Pain Management

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Table of Contents

Chapter 1

Pain

Pain

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Pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." It is the feeling common to such experiences as stubbing a toe, burning a finger, putting iodine on a cut, and bumping the "funny bone".

Pain motivates us to withdraw from potentially damaging situations, protect a damaged body part while it heals, and avoid those situations in the future. Most pain resolves promptly once the painful stimulus is removed and the body has healed, but sometimes pain persists despite removal of the stimulus and apparent healing of the body; and sometimes pain arises in the absence of any detectable stimulus, damage or disease.

Pain is the most common reason for physician consultation in the United States. It is a major symptom in many medical conditions, and can significantly interfere with a person's quality of life and general functioning. Social support, hypnotic suggestion, excitement in sport or war, distraction, and appraisal can all significantly modulate pain's intensity or unpleasantness.

Classification

The International Association for the Study of Pain (IASP) classification system describes pain according to five categories: duration and severity, anatomical location, body system involved, cause, and temporal characteristics (intermittent, constant, etc.). This system has been criticized by Woolf and others as inadequate for guiding research and treatment, and an additional category based on neurochemical mechanism has been proposed.

Duration

Pain is usually transitory, lasting only until the noxious stimulus is removed or the underlying damage or pathology has healed, but some painful conditions, such as rheumatoid arthritis, peripheral neuropathy, cancer and idiopathic pain, may persist for years. Pain that lasts a long time is called *chronic*, and pain that resolves quickly is called *acute*. Traditionally, the distinction between *acute* and *chronic* pain has relied upon an arbitrary interval of time from onset; the two most commonly used markers being 3 months and 6 months since the onset of pain, though some theorists and researchers have placed the transition from acute to chronic pain at 12 months. Others apply *acute* to pain that lasts less than 30 days, *chronic* to pain of more than six months duration, and *subacute* to pain that lasts from one to six months. A popular alternative definition of *chronic pain*, involving no arbitrarily fixed durations is "pain that extends beyond the expected period of healing." Chronic pain may be classified as "malignant" (caused by cancer) or "benign" (non-malignant).

Region and system

Pain can be classed according to its location in the body, as in headache, low back pain and pelvic pain; or according to the body system involved, such as myofascial pain (emanating from skeletal muscles or the fibrous sheath surrounding them), rheumatic pain (emanating from the joints and surrounding tissue), neuropathic pain (caused by damage or illness affecting the somatosensory system), or vascular (pain from blood vessels).

Cause

The crudest example of classification by cause simply distinguishes "somatogenic" pain (arising from a perturbation of the body) from psychogenic pain (arising from a perturbation of the mind: when a thorough physical exam, imaging, and laboratory tests

fail to detect the cause of pain, it is assumed to be the product of psychic conflict or psychopathology). Somatogenic pain is divided into "nociceptive" and "neuropathic".

Nociceptive

Nociceptive pain is caused by stimulation of peripheral nerve fibers that respond only to stimuli approaching or exceeding harmful intensity (nociceptors), and may be classified according to the mode of noxious stimulation; the most common categories being "thermal" (heat or cold), "mechanical" (crushing, tearing, etc.) and "chemical" (iodine in a cut, chili powder in the eyes).

Nociceptive pain may also be divided into "visceral," "deep somatic" and "superficial somatic" pain. *Visceral* pain originates in the viscera (organs) and often is extremely difficult to locate, and nociception from some visceral regions produces "referred" pain, where the sensation is located in an area distant from the site of the stimulus. *Deep somatic* pain is initiated by stimulation of nociceptors in ligaments, tendons, bones, blood vessels, fasciae and muscles, and is dull, aching, poorly-localized pain. Examples include sprains and broken bones. *Superficial* pain is initiated by activation of nociceptors in the skin or superficial tissues, and is sharp, well-defined and clearly located. Examples of injuries that produce superficial somatic pain include minor wounds and minor (first degree) burns.

Neuropathic

Neuropathic pain is caused by damage or disease affecting the central or peripheral portions of the nervous system involved in bodily feelings (the somatosensory system). Peripheral neuropathic pain is often described as “burning,” “tingling,” “electrical,” “stabbing,” or “pins and needles.” Bumping the "funny bone" elicits peripheral neuropathic pain.

Psychogenic

Psychogenic pain, also called *psychalgia* or *somatoform pain*, is pain caused, increased, or prolonged by mental, emotional, or behavioral factors. Headache, back pain, and stomach pain are sometimes diagnosed as psychogenic. Sufferers are often stigmatized, because both medical professionals and the general public tend to think that pain from a psychological source is not "real". However, specialists consider that it is no less actual or hurtful than pain from any other source.

People with long term pain frequently display psychological disturbance, with elevated scores on the Minnesota Multiphasic Personality Inventory scales of hysteria, depression and hypochondriasis (the "neurotic triad"). Some investigators have argued that it is this neuroticism that causes acute injuries to turn chronic, but clinical evidence points the other way, to chronic pain causing neuroticism. When long term pain is relieved by therapeutic intervention, scores on the neurotic triad and anxiety fall, often to normal

levels. Self-esteem, often low in chronic pain patients, also shows improvement once pain has resolved.

“The term 'psychogenic' assumes that medical diagnosis is so perfect that all organic causes of pain can be detected; regrettably, we are far from such infallibility... All too often, the diagnosis of neurosis as the cause of pain hides our ignorance of many aspects of pain medicine.”
— Ronald Melzack, 1996.

Phantom pain

Phantom pain is pain from a part of the body that has been lost or from which the brain no longer receives signals. It is a type of neuropathic pain. Phantom limb pain is a common experience of amputees.

The prevalence of phantom pain in upper limb amputees is nearly 82%, and in lower limb amputees is 54%. One study found that eight days after amputation, 72 percent of patients had phantom limb pain, and six months later, 65 percent reported it. Some amputees experience continuous pain that varies in intensity or quality; others experience several bouts a day, or it may occur only once every week or two. It is often described as shooting, crushing, burning or cramping. If the pain is continuous for a long period, parts of the intact body may become sensitized, so that touching them evokes pain in the phantom limb, or phantom limb pain may accompany urination or defecation.

Local anesthetic injections into the nerves or sensitive areas of the stump may relieve pain for days, weeks or, sometimes permanently, despite the drug wearing off in a matter of hours; and small injections of hypertonic saline into the soft tissue between vertebrae produces local pain that radiates into the phantom limb for ten minutes or so and may be followed by hours, weeks or even longer of partial or total relief from phantom pain. Vigorous vibration or electrical stimulation of the stump, or current from electrodes surgically implanted onto the spinal cord all produce relief in some patients.

Work by Vilayanur S. Ramachandran using Mirror box therapy allows for illusions of movement and touch in a phantom limb which in turn cause a reduction in pain.

Paraplegia, the loss of sensation and voluntary motor control after serious spinal cord damage, may be accompanied by girdle pain at the level of the spinal cord damage, visceral pain evoked by a filling bladder or bowel, or, in five to ten per cent of paraplegics, phantom body pain in areas of complete sensory loss. Phantom body pain is initially described as burning or tingling but may evolve into severe crushing or pinching pain, fire running down the legs, or a knife twisting in the flesh. Onset may be immediate or may not occur until years after the disabling injury. Surgical treatment rarely provides lasting relief.

Pain asymbolia and insensitivty

The ability to experience pain is essential for protection from injury, and recognition of the presence of injury. Episodic analgesia may occur under special circumstances, such as in the excitement of sport or war: a soldier on the battlefield may feel no pain for many hours from a traumatic amputation or other severe injury.

Although unpleasantness is an essential part of the IASP definition of pain, it is possible to induce a state described as intense pain devoid of unpleasantness in some patients, with morphine injection or psychosurgery. Such patients report that they have pain but are not bothered by it, they recognize the sensation of pain but suffer little, or not at all. Indifference to pain can also rarely be present from birth; these people have normal nerves on medical investigations, and find pain unpleasant, but do not avoid repetition of the pain stimulus.

Insensitivity to pain may also result from abnormalities in the nervous system. This is usually the result of acquired damage to the nerves, such as spinal cord injury, diabetes mellitus (diabetic neuropathy), or leprosy in countries where this is prevalent. These individuals are at risk of tissue damage due to undiscovered injury. People with diabetes-related nerve damage, for instance, sustain poorly healing foot ulcers as a result of decreased sensation.

A much smaller number of people are insensitive to pain due to an inborn abnormality of the nervous system, known as "congenital insensitivity to pain". Children with this condition incur carelessly repeated damage to their tongue, eyes, joints, skin, and muscles. They may attain adulthood, but have a reduced life expectancy. Most people with congenital insensitivity to pain have one of five hereditary sensory and autonomic neuropathies (which includes familial dysautonomia and congenital insensitivity to pain with anhidrosis).These conditions feature decreased sensitivity to pain together with other neurological abnormalties, particularly of the autonomic nervous system. A very rare syndrome with isolated congenital insensitivity to pain has been linked with mutations in the *SCN9A* gene, which codes for a sodium channel ($Na_v1.7$) necessary in conducting pain nerve stimuli.

Effect on psychological and psychosocial functioning

Experimental subjects challenged by acute pain and patients in chronic pain experience impairments in attention control, working memory, mental flexibility, problem solving, and information processing speed. Acute and chronic pain are also associated with increased depression, anxiety, fear, and anger.

"If I have matters right, the consequences of pain will include direct physical distress, unemployment, financial difficulties, marital disharmony, and difficulties in concentration and attention…"
—Harold Merskey 2000

Theory

Specificity

Descartes' pain pathway.

In his 1664 *Treatise of Man,* René Descartes traced a pain pathway. "Particles of heat" (A) activate a spot of skin (B) attached by a fine thread (cc) to a valve in the brain (de) where this activity opens the valve, allowing the animal spirits to flow from a cavity (F) into the muscles that then flinch from the stimulus, turn the head and eyes toward the affected body part, and move the hand and turn the body protectively. The underlying premise of this model - that pain is the direct product of a noxious stimulus activating a dedicated pain pathway, from a receptor in the skin, along a thread or chain of nerve fibers to the pain center in the brain, to a mechanical behavioral response - remained the dominant perspective on pain until the mid-nineteen sixties.

Pattern

This "specificity theory" (specific pain receptor and pathway) was challenged by the theory, proposed initially in 1874 by Wilhelm Erb, that a pain signal can be generated by stimulation of *any* sensory receptor, provided the stimulation is intense enough: the pattern of stimulation (intensity over time and area), not the receptor type, determines

whether nociception occurs. Alfred Goldscheider (1894) proposed that over time, activity from many sensory fibers might accumulate in the dorsal horns of the spinal cord and begin to signal pain once a certain threshold of accumulated stimulation has been crossed. In 1953, Willem Noordenbos observed that a signal carried from the area of injury along large diameter "touch, pressure or vibration" fibers may inhibit the signal carried by the thinner "pain" fibers - the ratio of large fiber signal to thin fiber signal determining pain intensity; hence, we rub a smack. This was taken as a demonstration that pattern of stimulation (of large and thin fibers in this instance) modulates pain intensity.

Gate control

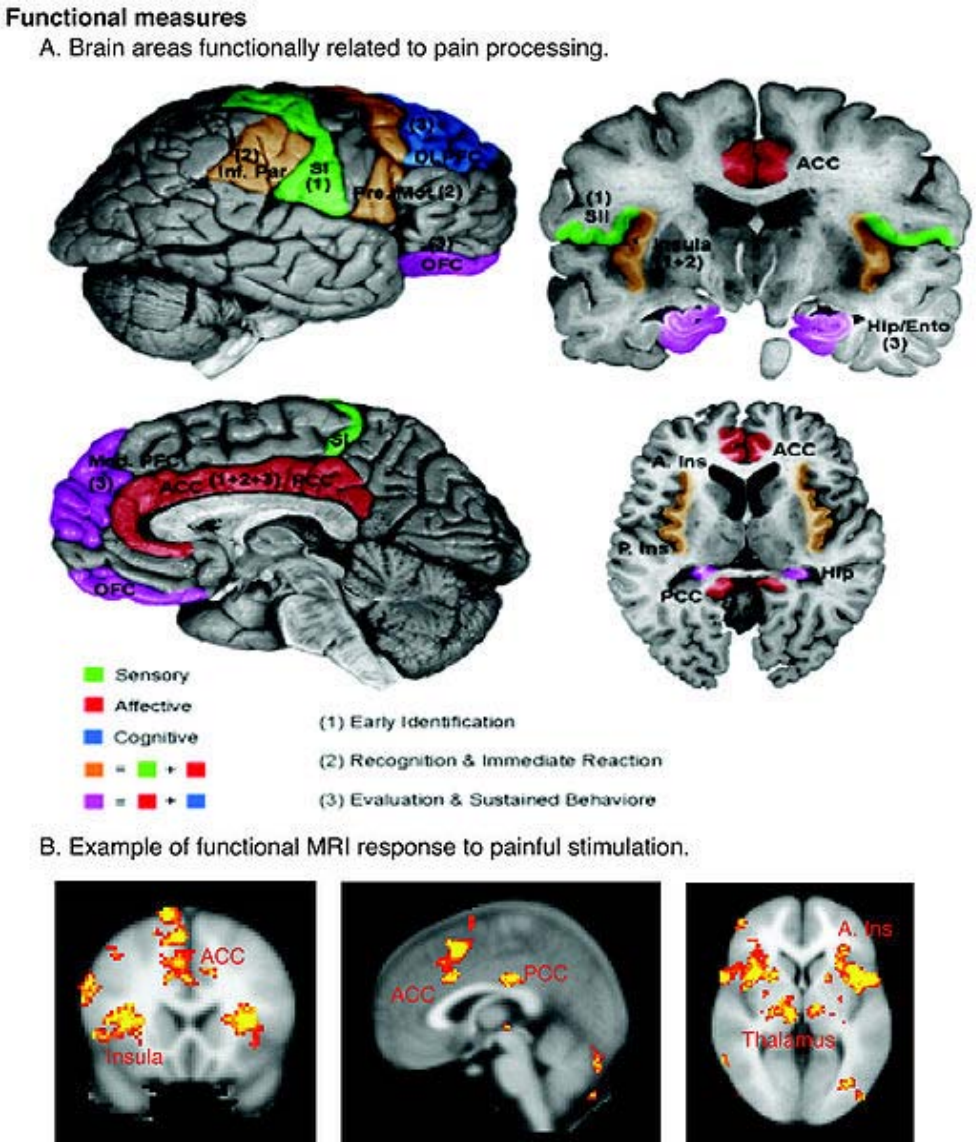
Melzack and Wall introduced their "gate control" theory of pain in the 1965 *Science* article "Pain Mechanisms: A New Theory". The authors proposed that thin (pain) and large diameter (touch, pressure, vibration) nerve fibers carry information from the site of injury to two destinations in the dorsal horn of the spinal cord: the "inhibitory" cells and the "transmission" cells. Signals from both thin and large diameter fibers excite the transmission cells, and when the output of the transmission cells exceeds a critical level, pain begins. The job of the inhibitory cells is to inhibit activation of the transmission cells. The transmission cells are the gate on pain, and inhibitory cells can shut the gate. When thin (pain) and large (touch, etc.) fibers, activated by a noxious event, excite a spinal cord transmission cell, they also act on its inhibitory cells. The thin fibers *impede* the inhibitory cells (tending to leave the gate open) while the large diameter fibers *excite* the inhibitory cells (tending to close the gate). So, the more large fiber activity relative to thin fiber activity coming from the inhibitory cell's receptive field, the less pain is felt. The authors had conceived a neural "circuit diagram" to explain why we rub a smack. They pictured not only a signal traveling from the site of injury to the inhibitory and transmission cells and up the spinal cord to the brain, but also a signal traveling from the site of injury directly up the cord to the brain (bypassing the inhibitory and transmission cells) where, depending on the state of the brain, it may trigger a signal back down the spinal cord to modulate inhibitory cell activity (and so pain intensity). This was the first theory to offer a physiological explanation for the previously reported effect of psychology on pain perception.

Dimensions

In 1968 Melzack and Casey described pain in terms of its three dimensions: "Sensory-discriminative" (sense of the intensity, location, quality and duration of the pain), "Affective-motivational" (unpleasantness and urge to escape the unpleasantness), and "Cognitive-evaluative" (cognitions such as appraisal, cultural values, distraction and hypnotic suggestion). They theorized that pain intensity (the sensory discriminative dimension) and unpleasantness (the affective-motivational dimension) are not simply determined by the magnitude of the painful stimulus, but “higher” cognitive activities (the cognitive-evaluative dimension) can influence perceived intensity and unpleasantness. Cognitive activities "may affect both sensory and affective experience or they may modify primarily the affective-motivational dimension. Thus, excitement in games or war appears to block both dimensions of pain, while suggestion and placebos

may modulate the affective-motivational dimension and leave the sensory-discriminative dimension relatively undisturbed." (p. 432) The paper ends with a call to action: "Pain can be treated not only by trying to cut down the sensory input by anesthetic block, surgical intervention and the like, but also by influencing the motivational-affective and cognitive factors as well." (p. 435)

Theory today



Regions of the cerebral cortex associated with pain.

Wilhelm Erb's (1874) early pattern theory hypothesis, that a pain signal can be generated by intense enough stimulation of *any* sensory receptor, has been soundly disproved. The thin (A-delta and C) peripheral nerve fibers carry information regarding the state of the body to the spinal cord. Some of these thin fibers do not differentiate noxious from non-noxious stimuli, while others, nociceptors, respond only to painfully intense stimuli.

Because the A-delta fiber is thinly sheathed in an electrically insulating material (myelin), it carries its signal faster (2.5–35 m/s) than the unmyelinated C fiber (0.5–2.0 m/s). Pain evoked by the (faster) A-delta fibers is described as sharp and is felt first. This is followed by a duller pain, often described as burning, carried by the C fibers.

Spinal cord fibers dedicated to carrying A-delta fiber pain signals, and others dedicated to carrying C fiber pain signals up the spinal cord to the thalamus in the brain have been identified. Pain-related activity in the thalamus spreads to the insular cortex (thought to embody, among other things, the feeling that distinguishes pain from other homeostatic emotions such as itch and nausea) and anterior cingulate cortex (thought to embody, among other things, the motivational element of pain);and pain that is distinctly located also activates the primary and secondary somatosensory cortices.

One study has found that pain reduction due to non-noxious touch or vibration can result from activity within the cerebral cortex, with minimal contribution at the spinal level. Melzack and Casey's 1968 picture of the dimensions of pain is as influential today as ever, firmly framing theory and guiding research in the functional neuroanatomy and psychology of pain.

Evolutionary and behavioral role

Pain is part of the body's defense system, producing a reflexive retraction from the painful stimulus, and tendencies to protect the affected body part while it heals, and avoid that harmful situation in the future. It is an important part of animal life, vital to healthy survival. People with congenital insensitivity to pain have reduced life expectancy. Idiopathic pain (pain that persists after the trauma or pathology has healed, or that arises without any apparent cause), may be an exception to the idea that pain is helpful to survival, although some psychodynamic psychologists argue that such pain is psychogenic, enlisted as a protective distraction to keep dangerous emotions unconscious. It is not clear what the survival benefit of some extreme forms of pain (e.g. toothache) might be, and the intensity of some forms of pain (for example as a result of injury to fingernails or toenails) seems to be out of all proportion to any survival benefits.

Thresholds

In pain science, thresholds are measured by gradually increasing the intensity of a stimulus such as electric current or heat applied to the body. The pain perception threshold is the point at which the stimulus begins to hurt, and the pain tolerance threshold is reached when the subject acts to stop the pain.

Differences in pain perception and tolerance thresholds are associated with, among other factors, ethnicity, genetics, and sex. People of Mediterranean origin report as painful some radiant heat intensities that northern Europeans describe as warmth, and Italian women tolerate less intense electric shock than Jewish or Native American women. Some individuals in all cultures have significantly higher than normal pain perception and tolerance thresholds. For instance, patients who experience painless heart attacks have

higher pain thresholds for electric shock, muscle cramp and heat. Women have lower pain perception and tolerance thresholds than men, and this sex difference appears to apply to all ages, including newborn infants.

Assessment

A person's self report is the most reliable measure of pain, with health care professionals tending to underestimate severity. A definition of pain widely employed in nursing, emphasizing its subjective nature and the importance of believing patient reports, was introduced by Margo McCaffery in 1968: "Pain is whatever the experiencing person says it is, existing whenever he says it does". To assess intensity, the patient may be asked to locate their pain on a scale of 0 to 10, with 0 being no pain at all, and 10 the worst pain they have ever felt. Quality can be established by having the patient complete the McGill Pain Questionnaire indicating which words best describe their pain.

Multidimensional pain inventory

The Multidimensional Pain Inventory (MPI) is a questionnaire designed to assess the psychosocial state of a person with chronic pain. Analysis of MPI results by Turk and Rudy (1988) found three classes of chronic pain patient: "(a) dysfunctional, people who perceived the severity of their pain to be high, reported that pain interfered with much of their lives, reported a higher degree of psychological distress caused by pain, and reported low levels of activity; (b) interpersonally distressed, people with a common perception that significant others were not very supportive of their pain problems; and (c) adaptive copers, patients who reported high levels of social support, relatively low levels of pain and perceived interference, and relatively high levels of activity." Combining the MPI characterization of the person with their IASP five-category pain profile is recommended for deriving the most useful case description.

In nonverbal patients

When a person is non-verbal and cannot self report pain, observation becomes critical, and specific behaviors can be monitored as pain indicators. Behaviors such as facial grimacing and guarding indicate pain, as well as an increase or decrease in vocalizations, changes in routine behavior patterns and mental status changes. Patients experiencing pain may exhibit withdrawn social behavior and possibly experience a decreased appetite and decreased nutritional intake. A change in condition that deviates from baseline such as moaning with movement or when manipulating a body part, and limited range of motion are also potential pain indicators. In patients who possess language but are incapable of expressing themselves effectively, such as those with dementia, an increase in confusion or display of aggressive behaviors or agitation, may signal that discomfort exists, and further assessment is necessary.

Infants feel pain but they lack the language needed to report it, so communicate distress by crying. A non-verbal pain assessment should be conducted involving the parents, who

will notice changes in the infant not obvious to the health care provider. Pre-term babies are more sensitive to painful stimuli than full term babies.

Other barriers to reporting

An aging adult may not respond to pain in the way that a younger person would. Their ability to recognize pain may be blunted by illness or the use of multiple prescription drugs. Depression may also keep the older adult from reporting they are in pain. The older adult may also quit doing activities they love because it hurts too much. Decline in self-care activities (dressing, grooming, walking, etc.) may also be indicators that the older adult is experiencing pain. The older adult may refrain from reporting pain because they are afraid they will have to have surgery or will be put on a drug they become addicted to. They may not want others to see them as weak, or may feel there is something impolite or shameful in complaining about pain, or they may feel the pain is deserved punishment for past transgressions.

Cultural barriers can also keep a person from telling someone they are in pain. Religious beliefs may prevent the individual from seeking help. They may feel certain pain treatment is against their religion. They may not report pain because they feel it is a sign that death is near. Many people fear the stigma of addiction and avoid pain treatment so as not to be prescribed addicting drugs. Many Asians do not want to lose respect in society by admitting they are in pain and need help, believing the pain should be borne in silence, while other cultures feel they should report pain right away and get immediate relief. Gender can also be a factor in reporting pain. Gender differences are usually the result of social and cultural expectations, with women expected to be emotional and show pain and men stoic, keeping pain to themselves.

As an aid to diagnosis

Pain is a symptom of many medical conditions. Knowing the time of onset, location, intensity, pattern of occurrence (continuous, intermittent, etc.), exacerbating and relieving factors, and quality (burning, sharp, etc.) of the pain will help the examining physician to accurately diagnose the problem. For example, chest pain described as extreme heaviness may indicate myocardial infarction, while chest pain described as tearing may indicate aortic dissection.

Management

Inadequate treatment of pain is widespread throughout surgical wards, intensive care units, accident and emergency departments, in general practice, in the management of all forms of chronic pain including cancer pain, and in end of life care. This neglect is extended to all ages, from neonates to the frail elderly. African and Hispanic Americans are more likely than others to suffer needlessly in the hands of a physician; and women's pain is more likely to be undertreated than men's.

The International Association for the Study of Pain advocates that the relief of pain should be recognized as a human right, that chronic pain should be considered a disease in its own right, and that pain medicine should have the full status of a specialty. It is a specialty only in China and Australia at this time. Elsewhere, pain medicine is a subspecialty under disciplines such as anesthesiology, physiatry, neurology, palliative medicine and psychiatry.

Medication

Acute pain is usually managed with medications such as analgesics and anesthetics. Management of chronic pain, however, is much more difficult and may require the coordinated efforts of a pain management team, which typically includes medical practitioners, clinical psychologists, physiotherapists, occupational therapists, and nurse practitioners.

Sugar taken orally reduces the total crying time but not the duration of the first cry in newborns undergoing a painful procedure (a single lancing of the heel). It does not moderate the effect of pain on heart rate and a recent single study found that sugar did not significantly affect pain-related electrical activity in the brains of newborns one second after the heel lance procedure. Sweet oral liquid moderately reduces the incidence and duration of crying caused by immunization injection in children between one and twelve months of age.

Psychological

Individuals with more social support experience less cancer pain, take less pain medication, report less labor pain and are less likely to use epidural anesthesia during childbirth or suffer from chest pain after coronary artery bypass surgery.

Suggestion can significantly affect pain intensity. About 35% of people report marked relief after receiving a saline injection they believe to have been morphine. This "placebo" effect is more pronounced in people who are prone to anxiety, so anxiety reduction may account for some of the effect, but it does not account for all of the effect. Placebos are more effective in intense pain than mild pain; and they produce progressively weaker effects with repeated administration.

It is possible for many chronic pain sufferers to become so absorbed in an activity or entertainment that the pain is no longer felt, or is greatly diminished.

Cognitive behavioral therapy (CBT) is effective in reducing the suffering associated with chronic pain in some patients but the reduction in suffering is quite modest, and the CBT method employed seems to have no effect on outcome.

Alternative medicine

Pain is the most common reason for people to use complementary and alternative medicine. An analysis of the 13 highest quality studies of pain treatment with acupuncture, published in January 2009 in the *British Medical Journal*, concluded there is little difference in the effect of real, sham and no acupuncture. There is interest in the relationship between vitamin D and pain, but the evidence so far from controlled trials for such a relationship, other than in osteomalacia, is unconvincing.

A 2007 review of 13 studies found evidence for the efficacy of hypnosis in the reduction of pain in some conditions, though the number of patients enrolled in the studies was low, bringing up issues of power to detect group differences, and most lacked credible controls for placebo and/or expectation. The authors concluded that "although the findings provide support for the general applicability of hypnosis in the treatment of chronic pain, considerably more research will be needed to fully determine the effects of hypnosis for different chronic-pain conditions."

A 2003 meta-analysis of randomized clinical trials found that spinal manipulation was "more effective than sham therapy but was no more or less effective than general practitioner care, analgesics, physical therapy, exercise, or back school" in the treatment of low back pain.

Epidemiology

Pain is the main reason for visiting the emergency department in more than 50% of cases and is present in 30% of family practice visits. Several epidemiological studies from different countries have reported widely varying prevalence rates for chronic pain, ranging from 12-80% of the population. It becomes more common as people approach death. A study of 4,703 patients found that 26% had pain in the last two years of life, increasing to 46% in the last month.

A survey of 6,636 children (0-18 years of age) found that, of the 5,424 respondents, 54% had experienced pain in the preceding three months. A quarter reported having experienced recurrent or continuous pain for three months or more, and a third of these reported frequent and intense pain. The intensity of chronic pain was higher for girls, and girls' reports of chronic pain increased markedly between ages12 and 14.

Society and culture

The okipa ceremony as witnessed by George Catlin, circa 1835.

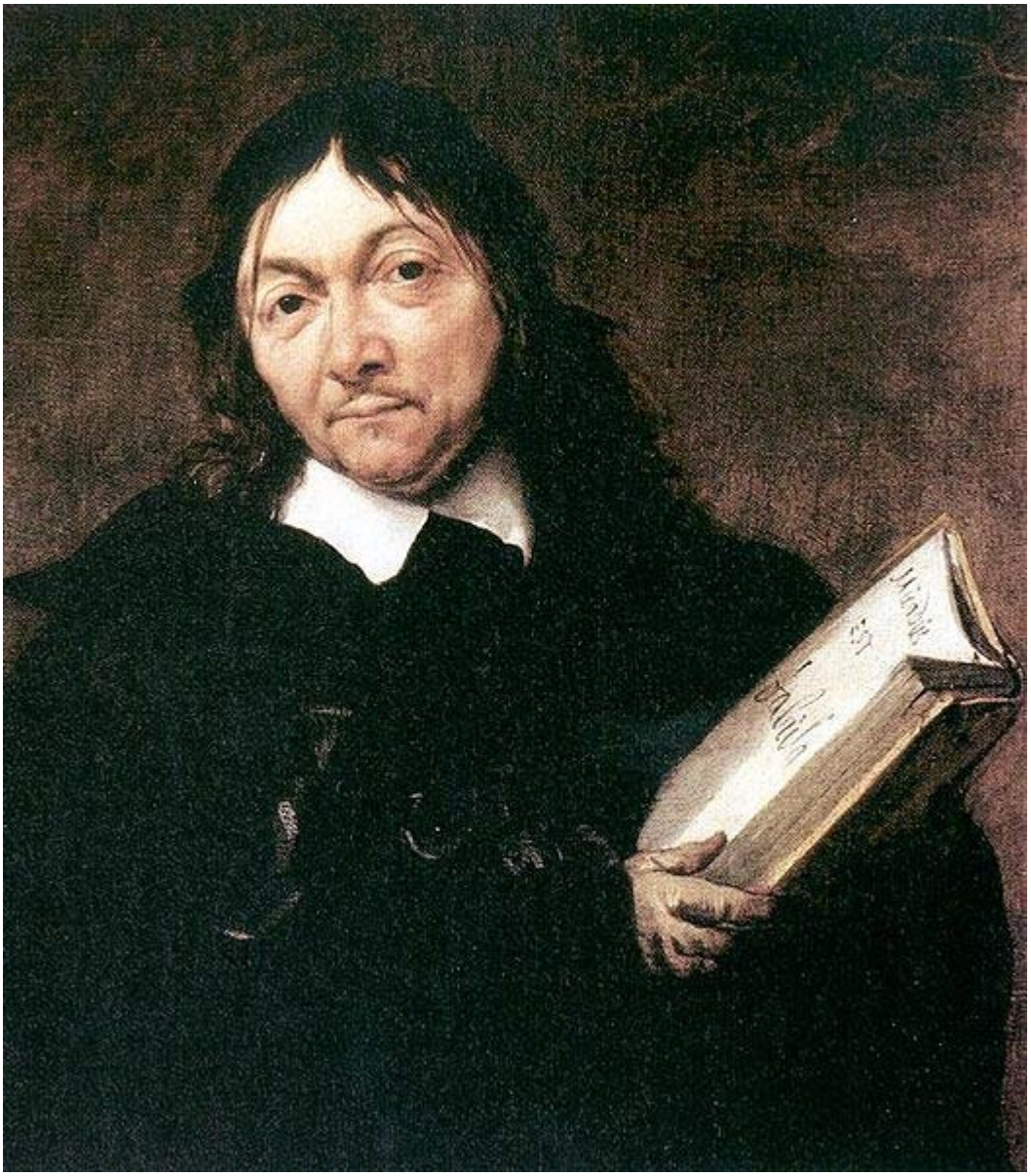
The nature or meaning of physical pain has been diversely understood by religious or secular traditions from antiquity to modern times.

Physical pain is an important political topic in relation to various issues, including pain management policy, drug control, animal rights or animal welfare, torture, pain compliance. In various contexts, the deliberate infliction of pain in the form of corporal punishment is used as retribution for an offence, or for the purpose of disciplining or reforming a wrongdoer, or to deter attitudes or behaviour deemed unacceptable. In some cultures, extreme practices such as mortification of the flesh or painful rites of passage are highly regarded.

Philosophy of pain is a branch of philosophy of mind that deals essentially with physical pain. Identity theorists assert that the mental state of pain is completely identical with some physiological state. Functionalists consider that pain as a mental state is constituted solely by its functional role, by its causal relations to other mental states, sensory inputs, and behavioral outputs.

More generally, it is often as a part of pain in the broad sense, i.e. suffering, that physical pain is dealt with in culture, religion, philosophy, or society.

In other animals



Portrait of René Descartes by Jan Baptist Weenix 1647-1649

The most reliable method for assessing pain in most humans is by asking a question: a person may report pain that cannot be detected by any known physiological measure. However, like infants (Latin *infans* meaning "unable to speak"), non-human animals cannot answer questions about whether they feel pain; thus the defining criterion for pain in humans cannot be applied to them. Philosophers and scientists have responded to this difficulty in a variety of ways. René Descartes for example argued that animals lack consciousness and therefore do not experience pain and suffering in the way that humans do. Bernard Rollin of Colorado State University, the principal author of two U.S. federal laws regulating pain relief for animals, writes that researchers remained unsure into the 1980s as to whether animals experience pain, and that veterinarians trained in the U.S.

before 1989 were simply taught to ignore animal pain. In his interactions with scientists and other veterinarians, he was regularly asked to "prove" that animals are conscious, and to provide "scientifically acceptable" grounds for claiming that they feel pain. Carbone writes that the view that animals feel pain differently is now a minority view. Academic reviews of the topic are more equivocal, noting that although the argument that animals have at least simple conscious thoughts and feelings has strong support, some critics continue to question how reliably animal mental states can be determined. The ability of invertebrate species of animals, such as insects, to feel pain and suffering is also unclear.

The presence of pain in an animal cannot be known for certain, but it can be inferred through physical and behavioral reactions. Specialists currently believe that all vertebrates can feel pain, and that certain invertebrates, like the octopus, might too. As for other animals, plants, or other entities, their ability to feel physical pain is at present a question beyond scientific reach, since no mechanism is known by which they could have such a feeling. In particular, there are no known nociceptors in groups such as plants, fungi, and most insects, except for instance in fruit flies.

In vertebrates, endogenous opioids are neurochemicals that moderate pain by interacting with opiate receptors. Opioids and opiate receptors occur naturally in crustaceans and, although at present no certain conclusion can be drawn, their presence indicates that lobsters may be able to experience pain. Opioids may mediate their pain in the same way as in vertebrates. Veterinary medicine uses, for actual or potential animal pain, the same analgesics and anesthetics as used in humans.

Etymology

First attested in English in 1297, the word *pain* comes from the Old French *peine*, in turn from Latin *poena*, "punishment, penalty" (in L.L. also "torment, hardship, suffering") and that from Greek "ποινή" (*poine*), generally "price paid", "penalty", "punishment".

Chapter 2

Chronic Pain and Psychogenic Pain

Chronic pain

	Chronic pain
ICD-10	R52.1-R52.2
ICD-9	338.2

Chronic pain has several different meanings in medicine. Traditionally, the distinction between *acute* and *chronic* pain has relied upon an arbitrary interval of time from onset; the two most commonly used markers being 3 months and 6 months since the initiation of pain, though some theorists and researchers have placed the transition from acute to chronic pain at 12 months. Others apply *acute* to pain that lasts less than 30 days, *chronic* to pain of more than six months duration, and *subacute* to pain that lasts from one to six months. A popular alternative definition of *chronic pain*, involving no arbitrarily fixed durations is "pain that extends beyond the expected period of healing."

Classification

Chronic pain may be divided into "nociceptive" (caused by activation of nociceptors), and "neuropathic" (caused by damage to or malfunction of the nervous system).

Nociceptive pain may be divided into "superficial somatic" and "deep", and *deep* pain into "deep somatic" and "visceral". *Superficial somatic* pain is initiated by activation of nociceptors in the skin or superficial tissues. *Deep somatic* pain is initiated by stimulation of nociceptors in ligaments, tendons, bones, blood vessels, fasciae and muscles, and is dull, aching, poorly-localized pain. *Visceral* pain originates in the viscera (organs). Visceral pain may be well-localized, but often it is extremely difficult to locate, and several visceral regions produce "referred" pain when injured, where the sensation is located in an area distant from the site of pathology or injury.

Neuropathic pain is divided into "peripheral" (originating in the peripheral nervous system) and "central" (origiiniting in the brain or spinal cord). Peripheral neuropathic pain is often described as “burning,” “tingling,” “electrical,” “stabbing,” or “pins and needles.” Bumping the "funny bone" elicits peripheral neuropathic pain.

Pathophysiology

Under persistent activation nociceptive transmission to the dorsal horn may induce a wind up phenomenon. This induces pathological changes that lower the threshold for pain signals to be transmitted. In addition it may generate nonnociceptive nerve fibers to respond to pain signals. Nonnociceptive nerve fibers may also be able to generate and transmit pain signals. In chronic pain this process is difficult to reverse or eradicate once established.

Chronic pain of different etiologies has been characterized as a disease affecting brain structure and function. Magnetic Resonance Imaging studies have shown abnormal anatomical and functional connectivity, even during rest involving areas related to the processing of pain. Also, persistent pain has been shown to cause grey matter loss, reversible once the pain has resolved.

Management

Complete and sustained remission of many neuropathies and most idiopathic chronic pain (pain that extends beyond the expected period of healing, or chronic pain that has no known underlying pathology) is rarely achieved, but much can be done to reduce suffering and improve quality of life.

Pain management (also called pain medicine) is that branch of medicine employing an interdisciplinary approach to the relief of pain and improvement in the quality of life of those living with pain. The typical pain management team includes medical practitioners, clinical psychologists, physiotherapists, occupational therapists, and nurse practitioners. Acute pain usually resolves with the efforts of one practitioner; however, the management of chronic pain frequently requires the coordinated efforts of the treatment team.

Epidemiology

In a recent large-scale telephone survey of 15 European countries and Israel, 19% of respondents over 18 years of age had suffered pain for more than 6 months, including the last month, and more than twice in the last week, with pain intensity of 5 or more for the last episode, on a scale of 1(no pain) to 10 (worst imaginable). 4839 of these respondents with chronic pain were interviewed in depth. Sixty six percent scored their pain intensity at moderate (5–7), and 34% at severe (8–10); 46% had constant pain, 56% intermittent; 49% had suffered pain for 2–15 years; and 21% had been diagnosed with depression due to the pain. Sixty one percent were unable or less able to work outside the home, 19%

had lost a job, and 13% had changed jobs due to their pain. Forty percent had inadequate pain management and less than 2% were seeing a pain management specialist.

Comorbidities and sequelae

Chronic pain is associated with higher rates of depression and anxiety. Sleep disturbance, and insomnia due to medication and illness symptoms are often experienced by those with chronic pain. Substance abuse is highly prevalent in some segments of the chronic pain population such as those with chronic headache. Chronic pain may contribute to decreased physical activity due to fear of exacerbating pain.

Psychology

Personality

Two of the most frequent personality profiles found in chronic pain patients by the Minnesota Multiphasic Personality Inventory (MMPI) are the *conversion V* and the *neurotic triad*. The conversion V personality, so called because the higher scores on MMPI scales 1 and 3, relative to scale 2, form a "V" shape on the graph, expresses exaggerated concern over body feelings, develops bodily symptoms in response to stress, and often fails to recognize their own emotional state, including depression. The neurotic triad personality, scoring high on scales 1, 2 and 3, also expresses exaggerated concern over body feelings and develops bodily symptoms in response to stress, but is demanding and complaining.

Some investigators have argued that it is this neuroticism that causes acute pain to turn chronic, but clinical evidence points the other way, to chronic pain causing neuroticism. When long term pain is relieved by therapeutic intervention, scores on the neurotic triad and anxiety fall, often to normal levels. Self-esteem, often low in chronic pain patients, also shows striking improvement once pain has resolved.

Effect on cognition

Chronic pain's impact on cognition is an under-researched area, but several tentative conclusions have been published. Most chronic pain patients complain of cognitive impairment, such as forgetfulness, difficulty with attention, and difficulty completing tasks. Objective testing has found that people in chronic pain tend to experience impairment in attention, memory, mental flexibility, verbal ability, speed of response in a cognitive task, and speed in executing structured tasks. In 2007, Shulamith Kreitler and David Niv advised clinicians to assess cognitive function in chronic pain patients in order to more precisely monitor therapeutic outcomes, and tailor treatment to address this aspect of the pain experience.

Psychogenic pain

Psychogenic pain	
ICD-10	F45.4
ICD-9	307.8
MedlinePlus	000922

Psychogenic pain, also called psychalgia, is physical pain that is caused, increased, or prolonged by mental, emotional, or behavioral factors.

Headache, back pain, or stomach pain are some of the most common types of psychogenic pain. It may occur, rarely, in persons with a mental disorder, but more commonly it accompanies or is induced by social rejection, broken heart, grief, love sickness, or other such emotional events.

Sufferers are often stigmatized, because both medical professionals and the general public tends to think that pain from psychological source is not "real". However, specialists consider that it is no less actual or hurtful than pain from other sources.

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, *or described in terms of such damage*" (emphasis added). In the note accompanying that definition, the following can be found about pain that happens for psychological reasons:

Many people report pain in the absence of tissue damage or any likely pathophysiological cause; usually this happens for psychological reasons. There is usually no way to distinguish their experience from that due to tissue damage if we take the subjective report. If they regard their experience as pain and if they report it in the same ways as pain caused by tissue damage, it should be accepted as pain.

Medicine refers also to psychogenic pain or psychalgia as a form of chronic pain under the name of *persistent somatoform pain disorder*. Causes may be linked to stress, unexpressed emotional conflicts, psychosocial problems, or various mental disorders. Some specialists believe that psychogenic chronic pain exists as a protective distraction to keep dangerous repressed emotions such as anger or rage unconscious.

It remains controversial, however, that chronic pain might arise purely from emotional causes. Treatment may include psychotherapy, antidepressants, analgesics, and other remedies that are used for chronic pain in general.

Chapter 3

Neuropathic Pain

"**Neuropathic pain** may arise as a consequence of a lesion or disease affecting the somatosensory system." It may be associated with abnormal sensations called dysesthesia, which occur spontaneously and allodynia that occurs in response to external stimuli. Neuropathic pain may have continuous and/or episodic (paroxysmal) components. The latter are likened to an electric shock. Common qualities include burning or coldness, "pins and needles" sensations, numbness and itching. Nociceptive pain is more commonly described as aching.

Up to 7% to 8% of the European population is affected and in 5% of persons it may be severe. Neuropathic pain may result from disorders of the peripheral nervous system or the central nervous system (brain and spinal cord). Thus, neuropathic pain may be divided into peripheral neuropathic pain, central neuropathic pain, or mixed (peripheral and central) neuropathic pain.

Central neuropathic pain is found in spinal cord injury, multiple sclerosis, and some strokes. Fibromyalgia, a disorder of chronic widespread pain, is potentially a central pain disorder and is responsive to medications that are effective for neuropathic pain.

Aside from diabetes and other metabolic conditions, the common causes of painful peripheral neuropathies are herpes zoster infection, HIV-related neuropathies, nutritional deficiencies, toxins, remote manifestations of malignancies, genetic, and immune mediated disorders or physical trauma to a nerve trunk.

Neuropathic pain is common in cancer as a direct result of cancer on peripheral nerves (e.g., compression by a tumor), or as a side effect of chemotherapy, radiation injury or surgery.

Mechanisms

The starting point for neuropathic pain is a lesion or dysfunction within the somatosensory system. Current knowledge regarding the mechanisms of neuropathic pain is incomplete and is biased by a focus on animal models of peripheral nerve injury.

Peripheral

Under normal circumstances, pain sensations are carried by unmyelinated and thinly myelinated nerve fibers, designated C-fibers and A-delta fibers, respectively. After a peripheral nerve lesion, aberrant regeneration may occur. Neurons become unusually sensitive and develop spontaneous pathological activity, abnormal excitability, and heightened sensitivity to chemical, thermal and mechanical stimuli. This phenomenon is called "peripheral sensitization".

Central

The dorsal horn neurons give rise to the spinothalamic tract (STT), which constitutes the major ascending nociceptive pathway. As a consequence of ongoing spontaneous activity arising in the periphery, STT neurons develop an increased background activity, enlarged receptive field and increased responses to afferent impulses, including normally innocuous tactile stimuli. This phenomenon is called central sensitization. Central sensitization has been proposed as an important mechanism of persistent neuropathic pain.

Other mechanisms, however, may take place at the central level after peripheral nerve damage. The loss of afferent signals induces functional changes in dorsal horn neurons. A decrease in the large fiber input decreases activity of interneurons inhibiting nociceptive neurons i.e. loss of afferent inhibition. Hypoactivity of the descending antinociceptive systems or loss of descending inhibition may be another factor. With loss of neuronal input (deafferentation) the STT neurons begin to fire spontaneously, a phenomenon designated "deafferentation hypersensitivity."

Non-neural glial cells may play a role in central sensitization. Peripheral nerve injury induces glial to releasing glial proinflammatory cytokines and glutamate which, in turn influence neurons.

Mechanisms at light-microscopic and submicroscopic levels

The phenomenon described above are dependent on changes at light-microscopic and submicroscopic levels. Altered expression of ion channels, changes in neurotransmitters and their receptors as well as altered gene expression in response to neural input are at play.

Treatments

Neuropathic pain can be very difficult to treat with only some 40-60% of patients achieving partial relief.

In addition to the work of Dworkin, O'Connor and Backonja et al., cited above, there have been several recent attempts to derive guidelines for pharmacological therapy. These have combined evidence from randomized controlled trials with expert opinion.

Determining the best treatment for individual patients remains challenging. Attempts to translate scientific studies into best practices are limited by factors such as differences in reference populations and a lack of head-to-head studies. Furthermore, multi-drug combinations and the needs of special populations, such as children, require more study.

It is common practice in medicine to designate classes of medication according to their most common or familiar use e.g. as "antidepressants" and "anti-epileptic drugs" (AED's). These drugs have alternate uses to treat pain because the human nervous system employs common mechanisms for different functions, for example ion channels for impulse generation and neurotransmitters for cell-to-cell signaling.

Favored treatments are certain antidepressants e.g. tricyclics and selective serotonin-norepinephrine reuptake inhibitors (SNRI's), anticonvulsants, especially pregabalin (Lyrica) and gabapentin (Neurontin), and topical lidocaine. Opioid analgesics and tramadol are recognized as useful agents but are not recommended as first line treatments. Many of the pharmacologic treatments for chronic neuropathic pain decrease the sensitivity of nociceptive receptors, or desensitize C fibers such that they transmit fewer signals.

Some drugs may exert their influence through descending pain modulating pathways. These descending pain modulating pathways originate in the brainstem.

Antidepressants

The functioning of antidepressants is different in neuropathic pain from that observed in depression. Activation of descending norepinephrinergic and serotonergic pathways to the spinal cord limit pain signals ascending to the brain. Antidepressants will relieve neuropathic pain in non-depressed persons.

In animal models of neuropathic pain it has been found that compounds which only block serotonin reuptake do not improve neuropathic pain. Similarly, compounds that only block norepinephrine reuptake also do not improve neuropathic pain. Dual serotonin-norepinephrine reuptake inhibitors such as duloxetine, venlafaxine, and milnacipran, as well as tricyclic antidepressants such as nortriptyline and desipramine improve neuropathic pain and are considered first-line medications for this condition.

Bupropion has been found to have efficacy in the treatment of neuropathic pain.

Tricyclic antidepressants may also have effects on sodium channels.

Anticonvulsants

Pregabalin (Lyrica) and gabapentin (Neurontin) work by blocking specific calcium channels on neurons and are preferred first-line medications for diabetic neuropathy. The actions of the anticonvulsants carbamazepine (Tegretol) and oxcarbazepine (Trileptal) are especially effective on trigeminal neuralgia, are principally on sodium channels.

Lamotrigine may have a special role in treating two conditions for which there are few alternatives, namely post stroke pain and HIV/AIDS-related neuropathy caused by antiretroviral therapy.

Opioids

Opioids, also known as narcotics, are increasingly recognized as important treatment options for chronic pain. They are not considered first line treatments in neuropathic pain but remain the most consistently effective class of drugs for this condition. Opioids must be used only in appropriate individuals and under close medical supervision.

Several opioids, particularly methadone, have NMDA antagonist activity in addition to their μ-opioid agonist properties.

Methadone and ketobemidone possess NMDA antagonism. Methadone does so because it is a racemic mixture; only the l-isomer is a potent μ-opioid agonist. The d-isomer does not have opioid agonist action and acts as an NMDA antagonist; d-methadone is analgesic in experimental models of chronic pain. . Clinical studies are in progress to test the efficacy of d-methadone in neuropathic pain syndromes.

There is little evidence to indicate that one strong opioid is more effective than another. Expert opinion leans toward the use of methadone for neuropathic pain, in part because of its NMDA antagonism. It is reasonable to base the choice of opioid on other factors.

Topical agents

In some forms of neuropathy, especially post-herpetic neuralgia, the topical application of local anesthetics such as lidocaine can provide relief. A transdermal patch containing lidocaine is available commercially in some countries.

Repeated topical applications of capsaicin, are followed by a prolonged period of reduced skin sensibility referred to as desensitization, or nociceptor inactivation. Capsaicin not only depletes substance P but also results in a reversible degeneration of epidermal nerve fibers. Nevertheless, benefits appear to be modest with standard (low) strength preparations.

Cannabinoids

Marijuana's active ingredients are called cannabinoids. Unfortunately, strongly held beliefs make discussion of the appropriate use of these substances, in a medical context, difficult. Similar considerations apply to opioids.

A recent study showed smoked marijuana is beneficial in treating symptoms of HIV-associated peripheral neuropathy. Nabilone is an artificial cannabinoid which is significantly more potent than delta-9-tetrahydrocannabinol (THC). Nabilone produces less relief of chronic neuropathic pain and had slightly more side effects than dihydrocodeine.

The predominant adverse effects are CNS depression and cardiovascular effects which are mild and well tolerated but, psychoactive side effects limit their use. A complicating issue may be a narrow therapeutic window; lower doses decrease pain but higher doses have the opposite effect.

Sativex, a fixed dose combination of delta-9-tetrahydrocannabinol (THC) and cannabidiol, is sold as an oromucosal spray. The product is approved in Canada as adjunctive treatment for the symptomatic relief of neuropathic pain in multiple sclerosis, and for cancer related pain.

Long-term studies are needed to assess the probability of weight gain, unwanted psychological influences and other adverse effects.

Botulinum Toxin Type A (Botox, BTX-A)

Botulinum Toxin Type A (BTX-A) is best know by its trade name, Botox. Local intradermal injection of BTX-A is helpful in chronic focal painful neuropathies. The analgesic effects are not dependent on changes in muscle tone. Benefits persist for at least 14 weeks from the time of administration.

The utility of BTX-A in other painful conditions remains to be established.

NMDA antagonism

The *N*-methyl-D-aspartate (NMDA) receptor seems to play a major role in neuropathic pain and in the development of opioid tolerance. Dextromethorphan is an NMDA antagonist at high doses. Experiments in both animals and humans have established that NMDA antagonists such as ketamine and dextromethorphan can alleviate neuropathic pain and reverse opioid tolerance. Unfortunately, only a few NMDA antagonists are clinically available and their use is limited by a very short half life (dextrometorphan), weak activity (memantine)or unacceptable side effects (ketamine).

Reducing sympathetic nervous stimulation

In some neuropathic pain syndromes, "crosstalk" occurs between descending sympathetic nerves and ascending sensory nerves. Increases in sympathetic nervous system activity result in an increase of pain; this is known as sympathetically-mediated pain.

Lesioning operations on the sympathetic branch of the autonomic nervous system are sometimes carried out.

There are methods of treating sympathetically maintained pain in peripheral tissues. This is done topically to a patient having sympathetically maintained pain at a peripheral site where the pain originates. Wherein the sympathetically maintained pain can be diagnosed by local anesthetic blockade of the appropriate sympathetic ganglion or adrenergic receptor blockade via intravenous administration of Phentolamine, and rekindled by intradermal injection of Norepinephrine.

Dietary supplements

There are two dietary supplements that have clinical evidence showing them to be effective treatments of diabetic neuropathy; alpha lipoic acid and benfotiamine.

A 2007 review of studies found that injected (parenteral) administration of alpha lipoic acid (ALA) was found to reduce the various symptoms of peripheral diabetic neuropathy. While some studies on orally administered ALA had suggested a reduction in both the positive symptoms of diabetic neuropathy (including stabbing and burning pain) as well as neuropathic deficits (paresthesia), the metanalysis showed "more conflicting data whether it improves sensory symptoms or just neuropathic deficits alone". There is some limited evidence that ALA is also helpful in some other non-diabetic neuropathies.

Benfotiamine is a lipid-soluble form of thiamine that has several placebo-controlled double-blind trials proving efficacy in treating neuropathy and various other diabetic comorbidities.

Other modalities

In addition to pharmacological treatment several other modalities are commonly recommended. While lacking adequate double blind trials, these have shown to reduce pain and improve patient quality of life for chronic neuropathic pain: chiropractic, yoga, massage, meditation, cognitive therapy, and prescribed exercise. Some pain management specialists will try acupuncture, with variable results.

Transcutaneous electrical nerve stimulation (TENS) may be worth considering in chronic neurogenic pain. TENS, with certain electrical waveforms, appears to have an acupuncture-like function.

Infrared photo therapy has been used to treat neuropathic symptoms. However, recent work has cast doubt on the value of this approach.

Neuromodulators

Neuromodulation is a field of science, medicine and bioengineering that encompasses both implantable and non-implantable technologies (electrical and chemical) for treatment purposes.

Implanted devices are expensive and carry the risk of complications. Available studies have focused on conditions having a different prevalence than neuropathic pain patients in general. More research is needed to define the range of conditions for which they might be beneficial.

Spinal cord stimulators and implanted spinal pumps

Spinal cord stimulators, use electrodes placed adjacent to, but outside the spinal cord. The overall complication rate is one-third, most commonly due to lead migration or breakage. Lack of pain relief sometimes prompts device removal.

Infusion pumps deliver medication directly to the fluid filled (subarachnoid) space surrounding the spinal cord. Opioids alone or opioids with adjunctive medication (either a local anesthetic or clonidine) or more recently ziconotide are infused. Complications such as, serious infection (meningitis), urinary retention, hormonal disturbance and intrathecal granuloma formation have been noted.

There are no randomized studies of infusion pumps. For selected patients 50% or greater pain relief is achieved in 38% to 56% at six months but declines with the passage of time. These results must be viewed skeptically since placebo effects cannot be evaluated.

Motor cortex stimulation

Stimulation of the primary motor cortex through electrodes placed within the skull but outside the thick meningeal membrane (dura) has been used to treat pain. The level of stimulation is below that for motor stimulation. As compared with spinal stimulation, which requires a noticeable tingling (paresthesia) for benefit, the only palpable effect is pain relief.

Deep brain stimulation

The best long-term results with deep brain stimulation have been reported with targets in the periventricular/periaqueductal grey matter (79%), or the periventricular/periaqueductal grey matter plus thalamus and/or internal capsule (87%). There is a significant complication rate which increase over time.

Chapter 4

Phantom Pain

Phantom pain	
ICD-9	353.6
DiseasesDB	29431

Phantom pain sensations are described as perceptions that an individual experiences relating to a limb or an organ that is not physically part of the body. Limb loss is a result of either removal by amputation or congenital limb deficiency (Giummarra et al., 2007). However, phantom limb sensations can also occur following nerve avulsion or spinal cord injury. Sensations are recorded most frequently following the amputation of an arm or a leg, but may also occur following the removal of a breast or an internal organ. Phantom limb pain is the feeling of pain in an absent limb or a portion of a limb. The pain sensation varies from individual to individual.

Phantom limb sensation is the term given to any sensory phenomenon (except pain) which is felt at an absent limb or a portion of the limb. It has been known that at least 80% of amputees experience phantom sensations at some time of their lives. Some experience some level of this phantom pain and feeling in the missing limb for the rest of their lives.

There are various types of sensations that may be felt:

- Sensations related to the phantom limb's posture, length and volume e.g. feeling that the phantom limb is behaving just like a normal limb like sitting with the knee bent or feeling that the phantom limb is as heavy as the other limb. Sometimes, an amputee will experience a sensation called telescoping. This is the feeling that the phantom limb is gradually shortening over time.
- Sensations of movement (e.g. feeling that the phantom foot is moving).
- Sensations of touch, temperature, pressure and itchiness. Many amputees report of feeling heat, tingling, itchiness, and pain.

The term “phantom limb” was first coined by American neurologist Silas Weir Mitchell in 1871 (Halligan, 2002). Mitchell described that “thousands of spirit limbs were haunting as many good soldiers, every now and then tormenting them” (Bittar et al., 2005). However, in 1551, French military surgeon Ambroise Paré recorded the first documentation of phantom limb pain when he reported that, “For the patients, long after the amputation is made, say that they still feel pain in the amputated part” (Bittar et al., 2005).

Signs and symptoms

Phantom pain involves the sensation of pain in a part of the body that has been removed.

Epidemiology

Phantom limb pain and phantom limb sensations are linked, but must be differentiated from one another. While phantom limb sensations are experienced by those with congenital limb deficiency, spinal cord injury, and amputation, phantom limb pain occurs almost exclusively as a result of amputation (Kooijman et al., 2000). Almost immediately following the amputation of a limb, 90-98% of patients report experiencing a phantom sensation. Nearly 75% of individuals experience the phantom as soon as anesthesia wears off, and the remaining 25% of patients experience phantoms within a few days or weeks (Ramachandran and Herstein, 1998). Of those experiencing innocuous sensations, a majority of patients also report distinct painful sensations.

The prevalence of phantom limb pain differs based on the location of the amputation. The prevalence of phantom pain in upper limb amputees is nearly 82%, while the prevalence of pain in lower limb amputees is only 54% (Kooijman et al., 2000). Age and gender have not been shown to affect the onset or duration of phantom limb pain. Although it has not been fully explored, one investigation of lower limb amputation observed that as stump length decreased, there was a greater incidence of moderate and severe phantom pain (Bittar et al., 2005).

Pathophysiology

The neurological basis and mechanisms for phantom limb pain are all derived from experimental theories and observations. Little is known about the true mechanism causing phantom pains, and many theories highly overlap. Historically, phantom pains were thought to originate from neuromas located at the stump tip. Traumatic neuromas, or non-tumor nerve injuries, often arise from surgeries and result from the abnormal growth of injured nerve fibers. Although stump neuromas contribute to phantom pains, they are not the sole cause. This is because patients with congenital limb deficiency can sometimes, although rarely, experience phantom pains. This suggests that there is a central representation of the limb responsible for painful sensations (Ramachandran and Herstein, 1998). Currently, theories are based on altered neurological pathways and cortical reorganization. Although they are highly intertwined, mechanisms are often separated into peripheral, spinal, and central mechanisms.

Peripheral mechanisms

Neuromas formed from injured nerve endings at the stump site are able to fire abnormal action potentials, and were historically thought to be the main cause of phantom limb pain. Although neuromas are able to contribute to phantom pain, pain is not completely eliminated when peripheral nerves are treated with conduction blocking agents (Ramachandran and Herstein, 1998). Physical stimulation of neuromas can increase C fiber activity, thus increasing phantom pain, but pain still persists once the neuromas have ceased firing action potentials. The peripheral nervous system is thought to have at most a modulation effect on phantom limb pain (Bitter et al., 2005)

Spinal mechanisms

In addition to peripheral mechanisms, spinal mechanisms are thought to have an influencing role in phantom pains. Peripheral nerve injury can lead to the degeneration of C fibers in the dorsal horn of the spinal cord, and terminating A fibers may subsequently branch into the same lamina (Bittar et al., 2005). If this occurs, A fiber inputs could be reported as noxious stimuli. Substance P, involved in the transmission of pain signals, is usually expressed by Aδ and C fibers, but following peripheral nerve damage, substance P is expressed by Aβ fibers (Bittar et al., 2005). This leads to hyperexcitability of the spinal cord, which usually occurs only in the presence of noxious stimuli. Because patients with complete spinal cord injury have experienced phantom pains, there must be an underlying central mechanism responsible for the generation of phantom pains.

Central mechanisms and cortical remapping

Under ordinary circumstances, the genetically determined circuitry in the brain remains largely stable throughout life. It was thought, until about 30 years ago, that no new neural circuits could be formed in the adult mammalian brain (Ramachandran and Hirstein, 1998). Recently, functional MRI studies in amputees have shown that almost all patients have experienced motor cortical remapping (Cruz et al., 2003). The majority of motor reorganization has occurred as a downward shift of the hand area of the cortex onto the area of face representation, especially the lips. Sometimes there is a side shift of the hand motor cortex to the ipsilateral cortex (Cruz et al., 2003). In patients with phantom limb pain, the reorganization was great enough to cause a change in cortical lip representation into the hand areas only during lip movements (Cruz et al., 2003). It has also been found that there is a high correlation between the magnitude of phantom limb pain and the extent to which the shift of the cortical representation of the mouth into the hand area in motor and somatosensory cortical reorganization has occurred (Karl et al., 2001). Additionally, as phantom pains in upper extremity amputees increased, there was a higher degree of medial shift of the facial motor representation (Karl et al., 2001). There are Multiple theories that try to explain how cortical remapping occurs in amputees, but none have been supported to a great extent.

The neuromatrix

The neuromatrix theory proposes that there is an extensive network connecting the thalamus and the cortex, and the cortex and the limbic system (Bittar et al., 2005). It is a theory that extends beyond body schema theory and incorporates the conscious awareness of oneself. This theory proposes that conscious awareness and the perception of self are generated in the brain via patterns of input that can be modified by different perceptual inputs (Giummarra et al., 2007). The network is genetically predetermined, and is modified throughout one's lifetime by various sensory inputs to create a neurosignature. It is the neurosignature of a specific body part that determines how it is consciously perceived (Bittar et al., 2005). The input systems contributing to the neurosignature are primarily the somatosensory, limbic, and thalamocortical systems. The neuromatrix theory aims to explain how certain activities associated with pain lead to the conscious perception of phantom pain. The persistence of the neurosignature, even after limb amputation, may be the cause of phantom sensations and pain. Phantom pain may arise from abnormal reorganization in the neuromatrix to a pre-existing pain state (Melzack, 1992).

Opposition to the neuromatrix theory exists largely because it fails to explain why relief from phantom sensations rarely eliminates phantom pains. It also does not address how sensations can spontaneously end and how some amputees do not experience phantom sensations at all (Bittar et al., 2005). In addition, a major limitation of the neuromatrix theory is that it too broadly accounts for various aspects of phantom limb perception. It is also likely that it is too difficult to be tested empirically, especially when testing painless phantom sensations (Giummarra et al., 2007).

Management

Various methods have been used to treat phantom limb pain. Doctors may prescribe medications to reduce the pain. Some antidepressants or antiepileptics have been shown to have a beneficial effect on reducing phantom limb pain. Often physical methods such as light massage, electrical stimulation, and hot and cold therapy have been used with variable results.

There are many different treatment options for phantom limb pain that are actively being researched. Most treatments do not take into account the mechanisms underlying phantom pains, and are therefore ineffective. However, there are a few treatment options that have been shown to alleviate pain in some patients, but these treatment options usually have a success rate less than 30% (Bittar et al., 2005). It is important to note that this rate of success does not exceed the placebo effect. It is also important to note that because the degree of cortical reorganization is proportional to phantom limb pains, any perturbations to the amputated regions may increase pain perception (Bittar et al., 2005).

Non surgical techniques

Mirror box therapy

Mirror box therapy allows for illusions of movement and touch in a phantom limb by inducing somatosensory and motor pathway coupling between the phantom and real limb (Giummarra et al., 2007). Many patients experience pain as a result of a clenched phantom limb, and because phantom limbs are not under voluntary control, unclenching becomes impossible (Ramachandran and Rogers-Ramachandran, 1996). The theory behind the mirror box treatment is that the brain has become accustomed to the fact that a phantom limb is paralyzed because there is no feedback from the phantom back to the brain to inform it otherwise. Ramachandran and Rogers-Ramachandran believed that if the brain received visual feedback that the limb had moved, then the phantom limb would become unparalyzed (Ramachandran and Rogers-Ramachandran, 1996).

To create the visual feedback, mirror boxes are constructed to create an illusion of a second limb. The mirror box is constructed so that it has a vertical mirror placed in the center, and the lid remains off. The intact limb is placed on one side of the mirror, and in the patient's sight, while the amputated limb is placed on the other side, out of sight. The patient sees an intact second limb through the mirror and sends motor commands to both limbs to make symmetric movements. The movement gives the brain positive feedback that the phantom has moved, and it becomes unparalyzed (Ramachandran and Rogers-Ramachandran, 1996).

In a study of ten patients with upper phantom limb paralysis, nine patients were able to move the phantom limb, and eight of the patients able to move the phantom limb had their pain alleviated (Ramachandran and Rogers-Ramachandran, 1996). Since Ramachandran and Ramachandran's pioneer study, there have been multiple additional studies to support the mirror box findings for patients with upper limb phantom pain. MacLachlan, McDonald, and Walcoch presented the first case of mirror box treatment for lower limb phantoms in 2004. The patient, Alan, experienced a painful crossing of his toes in the morning, and the pain worsened as the day progressed. After three weeks of mirror box treatment twice a day, Alan no longer felt any painful sensations from crossed toes (MacLachlan, McDonald, and Walcoch, 2004).

Pharmacological treatment

Pharmacological techniques are often continued in conjunction with other treatment options. Doses or pain medications needed often drop substantially when combined with other techniques, but rarely are discontinued completely. Tricyclic antidepressants, such as amitriptyline, and sodium channel blockers, mainly carbamazepine, are often used to relieve chronic pain, and recently have been used in an attempt to reduce phantom pains. Pain relief may also be achieved through use of opioids, ketamine, calcitonin, and lidocaine (Bittar et al., 2005).

Surgical techniques

Deep-brain stimulation

Deep brain stimulation is a surgical technique used to alleviate patients from phantom limb pain. Prior to surgery, patients undergo functional brain imaging techniques such as PET scans and functional MRI to determine an appropriate trajectory of where pain is originating. Surgery is then carried out under local anesthetic, because patient feedback during the operation is needed. In the study conducted by Bittar et al., a radiofrequency electrode with four contact points was placed on the brain. Once the electrode was in place, the contact locations were altered slightly according to where the patient felt the greatest relief from pain. Once the location of maximal relief was determined, the electrode was implanted and secured to the skull. After the primary surgery, a secondary surgery under general anesthesia was conducted. A subcutaneous pulse generator was implanted into a pectoral pocket below the clavicle to stimulate the electrode (Bittar et al., 2005). It was found that all three patients studied had gained satisfactory pain relief from the deep brain stimulation. Pain had not been completely eliminated, but the intensity had been reduced by over 50% and the burning component had completely vanished (Bittar et al., 2005).

Chapter 5

Pain Management

Pain management (also called pain medicine; algiatry) is a branch of medicine employing an interdisciplinary approach for easing the suffering and improving the quality of life of those living with pain. The typical pain management team includes medical practitioners, clinical psychologists, physiotherapists, occupational therapists, and nurse practitioners. Pain sometimes resolves promptly once the underlying trauma or pathology has healed, and is treated by one practitioner, with drugs such as analgesics and (occasionally) anxiolytics. Effective management of long term pain, however, frequently requires the coordinated efforts of the management team.

Medicine treats injury and pathology to support and speed healing; and treats distressing symptoms such as pain to relieve suffering during treatment and healing. When a painful injury or pathology is resistant to treatment and persists, when pain persists after the injury or pathology has healed, and when medical science cannot identify the cause of pain, the task of medicine is to relieve suffering. Treatment approaches to long term pain include pharmacologic measures, such as analgesics, tricyclic antidepressants and anticonvulsants, interventional procedures, physical therapy, physical exercise, application of ice and/or heat, and psychological measures, such as biofeedback and cognitive behavioral therapy.

Medical specialties

Pain management practitioners come from all fields of medicine. Most often, pain fellowship trained physicians are anesthesiologists, neurologists, physiatrists or psychiatrists. Palliative care doctors are also specialists in pain management. Some practitioners have not been fellowship trained and have opted for certification by the American Board of Pain Medicine which is not recognized by the American Board of Medical Specialties and does not indicate fellowship training. However, the American Board of Anesthesiology and the American Board of Physical Medicine and Rehabilitation have a subspecialty in pain management which is recognized by the American Board of Medical Specialties and does indicate fellowship training. Some practitioners focus more on the pharmacologic management of the patient, while others

are very proficient at the interventional management of pain. Interventional procedures - typically used for chronic back pain - include: epidural steroid injections, facet joint injections, neurolytic blocks, spinal cord stimulators and intrathecal drug delivery system implants. Over the last several years the number of interventional procedures done for pain has grown.

As well as medical practitioners, the area of pain management may often benefit from the input of physiotherapists, chiropractors, clinical psychologists and occupational therapists, amongst others. Together the multidisciplinary team can help create a package of care suitable to the patient.

Because of the fast growth in the field of pain medicine many practitioners have entered the field, with many of these practitioners being not board certified or being certified by unrecognized boards.

Medications

The World Health Organization (WHO) recommends a *pain ladder* for managing analgesia. It was first described for use in cancer pain, but it can be used by medical professionals as a general principle when dealing with analgesia for any type of pain. In the treatment of chronic pain, whether due to malignant or benign processes, the three-step WHO Analgesic Ladder provides guidelines for selecting the kind and stepping up the amount of analgesia. The exact medications recommended will vary with the country and the individual treatment center, but the following gives an example of the WHO approach to treating chronic pain with medications. If, at any point, treatment fails to provide adequate pain relief, then the doctor and patient move onto the next step.

Mild pain

Paracetamol (acetaminophen), or a non steroidal anti-inflammatory drug such as ibuprofen.

Mild to moderate pain

Paracetamol, an NSAID and/or paracetamol in a combination product with a weak opioid such as hydrocodone used in combination, may provide greater relief than their separate use.

Moderate to severe pain

When treating moderate to severe pain, the type of the pain, acute or chronic, needs to be considered. The type of pain can result in different medications being prescribed. Certain medications may work better for acute pain, others for chronic pain, and some may work equally well on both. Acute pain medication is for rapid onset of pain such as from an inflicted trauma or to treat post-operative pain. Chronic pain medication is for alleviating long-lasting, ongoing pain.

Morphine is the gold standard to which all narcotics are compared. Fentanyl has the benefit of less histamine release and thus fewer side effects. It can also be administered via transdermal patch which is convenient for chronic pain management. Oxycodone is used across the Americas and Europe for relief of serious chronic pain; its main slow-release formula is known as OxyContin, and short-acting tablets, capsules, syrups and ampoules are available making it suitable for acute intractable pain or breakthrough pain. Diamorphine, methadone and buprenorphine are used less frequently. Pethidine, known in North America as meperidine, is not recommended for pain management due to its low potency, short duration of action, and toxicity associated with repeated use. Pentazocine, dextromoramide and dipipanone are also not recommended in new patients except for acute pain where other analgesics are not tolerated or are inappropriate, for pharmacological and misuse-related reasons. Amitriptyline is prescribed for chronic muscular pain in the arms, legs, neck and lower back. While opiates are often used in the management of chronic pain, high doses are associated with an increased risk of opioid overdose.

Opioids

Opioid medications can provide a short, intermediate or long acting analgesia depending upon the specific properties of the medication and whether it is formulated as an extended release drug. Opioid medications may be administered orally, by injection, via nasal mucosa or oral mucosa, rectally, transdermally, intravenously, epidurally and intrathecally. In chronic pain conditions that are opioid responsive a combination of a long-acting or extended release medication is often prescribed in conjunction with a shorter-acting medication for breakthrough pain, or exacerbations.

Most opioid treatment is oral (tablet, capsule or liquid), but suppositories and skin patches can be prescribed. An opioid injection is rarely needed for patients with chronic pain.

Although opioids are strong analgesics, they do not provide complete analgesia regardless of whether the pain is acute or chronic in origin. Opioids are efficacious analgesics in chronic malignant pain and modestly effective in nonmalignant pain management. However, there are associated adverse effects, especially during the commencement or change in dose. When opioids are used for prolonged periods drug tolerance, chemical dependency, diversion and addiction may occur.

Clinical guidelines for prescribing opioids for chronic pain have been issued by the American Pain Society and the American Academy of Pain Medicine. Included in these guidelines is the importance of assessing the patient for the risk of substance abuse, misuse, or addiction; a personal or family history of substance abuse is the strongest predictor of aberrant drug-taking behavior. Physicians who prescribe opioids should integrate this treatment with any psychotherapeutic intervention the patient may be receiving. The guidelines also recommend monitoring not only the pain but also the level of functioning and the achievement of therapeutic goals. The prescribing physician

should be suspicious of abuse when a patient reports a reduction in pain but has no accompanying improvement in function or progress in achieving identified goals.

Non-steroidal anti-inflammatory drugs

The other major group of analgesics are non-steroidal anti-inflammatory drugs (NSAID). Acetaminophen is not always included in this class of medications. However, acetaminophen may be administered as a single medication or in combination with other analgesics (both NSAIDs and opioids). The alternatively prescribed NSAIDs such as ketoprofen and piroxicam, have limited benefit in chronic pain disorders and with long-term use is associated with significant adverse effects. The use of selective NSAIDs designated as selective COX-2 inhibitors have significant cardiovascular and cerebrovascular risks which have limited their utilization.

Antidepressants and antiepileptic drugs

Some antidepressant and antiepileptic drugs are used in chronic pain management and act primarily within the pain pathways of the central nervous system, though peripheral mechanisms have been attributed as well. These mechanisms vary and in general are more effective in neuropathic pain disorders as well as complex regional pain syndrome. Drugs such as gabapentin have been widely prescribed for the off-label use of pain control. The list of side effects for these classes of drugs are typically much longer than opiate or NSAID treatments for chronic pain, and many antiepileptics cannot be suddenly stopped without the risk of seizure.

Other analgesics

Other drugs are often used to help analgesics combat various types of pain and parts of the overall pain experience. In addition to gabapentin, the vast majority of which is used off-label for this purpose, orphenadrine, cyclobenzaprine, trazodone and other drugs with anticholinergic properties are useful in conjunction with opioids for neuropathic pain. Orphenadrine and cyclobenzaprine are also muscle relaxants and are therefore particularly useful in painful musculoskeletal conditions. Clonidine has found use as an analgesic for this same purpose and all of the mentioned drugs potentiate the effects of opioids overall.

Procedures

Pulsed radiofrequency, neuromodulation, direct introduction of medication and nerve ablation may be used to target either the tissue structures and organ/systems responsible for persistent nociception or the nociceptors from the structures implicated as the source of chronic pain.

An intrathecal pump used to deliver very small quantities of medications directly to the spinal fluid. This is similar to epidural infusions used in labour and postoperatively. The major differences are that it is much more common for the drug to be delivered into the

spinal fluid (intrathecal) rather than epidurally, and the pump can be fully implanted under the skin. This approach allows a higher dose of the drug to be delivered directly to the site of action, with fewer systemic side effects.

A spinal cord stimulator is an implantable medical device that creates electric impulses and applies them near the dorsal surface of the spinal cord provides a paresthesia ("tingling") sensation that alters the perception of pain by the patient.

Physical approach

Physiatry

Physical medicine and rehabilitation (physiatry) employs diverse physical techniques such as thermal agents and electrotherapy, as well as therapeutic exercise and behavioral therapy, alone or in tandem with interventional techniques and conventional pharmacotherapy to treat pain, usually as part of an interdisciplinary or multidisciplinary program.

TENS

Transcutaneous electrical nerve stimulation has been found to be ineffective for lower back pain, however, it might help with diabetic neuropathy.

Acupuncture

Acupuncture involves the insertion and manipulation of needles into specific points on the body to relieve pain or for therapeutic purposes. In 2003, the World Health Organization published an article synthesizing the scientific research (controlled trials) of the time, and concluded acupuncture is helpful for the treatment of pain in some cases of acute pain in the epigastric area, facial pain, headache, knee pain, low back pain, neck pain, pain in dentistry, postoperative pain, renal colic, and sciatica. The authors also concluded acupuncture has demonstrated effectiveness in other conditions for which further proof is needed. This review has been criticized for giving too much weight to low-quality clinical trials, and including a large number of trials originating in China. The latter issue is considered problematic because trials originating in the West include a mixture of positive, negative and neutral results while all trials in China are positive (attributed to publication bias rather than fraud). An analysis of the 13 highest quality studies of pain treatment with acupuncture, published in January 2009 in the *British Medical Journal*, concluded there was little difference in the effect of real, sham and no acupuncture. There is general agreement that acupuncture is safe when administered by well-trained practitioners using sterile needles, and that further research is appropriate.

LLLT

A 2007 review concluded low level laser therapy may be effective in reducing inflammation and pain, while a 2008 Cochrane collaboration review concluded that there

was insufficient evidence to support the use of LLLT in the management of low back pain.

Psychological approach

Cognitive and behavioral therapy

Mindfulness-based cognitive therapy, the use of stress reduction and relaxation, has been found to reduce chronic pain in some patients. Applied behavior analysis views chronic pain as a consequence of both respondent and operant conditioning, where a patient learns to display pain behavior in the presence of specific environmental antecedents and consequences. The model was first proposed by Fordyce in 1976. The behavioral model has shown effectiveness in reducing pain responses though operant based interventions. Though cognitive-behavioral intervention can be an effective and economical means of treating chronic pain, the effects are rather modest and a substantial portion of patients gain no benefit.

Biofeedback

Biofeedback based on behavioral principles has shown some success for chronic pain, demonstrating greater improvement in one study than peers undergoing cognitive-behavioral therapy and conservative medical treatment, though a different study showed improvements over wait-list controls but no difference between biofeedback and cognitive-behavioral therapy.

Hypnosis

A 2007 review of 13 studies found evidence for the efficacy of hypnosis in the reduction of pain in some conditions, though the number of patients enrolled in the studies was small, bringing up issues of power to detect group differences, and most lacked credible controls for placebo and/or expectation. The authors concluded that "although the findings provide support for the general applicability of hypnosis in the treatment of chronic pain, considerably more research will be needed to fully determine the effects of hypnosis for different chronic-pain conditions." (p. 283)

Under-treatment

Inadequate treatment of pain is widespread throughout surgical wards, intensive care units, accident and emergency departments, in general practice, in the management of all forms of chronic pain including cancer pain, and in end of life care. This neglect is extended to all ages, from neonates to the frail elderly. In September 2008, the World Health Organization (WHO) estimated that approximately 80 percent of the world population has either no or insufficient access to treatment for moderate to severe pain. Every year tens of millions of people around the world, including around four million cancer patients and 0.8 million HIV/AIDS patients at the end of their lives suffer from such pain without treatment. Yet the medications to treat pain are cheap, safe, effective,

generally straightforward to administer, and international law obliges countries to make adequate pain medications available.

Reasons for deficiencies in pain management include cultural, societal, religious, and political attitudes, including acceptance of torture. Moreover, the biomedical model of disease, focused on pathophysiology rather than quality of life, reinforces entrenched attitudes that marginalize pain management as a priority. Other reasons may have to do with inadequate training, personal biases or fear of prescription drug abuse.

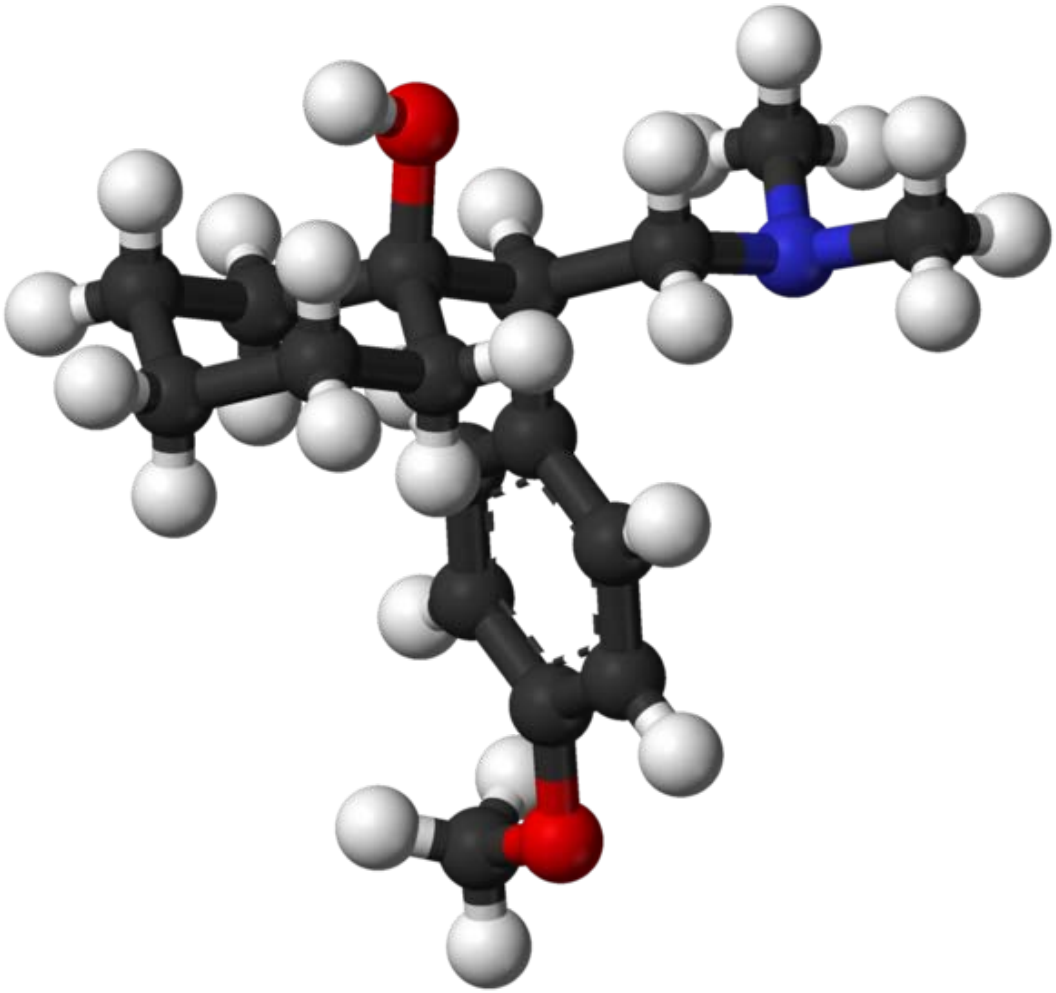
In the United States, Hispanic and African Americans are more likely to suffer needlessly in the hands of a physician than whites; and women's pain is more likely to be undertreated than men's. It is often recognized that a great number of patients suffering from chronic pain are being under-treated because physicians fail to provide comprehensive pain treatment. This failure may be due to physicians' fear of being accused of over-prescribing, despite the relative rarity of prosecutions (147 cases across USA in 2006), or physicians' poor understanding of the health risks attached to opioid prescription. As a result of two recent cases in California though, where physicians who failed to provide adequate pain relief were successfully sued for elder abuse, the North American medical and health care communities appear to be undergoing a shift in perspective. The California Medical Board publicly reprimanded the physician in the second case; the federal Center for Medicare and Medicaid Services has declared a willingness to charge with fraud health care providers who accept payment for providing adequate pain relief while failing to do so; and clinical practice guidelines and standards are evolving into clear, unambiguous statements on acceptable pain management, so health care providers, in California at least, can no longer avoid culpability by claiming that poor or no pain relief meets community standards.

Strategies currently applied for improvement in pain management include framing it as an ethical issue; promoting pain management as a legal right, providing constitutional guarantees and statutory regulations that span negligence law, criminal law, and elder abuse; defining pain management as a fundamental human right, categorizing failure to provide pain management as professional misconduct, and issuing guidelines and standards of practice by professional bodies.

Chapter 6

Antidepressant

Fluoxetine (Prozac), an SSRI



Venlafaxine, an SNRI

An **antidepressant** is a psychiatric medication used to alleviate mood disorders, such as major depression and dysthymia and anxiety disorders such as social anxiety disorder. According to Gelder, Mayou &*Geddes (2005) people with a depressive illness will experience a therapeutic effect to their mood, however this will not be experienced in healthy individuals. Drugs including the monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), tetracyclic antidepressants (TeCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) are most commonly associated with the term. These medications are among those most commonly prescribed by psychiatrists and other physicians, and their effectiveness and adverse effects are the subject of many studies and competing claims. Many drugs produce an antidepressant effect, but restrictions on their use have caused controversy and off-label prescription a risk, despite claims of superior efficacy.

The efficacy of modern thymoleptic anti-depressants has never been conclusively demonstrated to be greater than that of active placebo, according to two Cochrane Collaboration reviews. A review of all studies of anti-depressants ever submitted to the U.S. Food and Drug Administration (FDA), published and unpublished, was submitted to the FDA in 2004. In the published literature, anti-depressants had 94% success in treating depression. In the withheld literature, they had below 50% success. Combined, all studies showed 51% efficacy - only two points better than that of placebo. This increased the apparent efficacy of different anti-depressants from 11% to 69% over placebo. Possible exceptions are mirtazapine - a norepinephrine and serotonin antagonist - and venlafaxine, an SNRI with substantial similarity in chemical structure to the opioid derivative tramadol.

Opioids were used to treat major depression until the late 1950s. Amphetamines were used until the mid 1960s. Prescribing opioids or amphetamines for depression falls into a legal grey area. Research has only rarely been conducted in to the therapeutic potential of opioid derivatives for depression in the past sixty years, whereas amphetamines have found a thriving market for conditions as widely arrayed as attention deficit disorder, narcolepsy, and obesity, and continue to be studied for myriad applications. Both opioids and amphetamines induce a therapeutic response very quickly, showing results within twenty-four to forty-eight hours; the therapeutic ratios for both opioids and amphetamines are greater than those of the tricyclic anti-depressants. In some of this little, heavily restricted research, the opioid buprenorphine has shown the greatest potential for treating severe, treatment-resistant depression of any known pharmaceutical in a small study that is generally recognized and was published in 1995, but has never been pursued due to the social stigma attached to opioids in addition to that attached to mental illness in America.

Most typical antidepressants have a delayed onset of action (2–6 weeks) and are usually administered for anywhere from months to years. Despite the name, antidepressants are often used controversially, and with a dearth of empirical evidence to support their indication, off-label to treat other conditions, such as anxiety disorders, obsessive compulsive disorder, eating disorders, chronic pain, and some hormone-mediated disorders such as dysmenorrhea. Alone or together with anticonvulsants (e.g., Tegretol or Depakote), these medications can be used to treat attention-deficit hyperactivity disorder (ADHD) and substance abuse by addressing underlying depression. Also, antidepressants have been used sometimes to treat snoring and migraines.

Other medications that are not usually called antidepressants, including antipsychotics in low doses and benzodiazepines, may be used to manage depression, although benzodiazepines - along with all drugs called "anti-depressants" - cause a physical dependence to form. Stopping benzodiazepine (or SSRI) treatment abruptly can cause unpleasant withdrawal symptoms. An extract of the herb St John's Wort is commonly used as an antidepressant, although it is labeled as a dietary supplement in some countries. The term *antidepressant* is sometimes applied to any therapy (e.g., psychotherapy, electro-convulsive therapy, acupuncture) or process (e.g., sleep

disruption, increased light levels, regular exercise) found to improve a clinically depressed mood.

Inert placebos can have significant antidepressant effects, and so to establish a substance as an "antidepressant" in a clinical trial it is necessary to show superior efficacy to placebo.

History

St John's Wort

Various opiates (via the μ-opioid receptor and κ-opioid receptor) and amphetamines were commonly used as antidepressants until the mid-1950s, when they fell out of favor due to their addictive nature and side effects. Extracts from the herb St John's Wort have long been used (as a "nerve tonic") to alleviate depression.

Isoniazid and iproniazid

In 1951, two people from Sea View Hospital on Staten Island, Irving Selikoff and Edward Robitzek, began clinical trials on two new anti-tuberculosis agents from Hoffman-LaRoche, isoniazid and iproniazid. Only patients with a poor prognosis were initially treated; nevertheless, their condition improved dramatically. Selikoff and Robitzek noted "a subtle general stimulation . . . the patients exhibited renewed vigor and indeed this occasionally served to introduce disciplinary problems." The promise of a cure for tuberculosis in the Sea View Hospital trials was excitedly discussed in the

mainstream press. In 1952, learning of the stimulating side effects of isoniazid, the Cincinnati psychiatrist Max Lurie tried it on his patients. In the following year, he and Harry Salzer reported that isoniazid improved depression in two thirds of their patients and coined the term *antidepressant* to describe its action. A similar incident took place in Paris, where Jean Delay, head of psychiatry at Sainte-Anne Hospital, found out from his pulmonology colleagues at Cochin Hospital about the side effects of isoniazid. In 1952, before Lurie and Salzer, Delay, with the resident Jean-Francois Buisson, reported the positive effect of isoniazid on depressed patients. For reasons unrelated to its efficacy, isoniazid as an antidepressant was soon overshadowed by the more toxic iproniazid, although it remains a mainstay of tuberculosis treatment. The mode of antidepressant action of isoniazid is still unclear. It is speculated that its effect is due to the inhibition of diamine oxidase, coupled with a weak inhibition of monoamine oxidase A.

Another anti-tuberculosis drug tried at the same time by Selikoff and Robitzek, iproniazid, showed a greater "psychostimulant" effect, but more pronounced toxicity. After the publications on isoniazid, papers by Jackson Smith, Gordon Kamman, George Crane, and Frank Ayd appeared, describing the psychiatric applications of iproniazid. Ernst Zeller found iproniazid to be a potent monoamine oxidase inhibitor. Nevertheless, iproniazid remained relatively obscure until Nathan Kline, the influential and flamboyant head of research at Rockland State Hospital, began to popularize it in the medical and popular press as a "psychic energizer". Roche put a significant marketing effort behind iproniazid, including promoting its off-label use for depression. Its sales grew massively in the following years, until it was recalled from the market in 1961 due to cases of lethal hepatotoxicity.

Imipramine

The discovery that a tricyclic ("three ringed") compound had a significant antidepressant effect was first made in 1957 by Roland Kuhn in a Swiss psychiatric hospital. By that time antihistamine derivatives were increasingly used to treat surgical shock and then as psychiatric neuroleptics. Although in 1955 reserpine was shown to be more effective than placebo in alleviating anxious depression, neuroleptics (literally, "to seize the nerves" or "to take hold of nerves") were being developed as sedatives and antipsychotics.

Attempting to improve the effectiveness of chlorpromazine, Kuhn, in conjunction with the Geigy pharmaceutical company, discovered that compound "G 22355" (manufactured and patented in the US in 1951 by Häfliger and Schinder) had a beneficial effect in patients with depression accompanied by mental and motor retardation. Kuhn first reported his findings on what he called a "thymoleptic" (literally, "taking hold of the emotions," in contrast with neuroleptics, "taking hold of the nerves") in 1955-56. These gradually became established, resulting in marketing of the first tricyclic antidepressant, imipramine, soon followed by variants.

Later history

These new drug therapies became prescription drugs in the 1950s. It was estimated that no more than 50 to 100 people per million suffered from the kind of depression that these new drugs would treat, and pharmaceutical companies were not enthusiastic. Sales through the 1960s remained poor compared to the major tranquilizers (neuroleptics/antipsychotics) and minor tranquilizers (such as benzodiazepines), which were being marketed for different uses. Imipramine remained in common use and numerous successors were introduced. The field of MAO inhibitors remained quiet for many years until "reversible" forms affecting only the MAO-A subtype were introduced, avoiding some of the adverse effects.

Most pharmacologists by the 1960s thought the main therapeutic action of tricyclics was to inhibit norepinephrine reuptake, but it was gradually observed that this action was associated with energizing and motor stimulating effects, while some antidepressant compounds appeared to have differing effects through action on serotonin systems (notably proposed in 1969 by Carlsson and Lindqvist as well as Lapin and Oxenkrug).

Researchers began a process of rational drug design to isolate antihistamine-derived compounds that would selectively target these systems. The first such compound to be patented was zimelidine in 1971, while the first released clinically was indalpine. Fluoxetine was approved for commercial use by the Food and Drug Administration (United States) in 1988, becoming the first blockbuster SSRI. Fluoxetine was developed at Eli Lilly and Company in the early 1970s by Bryan Molloy, David Wong and others.

While it had fallen out of favor in most countries through the 19th and 20th centuries, the herb St John's Wort became increasingly popular in Germany, where Hypericum extracts were eventually licensed, packaged and prescribed by doctors. Small-scale efficacy trials were carried out in the 1970s and 1980s, and attention grew in the 1990s following a meta-analysis of these. It remained an over-the-counter drug (OTC) or supplement in most countries and research continued to investigate its neurotransmitter effects and active components, particularly hyperforin

SSRIs became known as "novel antidepressants" along with other newer drugs such as SNRIs and NRIs with various different selective effects, such as venlafaxine, duloxetine, nefazodone and mirtazapine.

Types of antidepressants

Selective serotonin reuptake inhibitors (SSRIs)

Selective serotonin reuptake inhibitors (SSRIs) are a class of antidepressants considered the current standard of drug treatment. A possible cause of depression is an inadequate amount of serotonin, a chemical used in the brain to transmit signals between neurons. SSRIs are said to work by preventing the reuptake of serotonin (also known as 5-hydroxytryptamine, or 5-HT) by the presynaptic neuron, thus maintaining higher levels

of 5-HT in the synapse. Chemists Klaus Schmiegel and Bryan Molloy of Eli Lilly discovered the first SSRI, fluoxetine. This class of drugs includes:

- Citalopram (Celexa, Cipramil)
- Escitalopram (Lexapro, Cipralex, Seroplex, Lexamil)
- Fluoxetine (Prozac, Sarafem, Symbyax)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil, Aropax)
- Sertraline (Zoloft)

These antidepressants typically have fewer adverse effects than the tricyclics or the MAOIs, although such effects as drowsiness, dry mouth, nervousness, anxiety, insomnia, decreased appetite, long-term weight gain and decreased ability to function sexually may occur. Some side effects may decrease as a person adjusts to the drug, but other side effects may be persistent. Though safer than first generation antidepressants, SSRIs may not work on as many patients as previous classes of antidepressants, suggesting the role of norepinephrine in depression is still important.

Work by two researchers has called into question the link between serotonin deficiency and symptoms of depression, noting that the efficacy of SSRIs as treatment does not in itself prove the link. Research indicates that these drugs may interact with transcription factors known as "clock genes", which may play a role in the addictive properties of drugs (drug abuse), and possibly in obesity.

A systematic review of randomized controlled trials published in the Archives of General Psychiatry showed that up to one-third of the 6-week effect of SSRI Treatment can be seen in the first week. The same study also found that patients treatment with SSRIs were 64% more likely to achieve a 50% absolute reduction in HRSD than patients given a placebo.

Serotonin-norepinephrine reuptake inhibitors (SNRIs)

Serotonin-norepinephrine reuptake inhibitors (SNRIs) are a newer form of antidepressant that work on both norepinephrine and 5-HT. They typically have similar side effects to the SSRIs, though there may be a withdrawal syndrome on discontinuation that may necessitate dosage tapering. These include:

- Desvenlafaxine (Pristiq)
- Duloxetine (Cymbalta)
- Milnacipran (Ixel)
- Venlafaxine (Effexor)

Noradrenergic and specific serotonergic antidepressants (NaSSAs)

Noradrenergic and specific serotonergic antidepressants (NaSSAs) form a newer class of antidepressants which purportedly work to increase norepinephrine (noradrenaline) and

serotonin neurotransmission by blocking presynaptic alpha-2 adrenergic receptors while at the same time blocking certain serotonin receptors. Side effects may include drowsiness, increased appetite, and weight gain. Examples include:

- Mianserin (Tolvon)
- Mirtazapine (Remeron, Avanza, Zispin)

Norepinephrine (noradrenaline) reuptake inhibitors (NRIs)

Norepinephrine (noradrenaline) reuptake inhibitors (NRIs) act via norepinephrine (also known as *noradrenaline*). NRIs are thought to have a positive effect on the concentration and motivation in particular. These include:

- Atomoxetine (Strattera)
- Mazindol (Mazanor, Sanorex)
- Reboxetine (Edronax)
- Viloxazine (Vivalan)

Norepinephrine-dopamine reuptake inhibitors (NDRIs)

Norepinephrine-dopamine reuptake inhibitors inhibit the neuronal reuptake of dopamine and norepinephrine (noradrenaline). These include:

- Bupropion (Wellbutrin, Zyban)

Selective serotonin reuptake enhancers (SSREs)

- Tianeptine (Stablon, Coaxil, Tatinol)

Norepinephrine-dopamine disinhibitors (NDDIs)

Norepinephrine-dopamine disinhibitors (NDDIs) act by antagonizing the serotonin 5-HT_{2C} receptor which normally acts to inhibit norepinephrine and dopamine release, thereby promoting outflow of these neurotransmitters.

- Agomelatine (Valdoxan, Melitor, Thymanax)

Tricyclic antidepressants (TCAs)

Tricyclic antidepressants are the oldest class of antidepressant drugs. Tricyclics block the reuptake of certain neurotransmitters such as norepinephrine (noradrenaline) and serotonin. They are used less commonly now due to the development of more selective and safer drugs. Side effects include increased heart rate, drowsiness, dry mouth, constipation, urinary retention, blurred vision, dizziness, confusion, and sexual dysfunction. Toxicity occurs at approximately ten times normal dosages; these drugs are often lethal in overdoses, as they may cause a fatal arrhythmia. However, tricyclic

antidepressants are still used because of their effectiveness, especially in severe cases of major depression. These include:

Tertiary amine tricyclic antidepressants:

- Amitriptyline (Elavil, Endep)
- Clomipramine (Anafranil)
- Doxepin (Adapin, Sinequan)
- Imipramine (Tofranil)
- Trimipramine (Surmontil)

Secondary amine tricyclic antidepressants

- Desipramine (Norpramin)
- Nortriptyline (Pamelor, Aventyl, Noritren)
- Protriptyline (Vivactil)

Monoamine oxidase inhibitor (MAOIs)

Monoamine oxidase inhibitors (MAOIs) may be used if other antidepressant medications are ineffective. MAOIs work by blocking the enzyme monoamine oxidase which breaks down the neurotransmitters dopamine, serotonin, and norepinephrine (noradrenaline). Because there are potentially fatal interactions between this class of medication and certain foods (particularly those containing tyramine), as well as certain drugs, classic MAOIs are rarely prescribed anymore. However, this does not apply to Emsam, the transdermal patch form of selegiline, which due to its bypassing of the stomach has a lesser propensity to induce such events. MAOIs can be as effective as tricyclic antidepressants, although they are generally used less frequently due to the fact that they have a higher incidence of dangerous side effects and interactions. A new generation of MAOIs has been introduced; moclobemide (Manerix), known as a reversible inhibitor of monoamine oxidase A (RIMA), acts in a more short-lived and selective manner and does not require a special diet. The MAOI group of medicines include:

- Isocarboxazid (Marplan)
- Moclobemide (Aurorix, Manerix)
- Phenelzine (Nardil)
- Selegiline (Eldepryl, Emsam)
- Tranylcypromine (Parnate)

Augmenter drugs

Some antidepressants have been found to work better in some patients when used in combination with another drug. Such "augmenter" drugs include:

- Buspirone (Buspar)
- Gepirone (Ariza)

- Nefazodone (Serzone)
- Tandospirone (Sediel)
- Trazodone (Desyrel)
- Bupropion (Wellbutrin/Zyban)

Tranquillizers and sedatives, typically the benzodiazepines, are prescribed to ease anxiety and promote sleep. Because of the high risk of dependency, these medications are intended only for short-term or occasional use. Medications are often used not for their primary functions, but to exploit what are normally side effects. Quetiapine fumarate (Seroquel) is designed primarily to treat schizophrenia and bipolar disorder, but frequently causes somnolence because of its affinity for histamine (H1 and H2) receptors, exploiting the same side effects as diphenhydramine (Benadryl).

Antipsychotics such as risperidone (Risperdal), olanzapine (Zyprexa), and quetiapine (Seroquel) are prescribed as mood stabilizers and to treat anxiety. Their use as mood stabilizers is a recent phenomenon, and controversial among some patients. Antipsychotics, whether typical or atypical, may also be prescribed to augment an antidepressant, to increase the blood concentration of another drug, or to relieve the psychotic or paranoid symptoms that often accompany clinical depression. However, they can cause serious side effects, particularly at high dosages, including blurred vision, muscle spasms, restlessness, tardive dyskinesia, and weight gain.

Psychostimulants are sometimes added to an antidepressant regimen if the patient suffers from anhedonia, hypersomnia and/or excessive eating as well as low motivation. These symptoms are common in atypical depression, and can be resolved by adding low to moderate doses of amphetamine (Adderall), methylphenidate (Ritalin) or modafinil (Provigil, Alertec), as these chemicals can enhance motivation and social behavior, and suppress appetite and sleep. Modafinil is unique in its effect on sleep: it increases alertness and reduces drowsiness while the patient is active, but does not inhibit normal sleep. These medications can also restore sexual drive, although this is a negative side effect and not a reason for the prescription of psychostimulants. Extreme caution must be used however with certain populations. Stimulants are known to trigger manic episodes in people suffering from bipolar disorder. Close supervision of those with substance abuse disorders is urged. Emotionally labile patients should avoid stimulants, as they exacerbate mood shifting.

Lithium remains the standard treatment for bipolar disorder and is often used in conjunction with other medications, depending on whether mania or depression is being treated. Lithium's potential side effects include thirst, tremors, light-headedness, nausea, and diarrhea. Some of the anticonvulsants, such as carbamazepine (Tegretol), sodium valproate (Epilim), and lamotrigine (Lamictal), are also used as mood stabilizers, particularly in bipolar disorder. Both lithium and lamotrigine have also been studied and used to augment antidepressants in treatment-resistant unipolar depression.

Herbal antidepressants

St. John's Wort is by far the most widely-used and well-studied herbal antidepressant. A number of other herbs have been used traditionally to treat depression and related ailments like anxiety, but the research on most of these treatments is sparse.

Saffron (*Crocus sativus L.*) has been found in a double-blind randomized clinical trial to be equally effective with imipramine for treating mild to moderate depression; the study also remarked that anticholinergic side effects were more frequent in the imipramine treatment group. Another 8-week double-blind randomized trial found saffron to have a similar effect to fluoxetine (Prozac) in the treatment of mild to moderate depression, including a similar remission rate and similar rate of side effects.

Lavender, *Lavandula angustifolia*, has been traditionally used to treat depression, although until recently there was little research on this plant. A 2003 double-blind, randomized clinical trial compared lavender to imipramine in the treatment of mild to moderate depression, testing both each treatments individually, and a combination of the two. Lavender was found to be less effective than imipramine, but the combination of both treatments was found to be more effective than either alone.

Several plants in the *Salvia* genus have been studied for antidepressant properties, although most of the research conducted so far has only been from mice and rat studies. Salvia elegans, also known as pineapple sage, is widely used in Mexican traditional medicine, and has been found in single study in mice to have antidepressant and antianxiety properties. Salvia sclarea, also known as clary, is known to have an antidepressant-like effect in rats, which is thought to be explained by modulation of dopamine.

Ocimum tenuiflorum, also known as Tulsi or holy basil, has been used in Ayurveda to treat anxiety and depression, and was shown in a clinical study to be effective at treating generalized anxiety disorder and depression.

Wormwood, *Artemisia absinthium*, has shown antidepressant effects in mice, similar activity to imipramine.

Nutrients and nutritional supplements as antidepressants

Nutrition has been implicated as one of the causes and risk factors for depression, and accordingly, one approach to depression involves the use of nutritional supplements or changes in diet. A study of older adults found that poor nutrition was a strong predictor of depressive symptoms a year later. A few nutrients have been studied directly for their antidepressant properties, both to treat and prevent depression, as well as related conditions such as anxiety.

Omega-3

Omega 3 fatty acids have been proposed as a treatment for depression, often suggested to be combined with other treatments. One small pilot study of childhood depression (ages 6–12) suggested that omega 3 may have therapeutic benefits for treating childhood depression. A 2005 review of the scientific literature concluded that there were several different independent lines of evidence suggesting that omega-3 fatty acids play a role in depression, and that the theory of omega-3's role in depression was biologically plausible. The evidence includes a few double-blind randomized control trials, epidemiological studies linking low fish consumption (the primary source of omega-3) to increased rates of depression, and case-control and cohort studies of unipolar and postpartum depression indicating low blood levels of omega-3 in depressed patients.

Other essential nutrients

Folic acid and Vitamin B12 have also been proposed as a treatment for depression, especially when used in conjunction with other treatments. In particular, folic acid has been shown to improve the treatment response to other antidepressants.

Prescription trends

In the United Kingdom the use of antidepressants increased by 234% in the 10 years up to 2002. In the United States a 2005 independent report stated that 11% of women and 5% of men in the non-institutionalized population (2002) take antidepressants A 1998 survey found that 67% of patients diagnosed with depression were prescribed an antidepressant. A 2007 study suggested that 25% of Americans were overdiagnosed with depression, regardless of any medical intervention. The findings were based on a national survey of 8,098 people.

A 2002 survey found that about 3.5% of all people in France were being prescribed antidepressants, compared to 1.7% in 1992, often for conditions other than depression and often not in line with authorizations or guidelines Between 1996 and 2004 in British Columbia, antidepressant use increased from 3.4% to 7.2% of the population. Data from 1992 to 2001 from the Netherlands indicated an increasing rate of prescriptions of SSRIs, and an increasing duration of treatment. Surveys indicate that antidepressant use, particularly of SSRIs, has increased rapidly in most developed countries, driven by an increased awareness of depression together with the availability and commercial promotion of new antidepressants. Antidepressants are also increasingly used worldwide for non-depressive patients as studies continue to show the potential of immunomodulatory, analgesic and anti-inflammatory properties in antidepressants.

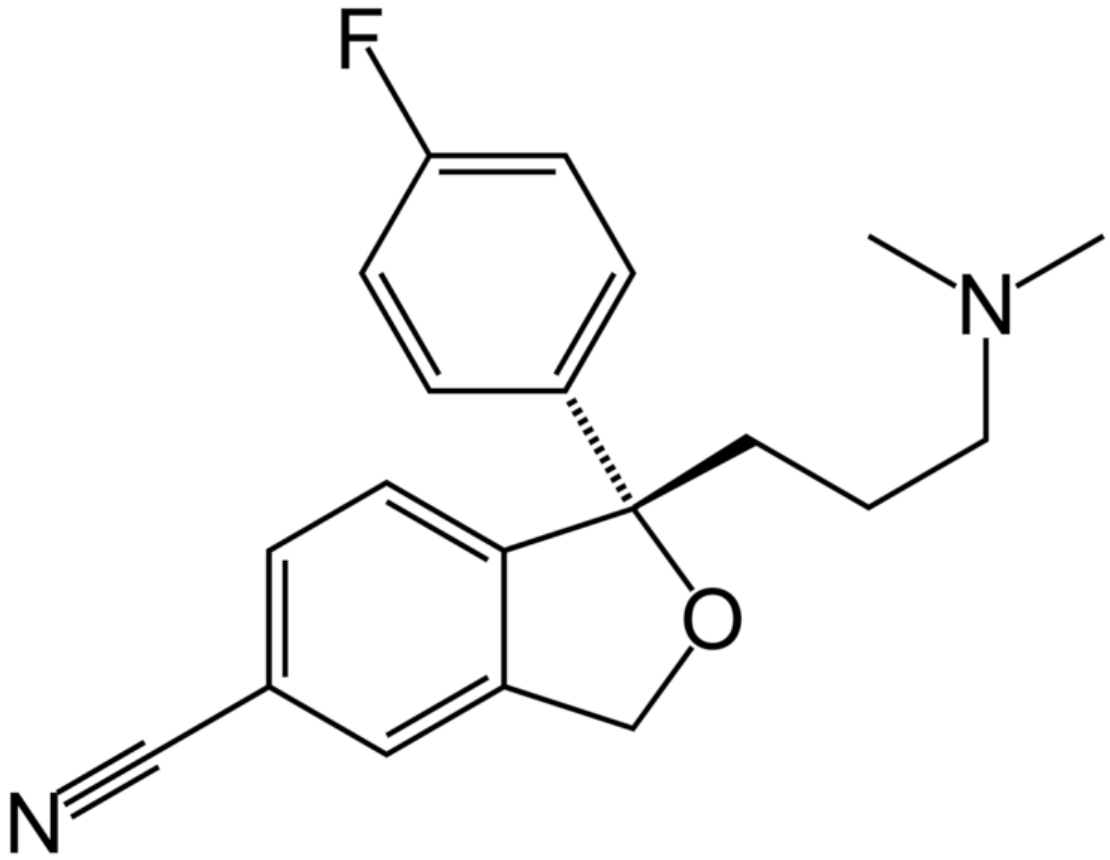
The choice of particular antidepressant is reported to be based, in the absence of research evidence of differences in efficacy, on seeking to avoid certain side effects, and taking into account comorbid (co-occurring) psychiatric disorders, specific clinical symptoms and prior treatment history.

It is also reported that, despite equivocal evidence of a significant difference in efficacy between older and newer antidepressants, clinicians perceive the newer drugs, including SSRIs and SNRIs, to be more effective than the older drugs (tricyclics and MAOIs). A survey in the UK found that male general physicians were more likely to prescribe antidepressants than female doctors.

The number of antidepressants prescribed by the NHS in the United Kingdom almost doubled during one decade, authorities reported in 2010. Furthermore the number highly increased in 2009 when 39.1 million prescriptions were issued compared with 20.1 million issued in 1999. Also, physicians issued 3.18 million more prescriptions in 2009 than in 2008. Health authorities believed the increase was partly linked to the recession. However, other reasons include a diagnosis improvement, a reduction of the stigma on mental ill-health, and more distress caused by the economic crisis. Furthermore, physicians concern is that some people who exhibit milder symptoms of depression are being prescribed drugs unnecessarily due to the lack of other options including talking therapies, counseling and cognitive behavior therapy. One more factor that may be increasing the consumption of antidepressants is the fact that these medications now are used for other conditions including social anxiety and post traumatic stress.

The use of antidepressants in the United States doubled over one decade, from 1996 to 2005. Antidepressant drugs were prescribed to 13 million in 1996 and to 27 million people by 2005. In 2008, more than 164 million prescriptions were written. During this period, patients were less likely to undergo psychotherapy.

Most commonly prescribed antidepressants



Structural formula of the SSRI escitalopram, in its free base form.

The most commonly prescribed antidepressants in the US retail market in 2007 were:

Drug	Brand	Class	2007 Prescriptions (in millions)
Sertraline	Zoloft	SSRI	29.652
Escitalopram	Lexapro	SSRI	27.023
Fluoxetine	Prozac	SSRI	22.266
Bupropion	Wellbutrin	NDRI	20.184
Paroxetine	Paxil	SSRI	18.141
Venlafaxine	Effexor	SNRI	17.200
Citalopram	Celexa	SSRI	16.246
Trazodone	Desyrel	SARI	15.473
Amitriptyline	Elavil	TCA	13.462
Duloxetine	Cymbalta	SNRI	12.551
Mirtazapine	Remeron	TeCA	5.129

Nortriptyline	Pamelor	TCA	3.105
Imipramine	Tofranil	TCA	1.524

The most commonly prescribed antidepressant in Germany is reported to be (concentrated extracts of) hypericum perforatum (St John's Wort). In the Netherlands, paroxetine, marketed as Seroxat among generic preparations, is the most prescribed antidepressant, followed by the tricyclic antidepressant amitriptyline, citalopram and venlafaxine.

Mechanisms of action

The therapeutic effects of antidepressants are believed to be caused by their effects on neurotransmitters and neurotransmission.

The Monoamine Hypothesis is a biological theory stating that depression is caused by the underactivity in the brain of monoamines, such as dopamine, serotonin, and norepinephrine. In the 1950s the monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants were accidentally discovered to be effective in the treatment of depression. These findings and other supporting evidence led Joseph Schildkraut to publish his paper called "The Catecholamine Hypothesis of Affective Disorders" in 1965. Schildkraut associated low levels of neurotransmitters with depression. Research into other mental impairments such as schizophrenia also found that too little activity of certain neurotransmitters were connected to these disorders. The hypothesis has been a major focus of research in the fields pathophysiology and pharmacotherapy for over 25 years.

Monoamine oxidase inhibitors (MAOIs) block the degradation of the monoamine neurotransmitters serotonin, norepinephrine, and dopamine by inhibiting the enzyme monoamine oxidase, leading to increased concentrations of these neurotransmitters in the brain and an increase in neurotransmission.

Tricyclic antidepressants (TCAs) prevent the reuptake of various neurotransmitters, including serotonin, norepinephrine, and to a much less extent, dopamine. Nowadays the most common antidepressants are selective serotonin reuptake inhibitors (SSRIs), which prevent the reuptake of serotonin (thereby increasing the level of active serotonin in synapses of the brain). Other novel antidepressants affect norepinephrine reuptake, or different receptors on the nerve cell.

While MAOIs, TCAs and SSRIs increase serotonin levels, others prevent serotonin from binding to 5-HT_{2A} receptors, suggesting it is too simplistic to say serotonin is a happy hormone. In fact, when the former antidepressants build up in the bloodstream and the serotonin level is increased, it is common for the patient to feel worse for the first weeks of treatment. One explanation of this is that 5-HT_{2A} receptors evolved as a saturation signal (people who use 5-HT_{2A} antagonists often gain weight), telling the animal to stop searching for food, a mate, etc., and to start looking for predators. In a threatening

situation it is beneficial for the animal not to feel hungry even if it needs to eat. Stimulation of 5-HT_{2A} receptors will achieve that. But if the threat is long lasting the animal needs to start eating and mating again - the fact that it survived shows that the threat was not so dangerous as the animal felt. So the number of 5-HT_{2A} receptors decreases through a process known as downregulation and the animal goes back to its normal behavior. This suggests that there are two ways to relieve anxiety in humans with serotonergic drugs: by blocking stimulation of 5-HT_{2A} receptors or by overstimulating them until they decrease via tolerance.

The stimulation or blocking of different receptors on a cell affects its genetic expression. Recent findings have shown that neurogenesis, and thus, changes in brain morphogenesis, mediate the effects of antidepressant drugs.

Another hypothesis is that antidepressants may have some longer-term effects due to the promotion of neurogenesis in the hippocampus, an effect found in mice. Other animal research suggests that antidepressants can affect the expression of genes in brain cells, by influencing "clock genes".

Other research suggests that delayed onset of clinical effects from antidepressants indicates involvement of adaptive changes in antidepressant effects. Rodent studies have consistently shown upregulation of the 3, 5-cyclic adenosine monophosphate (cAMP) system induced by different types of chronic but not acute antidepressant treatment, including serotonin and norepinephrine uptake inhibitors, monoamine oxidase inhibitors, tricyclic antidepressants, lithium and electroconvulsions. cAMP is synthesized from adenosine 5-triphosphate (ATP) by adenylyl cyclase and metabolized by cyclic nucleotide phosphodiesterases (PDEs). Data also suggest that antidepressants can modulate neural plasticity in longterm administration.

One theory regarding the cause of depression is that it is characterized by an overactive hypothalamic-pituitary-adrenal axis (HPA axis) that resembles the neuro-endocrine (cortisol) response to stress. These HPA axis abnormalities participate in the development of depressive symptoms, and antidepressants serve to regulate HPA axis function.

Comparison

A number of antidepressants have been compared below:

Compound	SERT	NET	DAT	H_1	M_{1-5}	α_1	α_2	5-HT_{1A}	5-HT_2	D_2
Agomelatine	?	?	?	?	?	?	?	?	270	?
Amitriptyline	4.3	35	3250	0.95	9.6	24	690	450	18	1460
Amoxapine	58	16	4310	25	1000	50	2600	?	?	?
Atomoxetine	8.9	2.03	1080	5500	2060	3800	8800	10900	940	35000+
Bupropion	45026	1389	2784	11800	35000+	4200	35000+	35000+	35000+	35000+
Buspirone	?	?	?	?	?	138	?	5.7	174	362
Butriptyline	1360	5100	3940	?	?	?	?	?	?	?

Citalopram	1.16	4070	28100	?	?	?	?	?	?	?
Clomipramine	0.28	38	2190	31	37	38	3200	?	?	?
Desipramine	17.6	0.83	3190	60	66	100	5500	6400	350	3500
Dosulepin	8.6	46	5310	?	?	?	?	?	?	?
Doxepin	68	29.5	12100	0.17	23	23.5	1270	276	27	360
Duloxetine	0.8	7.5	240	?	?	?	?	?	?	?
Etoperidone	890	20000	52000	3100	35000+	38	570	85	36	2300
Femoxetine	11	760	2050	4200	184	650	1970	2285	130	590
Fluoxetine	0.81	240	3600	5400	590	3800	13900	32400	280	12000
Fluvoxamine	0.81	240	3600	?	?	?	?	?	?	?
Imipramine	1.4	37	8500	37	46	32	3100	5800	150	620
Lofepramine	70	5.4	18000	360	67	100	2700	4600	200	2000
Maprotiline	5800	11.1	1000	2	570	90	9400	?	?	?
Mazindol	100	1.4	11	?	?	?	?	?	?	?
Mianserin	4000	71	9400	?	?	?	?	?	?	?
Milnacipran	123	200	10000+	?	?	?	?	?	?	?
Mirtazapine	1500+	1250~	1500+	1~	1000~	500~	100~	1500+	10~	1500+
Nefazodone	200	360	360	24000	11000	48	640	80	26	910
Nisoxetine	383	5.1	477	?	?	?	?	?	?	?
Nomifensine	1010	15.6	56	?	?	?	?	?	?	?
Nortriptyline	18	4.37	1140	6.3	37	55	2030	294	41	2570
Oxaprotiline	3900	4.9	4340	?	?	?	?	?	?	?
Paroxetine	0.13	40	490	22000	108	4600	17000	35000+	19000	32000
Protriptyline	19.6	1.41	2100	25	25	130	6600	?	?	?
Reboxetine	720	11	10000+	?	?	?	?	?	?	?
Sertraline	0.29	420	25	24000	630	380	4100	35000+	9900	10700
Trazodone	160	8500	7400	1100	35000+	42	320	96	25.0	35000+
Trimipramine	149	2450	3780	0.27	58	24	680	?	?	?
Venlafaxine	82	2480	7647	35000+	35000+	35000+	35000+	35000+	35000+	35000+
Viloxazine	17300	155	100000+	?	?	?	?	?	?	?
Zimelidine	152	9400	11700	?	?	?	?	?	?	?

The values above are expressed as equilibrium dissociation constants. It should be noted that less is more. SERT, NET, and DAT correspond to the abilities of the compounds to inhibit the reuptake of serotonin, norepinephrine, and dopamine, respectively. The other values correspond to their affinity for various receptors.

Anti-inflammatory and immunomodulation

Recent studies show pro-inflammatory cytokine processes take place during clinical depression, mania and bipolar disorder, and it is possible that symptoms of these conditions are attenuated by the pharmacological effect of antidepressants on the immune system.

Studies also show that the chronic secretion of stress hormones as a result of disease, including somatic infections or autoimmune syndromes, may reduce the effect of neurotransmitters or other receptors in the brain by cell-mediated pro-inflammatory pathways, thereby leading to the dysregulation of neurohormones. SSRIs, SNRIs and tricyclic antidepressants acting on serotonin, norepinephrine and dopamine receptors have been shown to be immunomodulatory and anti-inflammatory against pro-inflammatory cytokine processes, specifically on the regulation of Interferon-gamma (IFN-gamma) and Interleukin-10 (IL-10), as well as TNF-alpha and Interleukin-6 (IL-6). Antidepressants have also been shown to suppress TH1 upregulation.

Antidepressants, specifically TCAs and SNRIs (or SSRI-NRI combinations), have also shown analgesic properties.

These studies warrant investigation for antidepressants for use in both psychiatric and non-psychiatric illness and that a psycho-neuroimmunological approach may be required for optimal pharmacotherapy. Future antidepressants may be made to specifically target the immune system by either blocking the actions of pro-inflammatory cytokines or increasing the production of anti-inflammatory cytokines.

Therapeutic efficacy

There is a large amount of research evaluating the potential therapeutic effects of antidepressants, whether through efficacy studies under experimental conditions (including randomized clinical trials) or through studies of "real world" effectiveness. A sufficient *response* to a drug is often defined as at least a 50% reduction in self-reported or observed symptoms, with a *partial response* often defined as at least a 25% reduction. The term *remission* indicates a virtual elimination of depression symptoms, albeit with the risk of a *recurrence* of symptoms or complete *relapse*. Full remission or *recovery* signifies a full sustained return to a "normal" psychological state with full functioning.

There has also been a great deal of study about whether antidepressants address the underlying causes of depression. A 2002 review concluded that there was no evidence that antidepressants reduce the risk of recurrence of depression when their use is terminated. The authors of this review advocated that antidepressants be combined with therapy, and pointed to Interpersonal Psychotherapy (IPT) and Cognitive Behavioral Therapy (CBT).

Review studies

Recent clinical reviews include:

- A comparison of the relative efficacy of different classes of antidepressants in different settings and in regard to different kinds of depression
- An assessment of antidepressants compared with an "active placebo"
- An assessment of the newer types of the MAOI class
- A meta-analysis of randomized trials of St John's Wort
- A review of the use of antidepressants for childhood depression
- A review of all antidepressant trials submitted to the U.S. FDA from 1987 to 2004 has shown that around half of the trials failed to show any benefit over placebo. All but one of the successful trial results were published in scientific journals, while nearly all the unsuccessful trials were either not published or were presented in a misleadingly positive light (compared to the FDA's own evaluation of the data). This arose because whilst studies are required for medical approval, studies showing adverse findings are not necessarily required to be published or (if published) given similar prominence. As a result, while it appeared in the research literature that 94 percent of trials had positive outcomes, in the actual data submitted to the Food and Drug Administration, only 51 percent did. This publication bias inflated the apparent statistical effect of every antidepressant studied, by between 11% and 69%.
- A meta-analysis by UK, US and Canadian researchers, published in 2008, surveyed all pharmaceutical-company-sponsored drug trials on the six most widely prescribed new-generation antidepressants submitted for approval to the FDA between 1987 and 1999. The results showed, consistent with a prior metaanalysis, that the difference in efficacy between antidepressants and placebo was minimal, but that it increased from virtually no difference at moderate levels of initial depression to a relatively small difference for patients with very severe depression. The difference reached conventional criteria for clinical significance for patients at the upper end of the very severely depressed category, due to a reduction in the efficacy of placebo. The study received widespread media coverage in some countries, but was met with criticism from the professional community. Eli Lilly and Company responded by highlighting that the study did not take into account more recent studies on its product, Prozac, and that it was proud of the difference Prozac has made to millions of people. GlaxoSmithKline warned that this one study should not be used to cause unnecessary alarm and concern for patients. Wyeth pointed out that the data were good enough for FDA approval of the drugs. Two leading UK psychiatrists/pharmacologists, with financial and professional links to pharmaceutical companies, argued that short-term approval trials are not very suitable for evaluating effectiveness, that the unpublished ones are poorer quality, that the meta-analysis authors came from a "psychology background" rather than drug testing background, and that the media and "elements of the medico/scientific community" have "a down on antidepressants" and that the media does not appreciate the seriousness of

depression and blames and stigmatizes sufferers in a manner rooted in medieval religious attitudes.

- A May 7, 2002 article in The Washington Post titled "Against Depression, a Sugar Pill Is Hard to Beat" stated, "A new analysis has found that in the majority of trials conducted by drug companies in recent decades, sugar pills have done as well as—or better than—antidepressants. Companies have had to conduct numerous trials to get two that show a positive result, which is the Food and Drug Administration's minimum for approval. What's more, the sugar pills, or placebos, cause profound changes in the same areas of the brain affected by the medicines, according to research published last week... the makers of Prozac had to run five trials to obtain two that were positive, and the makers of Paxil and Zoloft had to run even more... When Leuchter compared the brain changes in patients on placebos, he was amazed to find that many of them had changes in the same parts of the brain that are thought to control important facets of mood... Once the trial was over and the patients who had been given placebos were told as much, they quickly deteriorated. People's belief in the power of antidepressants may explain why they do well on placebos..."

Clinical guidelines

The American Psychiatric Association 2000 Practice Guideline for the Treatment of Patients with Major Depressive Disorder indicates that, if preferred by the patient, antidepressant medications may be provided as an initial primary treatment for mild major depressive disorder; antidepressant medications should be provided for moderate to severe major depressive disorder unless electroconvulsive therapy is planned; and a combination of antipsychotic and antidepressant medications or electroconvulsive therapy should be used for psychotic depression. It states that efficacy is generally comparable between classes and within classes and that the initial selection will largely be based on the anticipated side effects for an individual patient, patient preference, quantity and quality of clinical trial data regarding the medication, and its cost.

The UK National Institute for Clinical Excellence (NICE) 2004 guidelines indicate that antidepressants should not be used for the initial treatment of mild depression, because the risk-benefit ratio is poor; that for moderate or severe depression an SSRI is more likely to be tolerated than a tricyclic; and that antidepressants for severe depression should be combined with a psychological treatment such as Cognitive Behavioural Therapy.

Efficacy limitations and strategies

Between 30% and 50% of individuals treated with a given antidepressant do not show a response. Even where there has been a robust response, significant continuing depression and dysfunction is common, with relapse rates 3 to 6 times higher in such cases. In addition, antidepressant drugs tend to lose efficacy over the course of treatment. A number of strategies are used in clinical practice to try to overcome these limits and variations.

"Trial and error" switching

The American Psychiatric Association 2000 Practice Guideline advises that where no response is achieved following six to eight weeks of treatment with an antidepressant, to switch to an antidepressant in the same class, then to a different class of antidepressant.

A recent meta-analysis review found wide variation in the findings of prior studies; for patients who had failed to respond to an SSRI antidepressant, between 12% and 86% showed a response to a new drug, with between 5% and 39% ending treatment due to adverse effects. The more antidepressants an individual had already tried, the less likely they were to benefit from a new antidepressant trial.

Augmentation and combination

For a partial response, the American Psychiatric Association guidelines advise adding a different kind of pharmaceutical agent to the antidepressant. Studies suggest that most patients fail to achieve remission on a given antidepressant, and augmentation strategies used in clinical practice include the use of lithium and thyroid augmentation, but there is not a good evidence base for these practices or for more novel strategies such as the use of selective dopamine agonists, sex steroids, NRI's, glucocorticoid-specific agents, or the newer anticonvulsants

A combination strategy involves adding one or more additional antidepressants, usually from different classes so as to have a diverse neurochemical effect. Although this may be used in clinical practice, there is little evidence for the relative efficacy or adverse effects of this strategy.

Long-term use

The therapeutic effects of antidepressants typically do not continue once the course of medication ends, resulting in a high rate of relapse. A recent meta-analysis of 31 placebo-controlled antidepressant trials, mostly limited to studies covering a period of one year, found that 18% of patients who had responded to an antidepressant relapsed while still taking it, compared to 41% whose antidepressant was switched for a placebo. The American Psychiatric Association guidelines advise four to five months of continuation treatment on an antidepressant following the resolution of symptoms. For patients with a history of depressive episodes, the British Association for Psychopharmacology's 2000 Guidelines for Treating Depressive Disorders with Antidepressants advise remaining on an antidepressant for at least six months and as long as five years or indefinitely.

Whether or not someone relapses after stopping an antidepressant does not appear to be related to the duration of prior treatment, however, and gradual loss of therapeutic benefit during the course also occurs. A strategy involving the use of pharmacotherapy in the treatment of the acute episode, followed by psychotherapy in its residual phase, has been suggested by some studies.

Medication failure

Approximately 30% of patients have remission of depression with medications. For patients with inadequate response, either adding sustained-release bupropion (initially 200 mg per day then increase by 100 mg up to total of 400 mg per day) or buspirone (up to 60 mg per day) for augmentation as a second drug can cause remission in approximately 30% of patients, while switching medications can achieve remission in about 25% of patients.

By pregnancy

There is uncertainty whether pregnancy contributes to medication failure, because the only report so far has drawn much controversy on itself:

In 2006, a widely reported study published in the *Journal of the American Medical Association* (*JAMA*) challenged the common assumption that hormonal changes during pregnancy protected expectant mothers against depression, finding that discontinuing anti-depressive medication during pregnancy led to more frequent relapse. The *JAMA* article did not disclose that several authors had financial ties to pharmaceutical companies making antidepressants. The *JAMA* later published a correction noting the ties and the authors maintain that the ties have no bearing on their research work. Obstetrician and perinatologist Adam Urato told the *Wall Street Journal* that patients and medical professionals need advice free of industry influence.

Withdrawal symptoms

In general, it may be impossible or very difficult to stop many antidepressant medications safely because nearly irreversible changes caused to central nervous system. These withdrawal symptoms can be reason for worsening of depression, manic or aggressive symptoms or suicide. When prescribing antidepressants, doctors don't often properly describe these withdrawal problems to patients with serious mental health problems.

If an SSRI medication is suddenly discontinued, it may produce both somatic and psychological withdrawal symptoms, a phenomenon known as "SSRI discontinuation syndrome" (Tamam & Ozpoyraz, 2002). When the decision is made to stop taking antidepressants it is common practice to "wean" off of them by slowly decreasing the dose over a period of several weeks. Most cases of discontinuation syndrome last between one and four weeks.

The selection of an antidepressant and dosage suitable for a certain case and a certain person is a lengthy and complicated process, requiring the knowledge of a professional. Certain antidepressants can initially make depression worse, can induce anxiety, or can make a patient aggressive, dysphoric or acutely suicidal. In rare cases, an antidepressant can induce a switch from depression to mania or hypomania.

Anecdotal evidence seems to show that many antidepressants can be withdrawn without major withdrawal symptoms if discontinued within the first week of treatment.

Chapter 7

Rebox Electrotherapy and Patient-Controlled Analgesia

Rebox electrotherapy

Rebox electrotherapeutic method is based on non-invasive transcutaneous application of specific electric currents to a living tissue. Main indications for using the Rebox include treatment of acute and chronic pain, immobility, musculoskeletal and neurological disorders and oedema.

Method description

Rebox electrotherapeutic rehabilitation has been clinically used in human and animal medicine since 1985. It was invented and patented by *Ing. Petr Slovak, Ph.D.*, a lecturer at Czech Technical University in Prague, CZ. The name Rebox is derived from the "Rehabilitation Box".

Rebox method is different from classic Transcutaneous Electric Nerve Stimulations (TENS) in many basic characteristics. Specific impulses (frequency 2–4 kHz, pulse width 100-300 μs) of weak electric currents (100-200 μA) are introduced transcutaneously to the affected region with a touch of a small non-invasive **treatment electrode (cathode)** while the patient holds a second **reference electrode (anode)** in a hand to complete electric circuit. The treatment electrode (active surface 1,5 mm2) is applied for 2–3 seconds in one spot, then proceeding approx. 1,5 cm to another point. About 20 points are treated per one session. Frequency of treatment sessions is individual for each patient.

Attraction of extracellular and intracellular positive ions (Na+, Ca2+, K+, H+) to the treatment electrode (cathode) leads to local changes in tissue microenvironment resulting in positive treatment effects.

Indications

Rebox electrotherapy is used by physiotherapists, rehabilitation providers, general practitioners, orthopedists, algesiologists, neurologists and sport-medicine providers. The devices are also used by patients themselves in homecare treatment. The most frequent applications include back pain, epicondylitis, sprained ankle, torticollis, knee ligament damage and other.

Acute and chronic pain

One of the main causes of pain is local acidosis due to inflammation and ischemic processes. Rebox is effective in immediate pain relief by correction of local acidosis (phenomena called *Transcutaneous Correction of Local Acidosis - TCLA*).

Immobility and hypertonia

Local changes in calcium ions (Ca2+) concentrations cause myorelaxation (decrease of muscular hypertonia and spasm) and significant improvement in range of motion.

Oedema

Rebox currents improve circulation of blood and lymphatic fluid (mainly due to Na+ movement) leading to antioedematous effect in affected area.

Neurological disorders

Rebox therapy is used in rehabilitation of after-stroke conditions, Multiple Sclerosis, phantom pain, Parkinson disease and other.

Healing processes

The method facilitates healing processes, this effect is mostly visible in wounds after surgery.

Diagnostic value

Tissue electric microcharacteristics can be visualized by the Rebox devices. The physiological curve differs from pathological situations and is specific for variety of disorders. This diagnostic value is helpful for monitoring of effectiveness and progress of treatment.

Patient-controlled analgesia

A patient-controlled analgesia infusion pump, configured for epidural administration of fentanyl and bupivacaine for postoperative analgesia

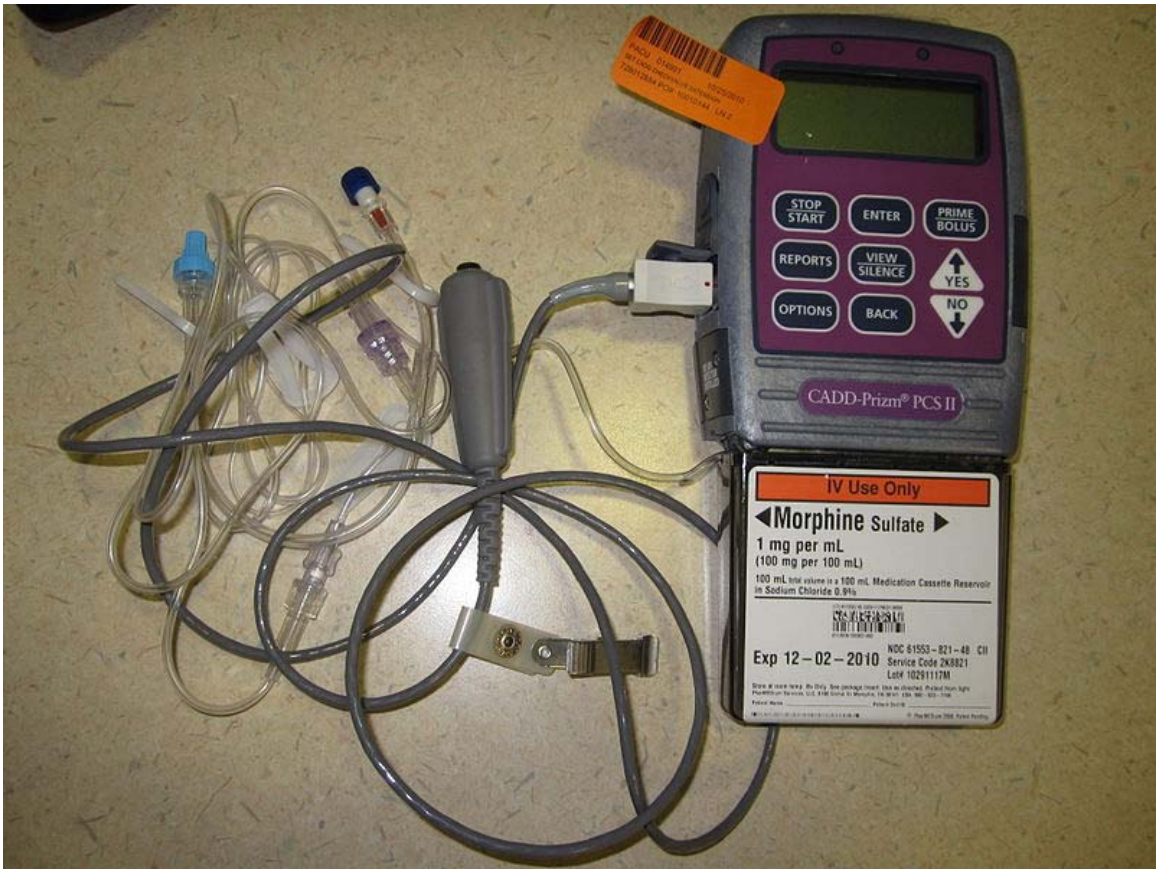
Patient-controlled analgesia (**PCA**) is any method of allowing a person in pain to administer their own pain relief. The infusion is programmable by the prescriber. If it is programmed and functioning as intended, the machine is unlikely to deliver an overdose of medication.

Routes of administration

Oral

The most common form of patient-controlled analgesia is self-administration of oral over-the-counter or prescription painkillers. For example, if a headache does not resolve with a small dose of an oral analgesic, more may be taken. As pain is a combination of tissue damage and emotional state, being in control means reducing the emotional component of pain.

Intravenous



A patient-controlled analgesia infusion pump, configured for intravenous administration of morphine for postoperative analgesia

In a hospital setting, a PCA refers to an electronically controlled infusion pump that delivers an amount of intravenous analgesic (usually an opioid) that is set by the patient. PCA can be used for both acute and chronic pain patients. It is commonly used for post-operative pain management, and for end-stage cancer patients.

Narcotics are the most common analgesics administered through PCAs. It is important for caregivers to monitor patients for the first two to twenty four hours to ensure they are using the device properly.

Epidural

Patient-controlled epidural analgesia (PCEA) is a related term describing the patient-controlled administration of analgesic medicine in the epidural space, by way of intermittent boluses or infusion pumps. This can be used by women in labour, terminally ill cancer patients or to manage post-operative pain.

Inhaled

In 1968, Robert Wexler of Abbott Laboratories developed the Analgizer, a disposable inhaler that allowed the self-administration of methoxyflurane vapor in air for analgesia. The Analgizer consisted of a polyethylene cylinder 5 inches in length and 1 inch in diameter with a 1 inch long mouthpiece. The device contained a rolled wick of polypropylene felt which held 15 milliliters of methoxyflurane. Because of the simplicity of the Analgizer and the pharmacological characteristics of methoxyflurane, it was easy for patients to self-administer the drug and rapidly achieve a level of conscious analgesia which could be maintained and adjusted as necessary over a period of time lasting from a few minutes to several hours. The 15 milliliter supply of methoxyflurane would typically last for two to three hours, during which time the user would often be partly amnesic to the sense of pain; the device could be refilled if necessary. The Analgizer was found to be safe, effective, and simple to administer in obstetric patients during childbirth, as well as for patients with bone fractures and joint dislocations, and for dressing changes on burn patients. When used for labor analgesia, the Analgizer allows labor to progress normally and with no apparent adverse effect on Apgar scores. All vital signs remain normal in obstetric patients, newborns, and injured patients. The Analgizer was widely utilized for analgesia and sedation until the early 1970s, in a manner that foreshadowed the patient-controlled analgesia infusion pumps of today. The Analgizer inhaler was withdrawn in 1974, but use of methoxyflurane as a sedative and analgesic continues in Australia and New Zealand in the form of the Penthrox inhaler.

Transcutaneous

Transcutaneous delivery systems, including iontophoretic systems, are available. These are popular for administration of opioids such as fentanyl, or local anesthetics such as lidocaine. Iontocaine is one example of such a system.

Advantages and disadvantages

Advantages of the use of Patient Controlled Analgesia include the lack of waiting time for patients requiring pain medication before a caregiver can increase the dosage of medication. In this way, the patient spends less time in pain and as a corollary to this, patients tend to use less medication than in cases in which medication is given according to a set schedule. Disadvantages include the possibility that the button can accidentally pressed, delivering an unneeded increase in the dosage of the medication. Many newer systems have mechanisms to prevent this. Also, if a PCA device is not programed properly for a patient it can result in an under-dose or overdose in a medicine.

History

The PCA pump was developed and introduced by Philip H. Sechzer in the late 1960s and described in 1971.

Chapter 8

Physical Therapy

Physical therapy

This physical therapist from the 1950s is assisting two children with polio to train their standing skills with help from calipers and rails, and use of a ball game.

Physical therapy (or **physiotherapy**), often abbreviated **PT**, is the art and science of physical care and rehabilitation. It is a primary care health profession, with **physical therapists** (or **physiotherapists**) providing services to individuals and populations to develop, maintain and restore maximum movement and functional ability throughout the

lifespan. This includes providing services in circumstances where movement and function are threatened by aging, injury, disease or environmental factors. Functional movement is central to what it means to be healthy.

Physical therapy is concerned with identifying and maximising quality of life and movement potential within the spheres of promotion, prevention, treatment/intervention, habilitation and rehabilitation. This encompasses physical, psychological, emotional, and social well being. Physical therapy involves the interaction between physical therapist, patients/clients, other health professionals, families, care givers, and communities in a process where movement potential is assessed and goals are agreed upon, using knowledge and skills unique to physical therapists. Physical therapy is performed by a physical therapist (PT) or physiotherapist (physio), and sometimes services are provided by an assistant (PTA) acting under their direction.

It involves the interaction between a physical therapist (PT) or physiotherapist (physio), patients/clients, other health professionals, families, care givers, and communities in a process where movement potential is assessed and goals are agreed upon, using knowledge and skills unique to physical therapists.

PTs use an individual's history and physical examination to arrive at a diagnosis and establish a management plan and, when necessary, incorporate the results of laboratory and imaging studies. Electrodiagnostic testing (e.g., electromyograms and nerve conduction velocity testing) may also be of assistance. PT management commonly includes prescription of or assistance with specific exercises, manual therapy, education and other interventions.

Physical therapy has many specialties including cardiopulmonary, geriatrics, neurologic, orthopaedic and pediatrics, to name some of the more common areas. PTs practice in many settings, such as outpatient clinics or offices, inpatient rehabilitation facilities, skilled nursing facilities, extended care facilities, private homes, education and research centers, schools, hospices, industrial workplaces or other occupational environments, fitness centers and sports training facilities.

Physical therapists also practice in non-patient care roles such as health policy, health insurance, health care administration and as health care executives. Physical therapists are involved in the medical-legal field serving as experts, performing peer review and independent medical examinations.

Education qualifications vary greatly by country. The span of education ranges from some countries having little formal education to others requiring masters or doctoral degrees.

History

Physicians like Hippocrates and later Galenus are believed to have been the first practitioners of physical therapy, advocating massage, manual therapy techniques and

hydrotherapy to treat people in 460 B.C. After the development of orthopedics in the eighteenth century, machines like the Gymnasticon were developed to treat gout and similar diseases by systematic exercise of the joints, similar to later developments in physical therapy.

The earliest documented origins of actual physical therapy as a professional group date back to Per Henrik Ling, “Father of Swedish Gymnastics,” who founded the Royal Central Institute of Gymnastics (RCIG) in 1813 for massage, manipulation, and exercise. The Swedish word for physical therapist is “sjukgymnast” = “sick-gymnast.” In 1887, PTs were given official registration by Sweden’s National Board of Health and Welfare.

Other countries soon followed. In 1894 four nurses in Great Britain formed the Chartered Society of Physiotherapy. The School of Physiotherapy at the University of Otago in New Zealand in 1913, and the United States' 1914 Reed College in Portland, Oregon, which graduated "reconstruction aides."

Modern physical therapy was established in Britain towards the end of the 19th century. Soon following American orthopedic surgeons began treating children with disabilities and began employing women trained in physical education, massage, and remedial exercise. These treatments were applied and promoted further during the Polio outbreak of 1916. During the First World War women were recruited to work with and restore physical function to injured soldiers, and the field of physical therapy was institutionalized. In 1918 the term "Reconstruction Aide" was used to refer to individuals practicing physical therapy. The first school of physical therapy was established at Walter Reed Army Hospital in Washtington D.C. following the outbreak of World War I.

Research catalyzed the physical therapy movement. The first physical therapy research was published in the United States in March 1921 in "The PT Review." In the same year, Mary McMillan organized the Physical Therapy Association (now called the American Physical Therapy Association (APTA). In 1924, the Georgia Warm Springs Foundation promoted the field by touting physical therapy as a treatment for polio.

Treatment through the 1940s primarily consisted of exercise, massage, and traction. Manipulative procedures to the spine and extremity joints began to be practiced, especially in the British Commonwealth countries, in the early 1950s. Later that decade, physical therapists started to move beyond hospital-based practice to outpatient orthopedic clinics, public schools, colleges/universities, geriatric settings (skilled nursing facilities), rehabilitation centers and medical centers.

In 1921 in the United States physical therapists formed the first professional association called the American Women's Physical Therapeutic Association. This gave birth to what is known today as the APTA (American Physical Therapy Association), and currently represents approximately 76,000 members throughout the United States. The APTA defines physical therapy as: "clinical applications in the restoration, maintenance, and promotion of optimal physical function."

Specialization for physical therapy in the U.S. occurred in 1974, with the Orthopaedic Section of the APTA being formed for those physical therapists specializing in orthopaedics. In the same year, the International Federation of Orthopaedic Manipulative Physical Therapists was formed, which has ever since played an important role in advancing manual therapy worldwide.

Education

World Confederation of Physical Therapy (WCPT) recognises there is considerable diversity in the social, economic, cultural, and political environments in which physical therapist education is conducted throughout the world. WCPT recommends physical therapist entry-level educational programs be based on university or university-level studies, of a minimum of four years, independently validated and accredited as being at a standard that accords graduates full statutory and professional recognition. WCPT acknowledges there is innovation and variation in program delivery and in entry-level qualifications, including first university degrees (Bachelors/Baccalaureate/Licensed or equivalent), Masters and Doctorate entry qualifications. What is expected is that any program should deliver a curriculum that will enable physical therapists to attain the knowledge, skills, and attributes described in these guidelines.

Professional education prepares physical therapists to be autonomous practitioners, that may work in collaboration with other members of the health care team.

Physical therapist entry-level educational programs integrate theory, evidence and practice along a continuum of learning. This begins with admission to an accredited physical therapy program and ending with retirement from active practice.

206 of 213 accredited physical therapy programs in the US are accredited at the doctoral level offering the Doctor of Physical Therapy degree (DPT)

Areas of study covered in a Doctor of Physical Therapy include: Basic Evaluation Techniques, Physical Agents, Biomechanics, Extremity and Spinal Orthopedics, Cardiopulmonary Physical Therapy, Women's Health, Anatomy, Neuroanatomy, Neuro Physical Therapy, Geriatrics, Pediatrics, Ethical and Legal Issues, Psychosocial Issues, and Business Management.

Students completing a Doctor of Physical Therapy program are also required to successfully complete clinical rotations prior to graduation.

Specialty areas

Because the body of knowledge of physical therapy is quite large, some PTs specialize in a specific clinical area. While there are many different types of physical therapy, the American Board of Physical Therapy Specialties list eight specialist certifications, including Sports Physical Therapy and Clinical Electrophysiology. Worldwide the six most common specialty areas in physical therapy are:

Cardiopulmonary

Cardiovascular and pulmonary rehabilitation physical therapists treat a wide variety of individuals with cardiopulmonary disorders or those who have had cardiac or pulmonary surgery. Primary goals of this specialty include increasing endurance and functional independence. Manual therapy is used in this field to assist in clearing lung secretions experienced with cystic fibrosis. Disorders, including heart attacks, post coronary bypass surgery, chronic obstructive pulmonary disease, and pulmonary fibrosis, treatments can benefit from cardiovascular and pulmonary specialized physical therapists.

Geriatric

Geriatric physical therapy covers a wide area of issues concerning people as they go through normal adult aging but is usually focused on the older adult. There are many conditions that affect many people as they grow older and include but are not limited to the following: arthritis, osteoporosis, cancer, Alzheimer's disease, hip and joint replacement, balance disorders, incontinence, etc. Geriatric physical therapists specialize in treating older adults.

Neurological

Neurological physical therapy is a field focused on working with individuals who have a neurological disorder or disease. These include Alzheimer's disease, Charcot-Marie-Tooth disease (CMT), ALS, brain injury, cerebral palsy, multiple sclerosis, Parkinson's disease, spinal cord injury, and stroke. Common impairments associated with neurologic conditions include impairments of vision, balance, ambulation, activities of daily living, movement, muscle strength and loss of functional independence.

Orthopedic

Orthopedic physical therapists diagnose, manage, and treat disorders and injuries of the musculoskeletal system including rehabilitation after orthopaedic surgery. This specialty of physical therapy is most often found in the out-patient clinical setting. Orthopedic therapists are trained in the treatment of post-operative orthopedic procedures, fractures, acute sports injuries, arthritis, sprains, strains, back and neck pain, spinal conditions and amputations.

Joint and spine mobilization/manipulation, therapeutic exercise, neuromuscular reeducation, hot/cold packs, and electrical muscle stimulation (e.g., cryotherapy, iontophoresis, electrotherapy) are modalities often used to expedite recovery in the orthopedic setting. Additionally, an emerging adjunct to diagnosis and treatment is the use of sonography for diagnosis and to guide treatments such as muscle retraining. Those who have suffered injury or disease affecting the muscles, bones, ligaments, or tendons such as ulnar collateral ligament of elbow joint will benefit from assessment by a physical therapist specialized in orthopedics.

Pediatric

Pediatric physical therapy assists in early detection of health problems and uses a wide variety of modalities to treat disorders in the pediatric population. These therapists are specialized in the diagnosis, treatment, and management of infants, children, and adolescents with a variety of congenital, developmental, neuromuscular, skeletal, or acquired disorders/diseases. Treatments focus on improving gross and fine motor skills, balance and coordination, strength and endurance as well as cognitive and sensory processing/integration. Children with developmental delays, cerebral palsy, spina bifida, or torticollis may be treated by pediatric physical therapists.

Integumentary

Integumentary (treatment of conditions involving the skin and related organs). Common conditions managed include wounds and burns. Physical therapists utilize surgical instruments, mechanical lavage, dressings and topical agents to debride necrotic tissue and promote tissue healing. Other commonly used interventions include exercise, edema control, splinting, and compression garments.

Womens Health

Womens Health physical therapy addresses womens issues related to child birth, and post partum. These conditions include lymphedema, osteoporosis, pelvic pain, prenatal & post partum periods, and urinary incontinence.

Chapter 9

Occupational Therapy

Occupational therapy promotes health by enabling people to perform meaningful and purposeful occupations. Occupation can be defined as "active process of living: from the beginning to the end of life, ... occupations are all the active processes of looking after ourselves and others, enjoying life, and being socially and economically productive over the lifespan and in various contexts" These include (but are not limited to) work, leisure, self care, domestic and community activities. Occupational therapists work with individuals, families, groups, communities and organizations to facilitate health, well-being and justice through engagement in occupation. Occupational therapists are becoming increasingly involved in addressing the impact of social, political and environmental factors that contribute to exclusion and occupational deprivation.

The World Federation of Occupational Therapists provides the following definition of Occupational Therapy: "Occupational therapy is as a profession concerned with promoting health and well being through occupation. The primary goal of occupational therapy is to enable people to participate in the activities of everyday life. Occupational therapists achieve this outcome by enabling people to do things that will enhance their ability to participate or by modifying the environment to better support participation." Occupational therapists use careful analysis of physical, environmental, psychosocial, mental, spiritual, political and cultural factors to identify barriers to occupation. Occupational therapy draws from the fields of medicine, psychology, sociology, anthropology, and many other disciplines in developing its knowledge base. A new discipline of occupational science has been developed to enhance the evidence base of the profession.

History of occupational therapy

The earliest evidence of using occupations as a method of therapy can be found in ancient times. In c. 100 BCE, Greek physician Asclepiades initiated humane treatment of patients with mental illness using therapeutic baths, massage, exercise, and music. Later, the Roman Celsus prescribed music, travel, conversation and exercise to his patients. However by medieval times the concept of humane treatment of people considered to be insane was rare, if not nonexistent.

In 18th century Europe, revolutionaries such as Philippe Pinel and Johann Christian Reil reformed the hospital system. Instead of the use of metal chains and restraint, their institutions utilized rigorous work and leisure activities in the late 18th century. Although it was thriving abroad, interest in the reform movement waxed and waned in the United States throughout the 19th century. At the turn of the 20th century, as physicians became increasingly interested in chronic disease, enthusiasm for the reform of the mental healthcare system was revived in the United States through work therapy .

The health profession of occupational therapy was conceived in the early 1910s. The focus was on promoting health in "invalids." Early professionals merged highly valued ideals, such as having a strong work ethic and the importance of crafting with one's own hands with scientific and medical principles. Early opponents of this view considered wood carving and crafting by ill patients trivial.

The emergence of occupational therapy challenged the views of mainstream scientific medicine. Instead of focusing on purely physical etiologies, they argued that a complex combination of social, economic, and biological reasons cause dysfunction. Principles and techniques were borrowed from many disciplines—including but not limited to nursing, psychiatry, rehabilitation, self-help, orthopedics, and social work—to enrich the profession's scope. Between 1900 and 1930, the founders defined the realm of practice and developed theories of practice. In a short 20-year span, they successfully convinced the public and medical world of the value of occupational therapy and established standards for the profession.

A substantial lack of primary sources of information has left today's occupational therapists with many questions concerning the founders of the field. Information is collected from early training institutions and hospitals, professional writings of practitioners, World War I records from government agencies, newspaper articles, and personal testimonials.

World War I forced the new profession to clarify its role in the medical domain and to standardize training and practice. In addition to clarifying its public image, OT also established clinics, workshops, and training schools nationwide. Due to the overwhelming number of wartime injuries, "reconstruction aides" (an umbrella term for physical therapists and occupational therapists) were recruited by the Surgeon General. Between 1917 and 1920, nearly 148,000 wounded men were placed in hospitals upon their return to the states. This number does not account for those wounded abroad. The success of the reconstruction aides, largely made up of women trying to "do their bit" to help with the war effort, was a great accomplishment. Post-war, however, there was a struggle to keep people in the profession. Emphasis was shifted from the altruistic war-time mentality to the financial, professional, and personal satisfaction that comes with being a therapist. To make the profession more appealing, practice was standardized, as was the curriculum. Entry and exit criteria were established, and AOTA advocated for steady employment, decent wages, and fair working conditions. Via these methods, occupational therapy sought and obtained medical legitimacy in the 1920s.

Occupational therapy. Toy making in psychiatric hospital. World War 1 era.

Evolution of the philosophy of occupational therapy

The philosophy of occupational therapy has evolved over the history of the profession. The philosophy articulated by the founders have owed much to the ideals of romanticism , pragmatism and humanism which are collectively considered the fundamental ideologies of the past century.

One of the most widely cited early papers about the philosophy of occupational therapy was presented by Adolf Meyer, a psychiatrist who had emigrated to the United States from Switzerland in the late 19th Century and who was invited to present his views to a gathering of the new occupational therapy society in 1922. At the time, Dr. Meyer was one of the leading psychiatrists in the United States and head of the new psychiatry department and Phipps Clinic at Johns Hopkins University in Baltimore, Maryland..

William Rush Dunton, a supporter of the National Society for the Promotion of Occupational Therapy, now the American Occupational Therapy Association, sought to promote the ideas that occupation is a basic human need, and that occupation was therapeutic. From his statements, came some of the basic assumptions of occupational therapy, which include:

- Occupation has an effect on health and well-being.

- Occupation creates structure and organizes time.
- Occupation brings meaning to life, culturally and personally.
- Occupations are individual. People value different occupations.

These have been elaborated over time in order to form the values which underpin the Codes of Ethics issued by each national association. However, the relevance of occupation to health and well-being remains the central theme. Influenced by criticism from medicine and the multitude of physical disabilities resulting from World War II , occupational therapy adopted a more reductionistic philosophy for a time. While this approach lead to developments in technical knowledge about occupational performance, clinicians became increasingly disillusioned and re-considered these beliefs. As a result, client centeredness and occupation are re-emerging as dominant themes in the profession, perhaps indicating growing maturity and self confidence. Over the past century, the underlying philosophy of occupational therapy has evolved from being a diversion from illness, to treatment, to enablement through meaningful occupation. This became evident through the development and widespread adoption of the Canadian Model of Occupational Performance.

The two most commonly mentioned values are that occupation is essential for health and the concept of holism. However, there have been some dissenting voices. Mocellin in particular advocated abandoning the notion of health through occupation as obsolete in the modern world and questioned the appropriateness of advocating holism when practice rarely supports it. The values formulated by the American Occupational Therapy Association have also been critiqued as being therapist centred and not reflecting the modern reality of multicultural practice.

Central to the philosophy of occupational therapy is the concept of occupational performance. In considering occupational performance the therapist must consider the many factors which comprise overall performance. This concept is made more tangible using models such as the person-environment-occupation model proposed by Law et al. (1996). This approach highlights the importance of satisfactions in one's occupations, broadening the aim of occupational therapy beyond the mere completion of tasks to the holistic achievement of personal wellbeing.

In recent times occupational therapists have challenged themselves to think more broadly about the potential scope of the profession, and expanded it to include working with groups experiencing occupational deprivation which stems from sources other than disability. Examples of new and emerging practice areas would include therapists working with refugees, and with people experiencing homelessness

The expanded version of the Canadian Model of Occupational Performance and Engagement (CMOP-E) encourages occupational therapists to think beyond just occupational performance and address other modes of occupational interaction such as occupational deprivation, competence, and justice. The broader notion of occupational engagement encompasses all that we do to become occupied and is congruent with how occupational therapists address issues of occupational enablement today.

Enabling occupation

Best practice in occupational therapy seeks to offer effective, client-centred services that enable people to engage in occupations of life. The Canadian Model of Client Centered Enablement (CMCE) embraces occupational enablement as the core competency of occupational therapy and the Canadian Practice Process Framework (CPPF) as the core process of occupational enablement.

Occupational therapy process

An Occupational Therapist works systematically through a sequence of actions known as the occupational therapy process. There are several versions of this process as described by numerous writers. Creek has sought to provide a comprehensive version based on extensive research. This version has 11 stages, which for the experienced therapist may not be linear in nature. The stages are:

- Referral
- Information gathering
- Initial assessment
- Needs identification/problem formation
- Goal setting
- Action planning
- Action
- Ongoing assessment and revision of action
- Outcome and outcome measurement
- End of intervention or discharge
- Review

Another process framework for occupational therapists to use is the Canadian Practice Process Framework (CPPF), which portrays eight action points and three contextual elements for the process of occupation-based, client-centred enablement. The contextual elements are:

- societal context
- practice context
- frame(s) of reference

The eight action points include:

- enter/initiate
- set the stage
- assess/evaluate
- agree on objectives and plan
- implement plan
- monitor/modify
- evaluate outcome

- conclude/exit

Fearing, Law, and Clark suggested a 7 stage process which includes:

- identifying of occupational performance issues
- choosing a theoretical frame of reference
- assessing factors contributing the identified occupational performance issue(s)
- considering the strengths and resources of both client and therapist
- negotiating targeted outcomes and developing an action plan
- implementing the plan through occupation
- evaluating outcomes

A central element of this process model is the focus on identifying both client and therapists strengths and resources prior to beginning to develop the outcomes and action plan.

Areas of practice in occupational therapy

The role of Occupational Therapy allows OT's to work in many different settings, work with many different populations and acquire many different specialties. This broad spectrum of practice lends itself to difficulty categorizing the areas of practice that exist, especially considering the many countries and different healthcare systems. Here, the categorization from the American Occupational Therapy Association is used. However, there are other ways to categorize areas of practice in OT, such as physical, mental, and community practice (AOTA, 2009). These divisions occur when the setting is defined by the population it serves. For example, acute physical or mental health settings (e.g.: hospitals), sub-acute settings (e.g.: aged care facilities), outpatient clinics and community settings.

In each area of practice below, an OT can work with different populations, diagnosis, specialities, and in different settings.

Physical health

Occupational therapy during WWI: bedridden wounded are knitting.

- Pediatrics - Schools, Community, inpatient hospital based child OT: Often, children need OT services for the same reasons an adult needs OT services. However, OTs approach intervention in a different way with children. OT delivers approaches treatment through occupation, and the occupations of a child are different from those of an adult, and include play, chores, self-care and schoolwork. Common conditions that are specific to or more common in the pediatric population creating a need for OT services include: developmental disorders, sensory regulation or sensory processing deficits, fine motor developmental delays or deficits, autism, emotional and behavioral disturbances (Lambert, 2005), among others. In addition, children are seen for every injury, illness or chronic condition that may cause a person of any age to have performance deficits in their daily life and thus benefit from OT services. Often, OT in pediatrics deals with the implications that certain medical conditions have for classroom learning and the remediation and strategies required. They need to be closely interwoven with existing teaching approaches to help the student achieve his or her educational potential.
- Acute care hospitals: Acute care is an inpatient hospital setting for individuals with a serious medical condition(s) usually due to a traumatic event, such as a traumatic brain injury, spinal cord injury, etc. The primary goal of acute care is to stabilize the patient's medical status and address any threats to his or her life and loss of function. Occupational therapy plays an important role in facilitating early

mobilization, restoring function, preventing further decline, and coordinating care, including transition and discharge planning. Furthermore, occupational therapy's role focuses on addressing deficits and barriers that limit the patient's ability to perform activities that they need or want to do related to independence in self-care, home management, work-related tasks, and participating in leisure and community pursuits.

- Inpatient rehabilitation (e.g., Spinal Cord Injuries):People with disabilities have the right and the privilege to live meaningful purposeful lives. When a disability occurs it is sometimes possible to recover – when it is not it is important to learn the skills to adapt capacity and environmental supports to be able to participate. OTs use their knowledge to help both with recovery and adaptation.
- Rehabilitation centers (e.g., Traumatic Brain Injury (TBI), Stroke (CVA), Spinal Cord Injuries, Head Injuries)
- Skilled nursing facilities: An occupational therapists role in a skilled nursing facility is centered on each client's individual needs. Many of the skills an OT works on are known as activities of daily living or self-care such as feeding or dressing. OTs can provide equipment to assist with activities or offer expertise in modifying the environment to maximize independence and facilitate independence. Other OT roles include education in adaptive equipment (shower bench), energy conservation, or task simplification (Hofmann, 2008).
- Home Health: Occupational therapists who work in this area of practice generally work with client's in the geriatric population who have one or more of the following diagnoses: Alzheimer's disease, arthritis, depression, CVA, generalized weakness, COPD, or Parkinson's disease. Occupational therapists working with these client's evaluate their level of independence, cognition, and safety. Moreover, occupational therapists provide intervention to maximize independence and function through remedial and compensatory strategies, with the ultimate goal of the client's regaining the ability to live independently at home (Swanson Anderson & Malaski, 1999).
- Outpatient clinics (e.g., Hand Therapy, orthopaedics) Hand therapy is a specialty practice area of occupational therapy that is mainly concerned with treating orthopedic-based upper extremity conditions to optimize the functional use of the hand and arm. Diagnoses seen by this practice area include: fractures of the hand or arm, lacerations and amputations, burns, and surgical repairs of tendons and nerves. Additionally, hand therapists treat acquired conditions such as tendonitis, rheumatoid arthritis and osteoarthritis, and carpal tunnel syndrome. Occupational therapists who work in this field address biomechanical issues underlying upper-extremity conditions. In addition, occupational therapists use an occupation-based and client-centered approach by identifying participation needs of the client, then tailoring intervention to improve performance in desired activities. (link for a picture of hand therapy)
- Specialist assessment centres (e.g., Electronic assistive technology, Posture and Mobility services)
- Hospices: An occupational therapists common role in hospice care is modifying and preventing. Modifying the demands of the activity to fit with the abilities of the client. The intervention may be directly with the client or with the client and

the client's caregivers. OT can offer the caregivers support an education. Progress is defined as improved quality of life in hospice care. (Hasselkaus, 1998)

- Assisted Living Facilities: In an assisted living facility OT services are provided by a home health agency, rehab agency, or a private practice. Medicare and some private insurance plans cover OT services in ALFs. Areas of treatment intervention often include: bathing, dressing, grooming, toileting, mobility, money management, laundry, and community participation. Can treat persons with occupational performance decline or at risk for a decline. Increase quality of life so less residents need the services of a long-term SNF. Special areas include mobility device assessment (scooter), continence training, psychosocial needs and low vision programs (Fagan, 2001).
- Productive Aging: An OT practicing in this area would provide skills and services to older adults to maximize independence, participation, and quality of life. Typical issues addressed: Any impairment or condition that would limit their ability to carry out meaningful occupations and tasks that are necessary for daily life. Skills taught include: energy conservation, education in adaptive equipment (such as a shower bench), task simplification, adapting and modifying activities to progress with a client's changing abilities (Opp Hoffman, 2008), caregiver education and support (AOTA, 2004), safety, social interactions and communication, memory skills training, mobility device assessment and training (i.e. scooters, wheelchairs, walkers), low vision interventions, continence training, and facilitating performance in basic ADL and IADL (Fagan, 2001).
- Work hardening is essentially a specialized program designed to enable people with physical, psychological, and psychosocial issues inhibiting a person's ability, to successfully return to work. The National Advisory Committee on Work Hardening best describes work hardening:

"Work hardening is a highly structured, goal oriented, individualized treatment program designed to maximize the individual's ability to return to work. Work hardening programs, which are interdisciplinary in nature, use real or simulated work activities in conjunction with conditioning tasks that are graded to progressively improve the biomechanical, neuromuscular, cardiovascular/metabolic and psychosocial functions of the individual. Work hardening provides a transition between acute care and return to work while addressing the issues of productivity, safety, physical tolerances, and worker behaviors" (Ogden-Niemeyer & Jacobs, 1989, p. 1).

- Work conditioning is similar to work hardening, except work conditioning purely involves improving physical capacities, whereas work hardening improves physical, psychological, and psychosocial factors.

Mental health

According to Medicare (2005) guidance, "Only a qualified occupational therapist has the knowledge, training, and experience required to evaluate and, as necessary, re-evaluate a patient's level of function, determine whether an occupational therapy program could

reasonably be expected to improve, restore, or compensate for lost function, and where appropriate, recommend to the physician a plan of treatment."

According to the American Occupational Therapy Association (AOTA), occupational therapists work with the Mental Health population throughout the life span and across many treatment settings where mental health services and psychiatric rehabilitation are provided (AOTA, 2009). Just as with other clients, the OT facilitates maximum independence in activities of daily living (dressing, grooming, etc.) and instrumental activities of daily living (medication management, grocery shopping, etc.). According to the American Occupational Therapy Association, OT improves functional capacity and quality of life for people with mental illness in the areas of employment, education, community living, and home and personal care through the use of real life activities in therapy treatments (AOTA, 2005).

Geriatric, Adult, Adolescents, and Children with any kind of mental illness or mental health issues. These conditions include but are not limited to: Schizophrenia, substance abuse, addiction, dementia, Alzheimer's, mood disorders, personality disorders, psychoses, eating disorders, anxiety disorders (including post-traumatic stress disorder, separation anxiety disorder) (Cara & MacRae, 2005), and reactive attachment disorder (children only) (Lambert, 2005).

Typical issues that are addressed are as follows: Helping people acquire the skills to care for themselves or others including; keeping a schedule, medication management, employment, education, increasing community participation, community access (grocery store, library, bank, etc.), money management skills, engaging in productive activities to fill the day, coping skills, routine building, building social skills, and childcare (Cara & MacRae, 2005).

In the UK, the College of Occupational Therapists (COT) have published Recovering Ordinary Lives , which details the strategy for OTs in mental health up to 2017, and makes explicit the goals that have been set for the profession, in line with government directives (COT 2006).

Areas that Mental Health OT's could work in are as follows:

- Mental health inpatient units
    - Adolescent, adult and older people's acute mental health wards
    - Adult and older people's rehabilitation wards
    - Prisons/secure units (Forensic psychiatry)
    - Psychiatric intensive care unit
    - Specialist units for Eating Disorders, Learning disabilities
- Community based mental health teams
    - Child and adolescent mental health teams
    - Adult and older people's community mental health teams
    - Rehabilitation and recovery and Assertive Outreach community teams
    - Primary care services in GP practices

- Home treatment teams
- early intervention in psychosis teams
- Specialist learning disability, eating disorder community services
- Day services
- Vocational Services
- Dementia & Alzheimer Care: OTs focus on adapting activities as the client progresses through the illness (Hofmann, 2008) OT also works with caregivers to teach them how to grade activities to the client's ability. Interventions are based on using the client's strengths to increase their quality of life and their relationships with caregivers. Use of social interactions, communication, memory, safety and self maintenance.

Community

Community based practice involves working with people in their own environment rather than in a hospital setting. It often combines the knowledge and skills related to physical and mental health. It can also involve working with atypical populations such as the homeless or at-risk populations. Examples of community-based practice settings:

- Health promotion and lifestyle change: Remaining healthy is the goal of all people in a society, including people with chronic disabling or health conditions. Achieving health requires skills to self-manage conditions that might limit their ability to function in daily life. The occupational therapist helps people acquire these skills (Wilcock, 2005).
- Private Practice
- Aging in place: Occupational therapists implement environmental modifications in senior housing, assisted living, long-term-care facilities, and homes (Yamkovenko, 2008) Environmental modifications can include rearranging furniture, building ramps, widening doorways, grab bars, special toilet seats, and other safety equipment to use performance capabilities to their fullest (Moyers & Christiansen, 2004).
- Low Vision: Occupational therapists help clients use their remaining vision to complete their daily routines with compensation, remediation, disability prevention and health promotion. Compensations or that modifications to the environment may include proper lighting, color contrast, reducing clutter and education on adaptive equipment (Golembiewski, 2004).
- Intermediate care services
- Driving Centers: Driving is an instrumental activity of daily living and an occupational therapist may evaluate and treat skills needed to drive such as vision, executive function or memory. If a client needs more skilled assessment and training they would refer them to an OT Driver Rehabilitation Specialist which could do on the road assessment, training in adaptive equipment and make more specific recommendations.
- Day centres
- Schools
- Child development centres

- People's own homes, carrying out therapy and providing equipment and adaptations
- Work and Industry: To be a healthy successful worker there must be a person environment fit between the task, the equipment, and the person's skills. Occupational therapists work to achieve that fit (Ellexson, 2000; Clinger, Dodson, Maltchev, & Page, 2007). Populations, conditions, and diagnoses: People of working age and ability who have been born with or developed a condition, injury, or illness that compromises their ability to work (Ellexson, 2000; Clinger, Dodson, Maltchev, & Page, 2007). Settings: Return to work programs, large organizations, consultants to large organizations, work hardening programs, work conditioning programs, transitional return to work programs (Ellexson, 2000; Clinger, Dodson, Maltchev, & Page, 2007). Typical issues addressed: assessment of ability to work, interventions to enhancing work performance by means of work hardening, work conditioning, and improvement of ergonomics in the workplace, identification of accommodations necessary to return-to-work following illness or injury, prevention of work related injury, illness, or disability (Ellexson, 2000; Clinger, Dodson, Maltchev, & Page, 2007).
- Homeless Shelters
- Educational Settings
- Refugee Camps

Emerging practice areas for therapy

- Children & Youth:
  - Psychosocial Needs of Children & Youth
  - Self-management for Physical & Occupational Therapy Students
  - Life Skills Trainings for children & Youth with Special Needs (Khemthong, 2006)
- Health & Wellness:
  - Health & Wellness Consulting
  - Design & Accessibility Consulting & Home Modification
  - Ergonomic Consulting
  - Private Practice Community Health Services
- Productive Aging:
  - Driver Rehabilitation & Training
  - Low Vision Services
  - Fatigue & Leisure Management (Khemthong, 2006)
  - Musical trainings for elderly (Khemthong, 2006)
- Rehabilitation, Disability, & Participation:
  - Technology & Assistive Device Development & Consulting
  - Meditation trainings for Diabetes Mellitus (Khemthong, 2006)
  - Leisure management for Chronic Obstructive Pulmonary Disease (Khemthong, 2006)
  - Health Systematization of Occupational Therapy for Stroke
  - Mental Practice & Recovery Programs (Khemthong, 2006)
  - Leisure Management for Mental Health (Khemthong, 2006)

    - Fatigue & Psychospirituality of Multi-Sensory Leisure for Cancer, Depression, Rheumatoid Arthritis(Khemthong, 2006)
- Work & Industry:
    - Ticket to Work Services
    - Welfare to Work Services
    - Leadership Maturity Fitness to Work Services (Khemthong, 2006)
    - Fatigue & Leisure Management to Work Services (Khemthong, 2006)

Occupational therapy approaches

Services typically include:

- Teaching new ways of approaching tasks
- How to break down activities into achievable components e.g. sequencing a complex task like cooking a complex meal
- Comprehensive home and job site evaluations with adaptation recommendations.
- Performance skills assessments and treatment.
- Adaptive equipment recommendations and usage training.
- Environmental adaptation including provision of equipment or designing adaptations to remove obstacles or make them manageable
- Guidance to family members and caregivers.
- The use of creative media as therapeutic activity

Activity analysis

Activity analysis has been defined as a process of dissecting an activity into its component parts and task sequence in order to identify its inherent properties and the skills required for its performance, thus allowing the therapist to evaluate its therapeutic potential

Theoretical Frameworks

Occupational Therapists use a number of theoretical frameworks to frame their practice. Note that terminology has differed between scholars. Theoretical bases for framing a human and their occupation being include the following:

Frames of Reference/Generic models

Frames of reference or generic models are the overarching title given to a collation of compatible knowledge, research and theories that form conceptual practice. More generally they can be defined as "those aspects which influence our perceptions, decisions and practice".

Occupational Therapy Frame of References/Models:

- Person Environment Occupation Performance Model (PEOP) (Charles Christiansen & Carolyn Baum)
- Occupational Therapy Intervention Process Model (OTIPM) (Anne Fisher and others)
- Occupational Performance Model (OPM)
- Model of Human Occupation (MOHO) (Gary Kielhofner and others)
    - MOHO was first published in 1980. It explains how people select, organise and undertake occupations within their environment. The model is supported with evidence generated over thirty years and has been successfully applied throughout the world.
- Canadian Model of Occupational Performance and Engagement (CMOP-E)
- Kawa (River) Model (Michael Iwama)
- Functional Information-Processing Model
- Biomechanical Frame of Reference
    - The Biomechanical Frame of Reference is primarily concerned with motion during occupation. It is used with individuals who experience limitations in movement, inadequate muscle strength or loss of endurance in occupations. The Frame of Reference was not originally compiled by Occupational Therapists, and Therapists should translate it to the Occupational Therapy perspective, to avoid the risk of movement or exercise becoming the main focus.
- Rehabilitative (compensatory)
- Neurofunctional (Gordon Muir Giles and Clark-Wilson)
- Cognitive Disabilities
- Sensory Integration
- Lifestyle Performance Model (Fidler)
- Client-Centered Frame of Reference
    - This Frame of Reference is developed from the work of Carl Rogers. It views the client as the center of all therapeutic activity, and the client's needs and goals direct the delivery of the Occupational Therapy Process.
- Cognitive-Behavioural Frame of Reference
- Psychodynamic Frame of Reference
- Ecological of Human Development Model
- Recovery Models & Self-Management Models
    - Curtin pARTicipation Model
    - Knowledge Translation of Self-Management Models
    - Life-Skills Tree Model
    - Occupational Therapy - Mahidol Clinical System (OT-MCS) Model

Challenges for occupational therapy

A key challenge for occupational therapy is to develop and maintain a definition of its nature and scope assert that while this presents a challenge, it also results in a unique flexibility which allows the discipline to move with the flow of social, cultural and environmental change. This difficulty in definition may be a cause of chronic strain for practitioners and may also contribute to a lack of role definition and subsequent blurring

Recent literature has also called for occupational therapy to address the political nature of who occupational therapists are and what they do (Kronenberg & Pollard, 2005). Profession specific models of occupational therapy have also been critiqued for being biased towards a western, ableist and generally unrepresentative of the most occupationally deprived groups

Occupational therapy and ICF

The International Classification of Functioning, Disability and Health (ICF) is a framework to measure health and ability by illustrating how these components impact one's function. This relates very closely to the Occupational Therapy Practice Framework as it is stated, "The profession's core beliefs are in the positive relationship between occupation and health and its view of people as occupational beings" . The ICF is also built into the 2nd edition of the practice framework. Activities and participation examples from the ICF overlap Areas of Occupation, Performance Skills, and Performance Patterns in the framework. The ICF also includes contextual factors (environmental and personal factors) that relate to the context in the framework. In addition, body functions and structures classified within the ICF help describe the client factors as described in the OT framework

Further exploration of the relationship between occupational therapy and the components of the ICIDH-2 (revision of the original International Classification of Impairments, Disabilities, and Handicaps (ICIDH); later becoming the ICF) was conducted by McLaughlin Gray . First, the ICF is an international framework and provides an opportunity for the occupational therapy field to become better known across the globe. Second, the ICF provides occupational therapists with a global language to describe their expertise to the larger international health care community. The ICF uses a positive, holistic language emphasizing skills, capacities, and strengths of an individual rather than focusing on one's deficits and disabilities. This is similar to the outlook of occupational therapists. Third, the ICF includes environmental and personal contextual factors which are incorporated into the theory behind occupational therapy. It is important to take into consideration an individual's personal, environmental, and occupational factors to develop an effective intervention . The last notable application of the ICF to occupational therapy is the recognition of cultural patterns in occupation. Culture has significance on an individual's activities and participation and it is important to keep this in mind when treating an individual.

Although the ICF can be very useful for occupational therapists, it is noted in the literature that occupational therapists should use specific occupational therapy vocabulary along with the ICF in order to ensure correct communication about specific concepts . The ICF might lack certain categories to describe what occupational therapists need to communicate to clients and colleagues. It also may not be possible to exactly match the connotations of the ICF categories to occupational therapy terms. The ICF is not an assessment and specialized occupational therapy vocabulary should not be replaced with ICF terminology The ICF is an overarching framework for current therapy practices.

Chapter 10

Occupational Therapist

An **occupational therapist** (OT) is trained in the practice of occupational therapy. The role of an occupational therapist is to work with a client to help them achieve a fulfilled and satisfied state in life through the use of "purposeful activity or interventions designed to achieve functional outcomes which promote health, prevent injury or disability and which develop, improve, sustain or restore the highest possible level of independence.". A practical definition for OT can also be illustrated with the use of models such as the Occupational Performance Model (Australia), known as the OPM(A). At the core of this approach is the ideology that occupational therapists are concerned with the occupations of people and how these contribute to health. Specifically it is a person's occupational performance that influences their health and personal satisfaction of their individual needs. The OPM(A) is constructed on the following definition of Occupational Performance:

"The ability to perceive, desire, recall, plan and carry out roles, routines, tasks and sub-tasks for the purpose of self-maintenance, productivity, leisure and rest in response to demands of the internal and/or external environment."

It can be seen that occupational performance, the roles it creates for a client, and the areas it can encompass are so far-reaching that an occupational therapist can work with a wide range of clients of various limitations who are being cared for in an array of settings. Occupational therapy is about helping people do the day-to-day tasks that "occupy" their time, sustain themselves, and enable them to contribute to the wider community. Its these opportunities to "do" that occupational therapy provides that prove important and meaningful to the health of people.

Role

Occupational therapists (OTs) help people of all ages to improve their ability to perform tasks in their daily living and working environments. They work with individuals who have conditions that are mentally, physically, developmentally, socially or emotionally disabling. They also help them to develop, recover, or maintain daily living and work skills. Occupational therapists help clients not only to improve their basic motor

functions and reasoning abilities, but also to compensate for permanent loss of function. Their goal is to help clients have independent, productive, and satisfying lives.

Occupational therapists assist clients in performing activities of all types, ranging from using a computer to caring for daily needs such as dressing, cooking, and eating. Physical exercises may be used to increase strength and dexterity, while other activities may be chosen to improve visual acuity and the ability to discern patterns. For example, a client with short-term memory loss might be encouraged to make lists to aid recall, and a person with coordination problems might be assigned exercises to improve hand-eye coordination. Occupational therapists also use computer programs to help clients improve decision-making, abstract-reasoning, problem solving, and perceptual skills, as well as memory, sequencing, and coordination —- all of which are important for independent living. Occupational therapists are often skilled in psychological strategies such as cognitive behavioural therapy and Acceptance and Commitment Therapy, and may use cognitive therapy especially when introducing people to new strategies for carrying out daily activities such as activity pacing or using effective communication strategies.

Clients with permanent disabilities

Therapists instruct those with permanent disabilities, such as spinal cord injuries, cerebral palsy, or muscular dystrophy, in the use of adaptive equipment, including wheelchairs, orthotics, and aids for eating and dressing. They also design or make special equipment needed at home or at work. Therapists develop computer-aided adaptive equipment and teach clients with severe limitations how to use that equipment in order to communicate better and control various aspects of their environment.

Work-related therapy

Some occupational therapists treat individuals whose ability to function in a work environment has been impaired. These practitioners arrange employment, evaluate the work environment, plan work activities, and assess the client's progress. Therapists also may collaborate with the client and the employer to modify the work environment so that the work can be successfully completed.

With children

Occupational therapists may work exclusively with individuals in a particular age group or with particular disabilities. In schools, for example, they evaluate children's abilities, recommend and provide therapy, modify classroom equipment, and help children participate as fully as possible in school programs and activities. A therapist may work with children individually, lead small groups in the classroom, consult with a teacher, or serve on a curriculum or other administrative committee. Early intervention therapy services are provided to infants and toddlers who have, or are at the risk of having, developmental delays. Specific therapies may include facilitating the use of the hands, promoting skills for listening and following directions, fostering social skills, or teaching dressing and grooming skills.

With the elderly

Occupational therapy is very beneficial to the elderly population. Therapists help the elderly lead more productive, active, and independent lives through a variety of methods, including the use of adaptive equipment. Occupational therapists work with the elderly in many varied environments, such as in their homes in the community, in hospital, and in residential care facilities to name a few. In the home environment, occupational therapists may work with the client to assess for hazards and to identify environmental factors that contribute to falls. Occupational therapists are often instrumental in assessing for appropriate wheelchairs for the elderly. In addition, therapists with specialized training in driver rehabilitation assess an individual's ability to drive using both clinical and on-the-road tests. The evaluations allow the therapist to make recommendations for adaptive equipment, training to prolong driving independence, and alternative transportation options.

Mental health

Occupational therapists also work with people who have mental health problems and learning disabilities. In this work, therapists choose activities that help people learn to engage in and cope with daily life. Activities include time management skills, budgeting, shopping, homemaking, and the use of public transportation. Occupational therapists also may work with individuals who are dealing with alcoholism, drug abuse, depression, eating disorders, or stress-related disorders. The ultimate aim would be to help people to engage in a personally satisfying and socially adaptive range of occupations.

With Terminally Ill Patient

Occupational therapists works with patients with terminal illness like cancer, Muscular dystrophy,etc. All performance areas including, work play and leisure are widely affected in these sets of patients. An occupational therapist provides various means to these patients to restore or maintain their deteriorating performance components by using their residual capacities and capabilities to give them a sense of importance.

With People with Chronic Pain

Occupational therapists often work within interdisciplinary or multidisciplinary teams to help individuals with chronic pain develop active self management strategies. An area of specific concern to occupational therapists is the use of time but it is also common for occupational therapists to help people return to work, and to return to leisure and family activities . Occupational therapists may use a variety of interventions including biofeedback, relaxation, goal setting, problem solving, planning, and carry this out within both group and individual settings . Therapists may work within a clinic setting, or in the community including the workplace, school, home and health care centres. Occupational therapists may assess occupational performance before and after intervention, as a measure of effectiveness and reduction in disability.

Assessment

Assessing and recording a client's activities and progress is an important part of an occupational therapist's job. Accurate records are essential for evaluating clients, for billing, and for reporting to physicians and other health care providers.

Thorough and accurate assessment ensures that Occupational Therapists select appropriate and effective interventions for their clients. Assessment in Occupational Therapy is complex and multifaceted, and is an essential component of the Occupational Therapy Process. Assessment occurs at the beginning of the Process (providing the foundation for effective treatment), at the end (evaluation). Reassessment also occurs throughout intervention.

Chapter 11

Anesthesia

Anesthesia, or **anaesthesia**, traditionally meant the condition of having sensation (including the feeling of pain) blocked or temporarily taken away. It is a pharmacologically induced and reversible state of amnesia, analgesia, loss of responsiveness, loss of skeletal muscle reflexes or decreased stress response, or all simultaneously. This allows patients to undergo surgery and other procedures without the distress and pain they would otherwise experience. An alternative definition is a "reversible lack of awareness," including a total lack of awareness (e.g. a general anesthetic) or a lack of awareness of a part of the body such as a spinal anesthetic. The word *anesthesia* was coined by Oliver Wendell Holmes, Sr. in 1846.

Types of anesthesia include local anesthesia, regional anesthesia, general anesthesia, and dissociative anesthesia. Local anesthesia inhibits sensory perception within a specific location on the body, such as a tooth or the urinary bladder. Regional anesthesia renders a larger area of the body insensate by blocking transmission of nerve impulses between a part of the body and the spinal cord. Two frequently used types of regional anesthesia are spinal anesthesia and epidural anesthesia. General anesthesia refers to inhibition of sensory, motor and sympathetic nerve transmission at the level of the brain, resulting in unconsciousness and lack of sensation. Dissociative anesthesia uses agents that inhibit transmission of nerve impulses between higher centers of the brain (such as the cerebral cortex) and the lower centers, such as those found within the limbic system.

History

Plant derivatives

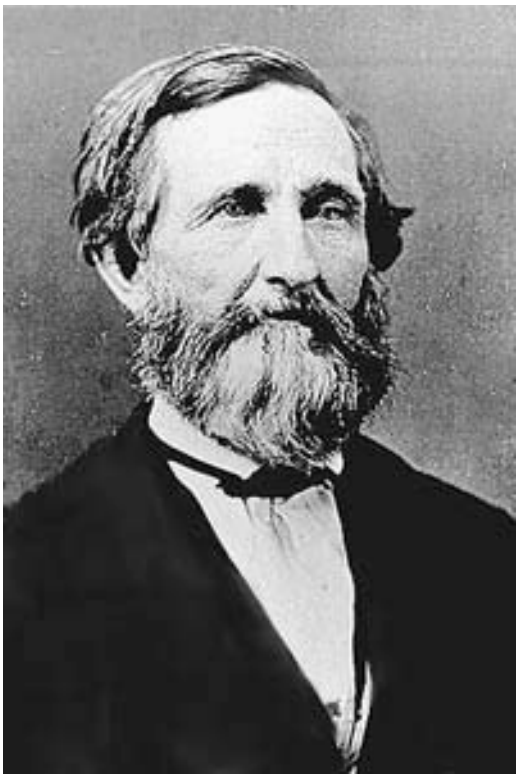
Throughout Europe, Asia, and the Americas a variety of *Solanum* species containing potent tropane alkaloids were used, such as mandrake, henbane, Datura metel, and Datura inoxia. Ancient Greek and Roman medical texts by Hippocrates, Theophrastus, Aulus Cornelius Celsus, Pedanius Dioscorides, and Pliny the Elder discussed the use of opium and *Solanum* species. In 13th century Italy, Theodoric Borgognoni used similar mixtures along with opiates to induce unconsciousness, and treatment with the combined alkaloids proved a mainstay of anesthesia until the nineteenth century. In the Americas coca was

also an important anesthetic used in trephining operations. Incan shamans chewed coca leaves and performed operations on the skull while spitting into the wounds they had inflicted to anesthetize the site. Alcohol was also used, its vasodilatory properties being unknown. Ancient herbal anesthetics have variously been called soporifics, anodynes, and narcotics, depending on whether the emphasis is on producing unconsciousness or relieving pain.

The use of herbal anesthesia had a crucial drawback compared to modern practice—as lamented by Fallopius, "When soporifics are weak, they are useless, and when strong, they kill." To overcome this, production was typically standardized as much as feasible, with production occurring from specific locations (such as opium from the fields of Thebes in ancient Egypt). Anesthetics were sometimes administered in the "spongia somnifera", a sponge into which a large quantity of drug was allowed to dry, from which a saturated solution could be trickled into the nose of the patient. At least in more recent centuries, trade was often highly standardized, with the drying and packing of opium in standard chests, for example. In the 19th century, varying aconitum alkaloids from a variety of species were standardized by testing with guinea pigs. Trumping this method was the discovery of morphine, a purified alkaloid that could be injected by hypodermic needle for a consistent dosage. The enthusiastic reception of morphine led to the foundation of the modern pharmaceutical industry.

The first effective local anesthetic was cocaine. Isolated in 1859, it was first used by Karl Koller, at the suggestion of Sigmund Freud, in eye surgery in 1884. German surgeon August Bier (1861–1949) was the first to use cocaine for intrathecal anesthesia in 1898. Romanian surgeon Nicolae Racoviceanu-Piteşti (1860–1942) was the first to use opioids for intrathecal analgesia; he presented his experience in Paris in 1901. A number of newer local anesthetic agents, many of them derivatives of cocaine, were synthesized in the 20th century, including eucaine (1900), amylocaine (1904), procaine (1905), and lidocaine (1943).

Early inhalational anesthetics



Anesthesia pioneer Crawford W. Long

Contemporary re-enactment of Morton's October 16, 1846, ether operation; daguerrotype by Southworth & Hawes

On 16 October 1846 William Thomas Green Morton, a Boston dentist was invited to the Massachusetts General Hospital to demonstrate his new technique for painless surgery. After Morton had induced anesthesia by administration of diethyl ether by inhalation, surgeon John Collins Warren removed a tumor from the neck of Edward Gilbert Abbott. This first public demonstration of ether anesthesia occurred in the surgical amphitheater now called the Ether Dome. The previously skeptical Dr. Warren was impressed and stated "Gentlemen, this is no humbug." In a letter to Morton shortly thereafter, physician and writer Oliver Wendell Holmes, Sr. proposed naming the state produced "anesthesia", and the procedure an "anesthetic".

Morton at first attempted to hide the actual nature of his anesthetic substance, referring to it as Letheon. He received a US patent for his substance, but news of the successful anesthetic spread quickly by late 1846. Respected surgeons in Europe including Liston, Dieffenbach, Pirogov, and Syme, quickly undertook numerous operations with ether. An American-born physician, Boott, encouraged London dentist James Robinson to perform a dental procedure on a Miss Lonsdale. This was the first case of an operator-anesthetist. On the same day, 19 December 1846, in Dumfries Royal Infirmary, Scotland, a Dr. Scott used ether for a surgical procedure. The first use of anesthesia in the Southern

Hemisphere took place in Launceston, Tasmania, that same year. Drawbacks with ether such as excessive vomiting and its flammability led to its replacement in England with chloroform.

Discovered in 1831, the use of chloroform in anesthesia is linked to James Young Simpson, who, in a wide-ranging study of organic compounds, found chloroform's efficacy on 4 November 1847. Its use spread quickly and gained royal approval in 1853 when John Snow gave it to Queen Victoria during the birth of Prince Leopold. Unfortunately, chloroform is not as safe an agent as ether, especially when administered by an untrained practitioner (medical students, nurses, and occasionally members of the public were often pressed into giving anesthetics at this time). This led to many deaths from the use of chloroform that (with hindsight) might have been preventable. The first fatality directly attributed to chloroform anesthesia was recorded on 28 January 1848 after the death of Hannah Greener.

John Snow of London published articles from May 1848 onwards "On Narcotism by the Inhalation of Vapours" in the London Medical Gazette. Snow also involved himself in the production of equipment needed for the administration of inhalational anesthetics.

Non-pharmacological methods

There is a long history of the use of hypnotism as an anesthetic techniques. Chilling tissue (e.g. with a mixture of salt and ice or a spray of diethyl ether or ethyl chloride) can temporarily inhibit the ability of nerve fibers (axons) to conduct sensation. The hypocapnia that results from hyperventilation can temporarily inhibit the conscious perception of sensory stimuli, including pain. These techniques are seldom employed in modern anesthetic practice.

Anesthesia providers

Physicians specializing in perioperative care, development of an anesthetic plan, and the administration of anesthetics are known in the United States as *anesthesiologists* and in the United Kingdom and Canada as *anaesthetists* or *anaesthesiologists*. All anesthetics in the UK, Australia, New Zealand, Hong Kong and Japan are administered by physicians. Nurse anesthetists also administer anesthesia in 109 nations. In the US, 35% of anesthetics are provided by physicians in solo practice, about 55% are provided by anesthesia care teams (ACTs) with anesthesiologists medically directing anesthesiologist assistants or certified registered nurse anesthetists (CRNAs), and about 10% are provided by CRNAs in solo practice.

Physicians

Anesthesia students training with a patient simulator

In the strict sense, the term *anesthetist* refers to any individual who administers anesthesia. However, in the US the term is most commonly employed to refer to registered nurses who have completed specialized education and training in anesthesia to become certified registered nurse anesthetists (CRNAs). In the US and Canada, medical doctors who specialize in anesthesiology are called *anesthesiologists*. Such physicians in the United Kingdom (UK), Australia and New Zealand are called *anaesthetists* or *anaesthesiologists*.

In the US, a physician specializing in anesthesiology typically completes 4 years of college, 4 years of medical school, and four years of postgraduate medical training or residency According to the American Society of Anesthesiologists, anesthesiologists provide or participate in more than 90 percent of the 40 million anesthetics delivered annually. In the UK, this training lasts a minimum of seven years after the awarding of a medical degree and two years of basic residency, and takes place under the supervision of the Royal College of Anaesthetists. In Australia and New Zealand, it lasts five years after the awarding of a medical degree and two years of basic residency, under the supervision of the Australian and New Zealand College of Anaesthetists. Other countries have similar systems, including Ireland (the Faculty of Anaesthetists of the Royal College of Surgeons in Ireland), Canada and South Africa (the College of Anaesthetists of South Africa).

In the US, satisfactory completion of the written and oral Board examinations allows an anesthesiologist to be called a "Diplomate" of the American Board of Anesthesiology (or of the American Osteopathic Board of Anesthesiology, for osteopathic physicians). This is often referred to colloquially as being "Board Certified". In the UK, Fellowship of the Royal College of Anaesthetists (FRCA) is conferred upon medical doctors following satisfactory completion of the written and oral parts of the Royal College's examination.

The role of the anesthesiologist is no longer limited to the operation itself — Many anesthesiologists function as perioperative physicians, ensuring optimal analgesia and maintenance of physiologic homeostasis throughout the preoperative, intraoperative, and postoperative periods. Anesthesiologists may elect to subspecialize in anesthesia for

particular types of surgery (cardiothoracic, obstetrical, neurosurgical, pediatric), regional anesthesia, acute or chronic pain medicine, or Intensive Care Medicine.

Anesthesia providers are often trained using full scale human simulators. The field was an early adopter of this technology and has used it to train students and practitioners at all levels for the past several decades. Notable centers in the United States can be found at the Johns Hopkins Medicine Simulation Center, Harvard's Center for Medical Simulation, Stanford, The Mount Sinai School of Medicine HELPS Center in New York, and Duke University.

Nurse anesthetists

In the United States, advanced practice nurses specializing in the provision of anesthesia care are known as Certified Registered Nurse anesthetists (CRNAs). According to the American Association of Nurse Anesthetists, the 39,000 CRNAs in the US administer approximately 30 million anesthetics each year, roughly two thirds of the US total. 34% of nurse anesthetists practice in communities of less than 50,000. CRNAs start school with a bachelors degree and at least 1 year of acute care nursing experience, and gain a masters degree in nurse anesthesia before passing the mandatory Certification Exam. Masters-level CRNA training programs range in length from 24 to 36 months.

CRNAs may work with podiatrists, dentists, anesthesiologists, surgeons, obstetricians and other professionals requiring their services. CRNAs administer anesthesia in all types of surgical cases, and are able to apply all the accepted anesthetic techniques—general, regional, local, or sedation. Many states place restrictions on practice, and hospitals often regulate what CRNAs and other midlevel providers can or can not do based on local laws, provider training and experience, and hospital and physician preferences.

In the United States, the Centers for Medicare and Medicaid Services (CMS), a federal agency within the United States Department of Health and Human Services, determines the conditions for payment for all anesthesia services provided under the Medicare, Medicaid, and State Children's Health Insurance Program (SCHIP) programs. For the purposes of payment for anesthesiology services, CMS defines an *anesthesia practitioner* as a physician who performs the anesthesia service alone, a CRNA who is not medically directed, or a CRNA or AA who is medically directed. Under the *QZ* Anesthesia Claims Modifier, CMS allows payment to a CRNA for anesthesiology services provided under these programs without medical direction by a physician. Furthermore, under CMS regulations, anesthesia must be administered only by:

- a qualified doctor of medicine or osteopathic medicine, dentist, oral surgeon, or podiatrist;
- a CRNA who, unless exempted, is under the supervision of the operating practitioner or of an anesthesiologist;
- an anesthesiologist's assistant who is under the supervision of an anesthesiologist.

The aforementioned exemption for CRNAs is the *State exemption* (also referred to as an "opt-out"). Under the State exemption, if the State in which the hospital is located submits a letter to CMS requesting exemption from physician supervision of CRNAs, and that letter has been signed by the Governor of that State, then hospitals within that State may be exempted from the requirement for physician supervision of CRNAs. In 2001, CMS established this exemption for CRNAs from the physician supervision requirement by recognizing a Governor's written request to CMS attesting that it is in the best interests of the State's citizens to exercise this exemption. As of July 2009, fifteen states (California, Iowa, Nebraska, Idaho, Minnesota, New Hampshire, New Mexico, Kansas, North Dakota, Washington, Alaska, Oregon, South Dakota, Wisconsin and Montana) have chosen to opt-out of the CRNA physician supervision regulation.

Anesthesiologist assistants

In the United States, anesthesiologist assistants (AAs) are graduate-level trained specialists who have undertaken specialized education and training to provide anesthesia care under the direction of an anesthesiologist. AAs typically hold a masters degree and practice under anesthesiologist supervision in 18 states through licensing, certification or physician delegation.

In the UK, a similar group of assistants are currently being evaluated. They are referred to as "physician assistant (anaesthesia)" (PAA). Their background can be nursing, operating department practice, another of the allied medical professions, or even one of the natural sciences. Training is in the form of a postgraduate diploma and takes 27 months to complete.

Operating department practitioners

In the United Kingdom, operating department practitioners provide assistance and support to the anesthetist or anesthesiologist. They can also assist the surgeon with surgical procedures and provide postoperative care to patients emerging from anesthesia. ODPs can be found in the operating department, accident and emergency department, intensive care unit, high dependency unit and in radiology, cardiology and endoscopy suites which require anesthesia support. They may also work with organ transplantation teams, as well as provide pre-hospital care to trauma victims. They are state-registered in the UK. The ODP is a mid-level practitioner of perioperative medicine. ODPs also function as lecturers and trainers in cardiopulmonary resuscitation, and work in management positions in operating departments.

Veterinary anesthetists/anesthesiologists

Much of the equipment and drugs utilized by veterinary anesthetists is similar or identical to that used in anesthesia for human patients. There are vast differences in the physiology of different animal species, which may influence the choice of anesthetic agents and delivery systems in organisms ranging in diversity from (for example) annelids to elephants. For many wild animals, anesthetic drugs must often be delivered from a

distance by means of remote projector systems ("dart guns") before the animal can even be approached. Large domestic livestock can often be anesthetized for certain types of surgery in the standing position using only local anesthetics and sedative drugs. While most clinical veterinarians and veterinary technicians routinely function as anesthetists in the course of their professional duties, veterinary anesthesiologists in the U.S. are veterinarians who have completed a three year residency in anesthesia and have qualified for certification by the American College of Veterinary Anesthesiologists.

Other personnel

Anesthesia technicians are specially trained biomedical technicians. They do not administer anesthesia, but rather they assist anesthesia providers similar to the way in which scrub technicians assist surgeons. Commonly these services are collectively called perioperative services, and thus the term perioperative service technician (PST) is used interchangeably with anesthesia technician. In the United States, an anesthesia technician can become a Certified Anesthesia Technician (Cer.A.T.), followed by becoming a Certified Anesthesia Technologist (Cer.A.T.T.) through American Society of Anesthesia Technologists & Technicians (ASATT). In New Zealand, an anesthetic technician completes a course of study recognized by the New Zealand Anaesthetic Technicians Society.

Anesthetic agents

An anesthetic agent is a drug that brings about a state of anesthesia. A wide variety of drugs are used in modern anesthetic practice. Many are rarely used outside of anesthesia, although others are used commonly by all disciplines. Anesthetics are categorized in to two categories: general anesthetics cause a reversible loss of consciousness (general anesthesia), while local anesthetics cause reversible local anesthesia and a loss of nociception.

Anesthetic equipment

In modern anesthesia, a wide variety of medical equipment is desirable depending on the necessity for portable field use, surgical operations or intensive care support, and the type(s) of anesthetic(s) to be administered. Anesthesia practitioners must possess a comprehensive and intricate knowledge of the production and use of various medical gases, anesthetic agents and vapors, medical breathing circuits and the variety of anesthetic machines (including vaporizers, ventilators and pressure gauges) and their corresponding safety features, hazards and limitations of each piece of equipment, for the safe, clinical competence and practical application for day to day practice. The risk of transmission of infection by anesthetic equipment has been a problem since the beginnings of anesthesia. Although most equipment that comes into contact with patients is disposable, there is still a risk of contamination from the anesthetic machine itself or because of bacterial passage through protective filters.

Anesthetic monitoring

Patients under general anesthesia must undergo continuous physiological monitoring to ensure safety. In the US, the American Society of Anesthesiologists have established mininum monitoring guidelines for patients receiving general anesthesia, regional anesthesia, or sedation. This includes electrocardiography (ECG), heart rate, blood pressure, inspired and expired gases, oxygen saturation of the blood (pulse oximetry), and temperature. In the UK the Association of Anaesthetists (AAGBI) have set minimum monitoring guidelines for general and regional anesthesia. For minor surgery, this generally includes monitoring of heart rate, oxygen saturation, blood pressure, and inspired and expired concentrations for oxygen, carbon dioxide, and inhalational anesthetic agents. For more invasive surgery, monitoring may also include temperature, urine output, blood pressure, central venous pressure, pulmonary artery pressure and pulmonary artery occlusion pressure, cardiac output, cerebral activity, and neuromuscular function. In addition, the operating room environment must be monitored for ambient temperature and humidity, as well as for accumulation of exhaled inhalational anesthetic agents, which might be deleterious to the health of operating room personnel.

Anesthesia record

The anesthesia record is the medical and legal documentation of events while a patient is under anesthesia. It reflects a detailed and continuous account of drugs, fluids, and blood products administered and procedures undertaken, and also includes the observation of cardiovascular responses, estimated blood loss, urine output and data from physiologic monitors while a patient is under anesthesia.

Traditionally handwritten on paper, the anesthesia record is increasingly being replaced by an electronic record as part of an Anesthesia Information Management System (AIMS), especially since 2007. An AIMS is any information system that is used as an automated electronic anesthesia record keeper (i.e., connection to patient physiologic monitors and/or the anesthetic machine) and which also may allow the collection and analysis of anesthesia-related perioperative patient data gathered from monitors and/or the anesthesia machine. These systems typically run on medical-grade hardware in the operating room. AIMS can be stand-alone systems or integrated modules of a hospital information system. AIMS have several benefits to the anesthesia departments as well to the hospital administration as documented in the scientific literature:

- Reducing anesthesia-related drug costs
- Increased anesthesia billing and capture of anesthesia-related charges
- Increased hospital reimbursement through improved hospital coding
- Improvement of the data quality of the intraoperative anesthesia record
- Support training and education of the anesthesia workforce
- Support of clinical decision-making
- Support of patient care and safety
- Enhancement of clinical studies
- Enhancement of clinical quality improvement programs

- Support of clinical risk management
- Monitoring for diversion of controlled substances