injuries are a common problem in trauma and orthopedic surgery. Since a damaged disk does not necessarily hurt, it might be a coincidence that you have a sore back and ruptured disk. Disks are the soft, rounded cartilage between the bones of the spine. A ruptured disk occurs if the jellylike the interior of the disk is pushed out of its usual place and extends beyond the bones of the spine. Ruptured disks also are called herniated, protruding, or slipped disks. Often, ruptured disks shrink over time, returning to fit their normal spaces again. However, interpretations of an MRI scan can vary from doctor to doctor. Hence, if your doctor suggests back surgery based on the results of imaging testing, get a second opinion. Keep in mind that 96% of all back injuries will heal with rest and rehabilitative exercises.^[39] Researchers at the Pittsburgh Medical Center discovered that under certain conditions taking just two more acetaminophen pills per day than the label recommends can seriously damage your liver. The maximum number of acetaminophen pills an adult should take in 1 day is eight extra strength tablets, you are posing a serious risk to your liver. A study, conducted at Johns Hopkins University in Maryland, indicated that people.

The WHO take more than one acetaminophen tablet a day for 1 year double their risk of kidney failure. As for the NSAIDs containing ibuprofen, such as Advil, research shows that people who have taken as many as 5000 pills in their lifetime have 8.8 times higher risk of kidney failure.^[40]

CONCLUSION

The ideal treatment of any pain is to remove the cause. Some conditions are so painful that rapid and effective analgesia is essential (e.g., post-operative state, burns, trauma, cancer, and sickle cell crisis). Analgesic mediators are the first line of treatment in these cases and all practitioners should be familiar with their use. Managing patients with chronic pain are intellectually and emotionally challenging. The patient’s problem is often difficult or impossible to diagnose with certainty.

Such patients are highly emotional. In these cases, psychological evaluation and behaviorally based treatment methods are useful. There are certain areas to which special attention should be paid in patient’s medical history. Since depression is the most common emotional disturbance in patients with chronic pain, patients should be questioned about their mood, appetite, sleep patterns, and daily activity.^[41] Pain is a complex perceptual experience. Pain is a major public health problem. Back pain without surgery and conquer pain without painkillers. Delays have dangerous ends. Knee braces invite injury. Chronic pain affects one in three people in the United States. There are more Americans suffering from chronic pain than with diabetes, heart disease, and cancer combined. Chronic pain is caused by degeneration, illnesses, injuries, surgeries, and treatment side effects. Pain is a major public health problem and is the most common reason why Americans use complementary and integrative health practices. Recent imaging evidence suggests a possible hypothalamic origin for a headache attack, but further research is needed. A migraine is associated with a modest increase in the risk of ischemic stroke. The etiology for this association remains unclear.

Codeine is a naturally occurring opioid that is a weak analgesic compared to morphine. It should be used only for mild-to-moderate pain. Its activity varies in patients, and ultrarapid metabolizers may experience higher levels of morphine, leading to possible overdose. Codeine is commonly used to combine with acetaminophen for the management of pain. Codeine exhibits good antitussive activity at doses that do not cause analgesia. Oxycodone is a semi-synthetic derivative of morphine. Oxymorphone is a semi-synthetic opioid analgesic. The oral formulation has a lower relative potency and is about 3 times more potent than oral morphine. Oxymorphone is available in both immediate-acting and extended-release oral formulations.

Fentanyl, a synthetic opioid chemically related to meperidine, has 100-fold the analgesic potency of morphine and is used for anesthesia. Methadone induces less euphoria and has a longer duration of action.^[42]

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