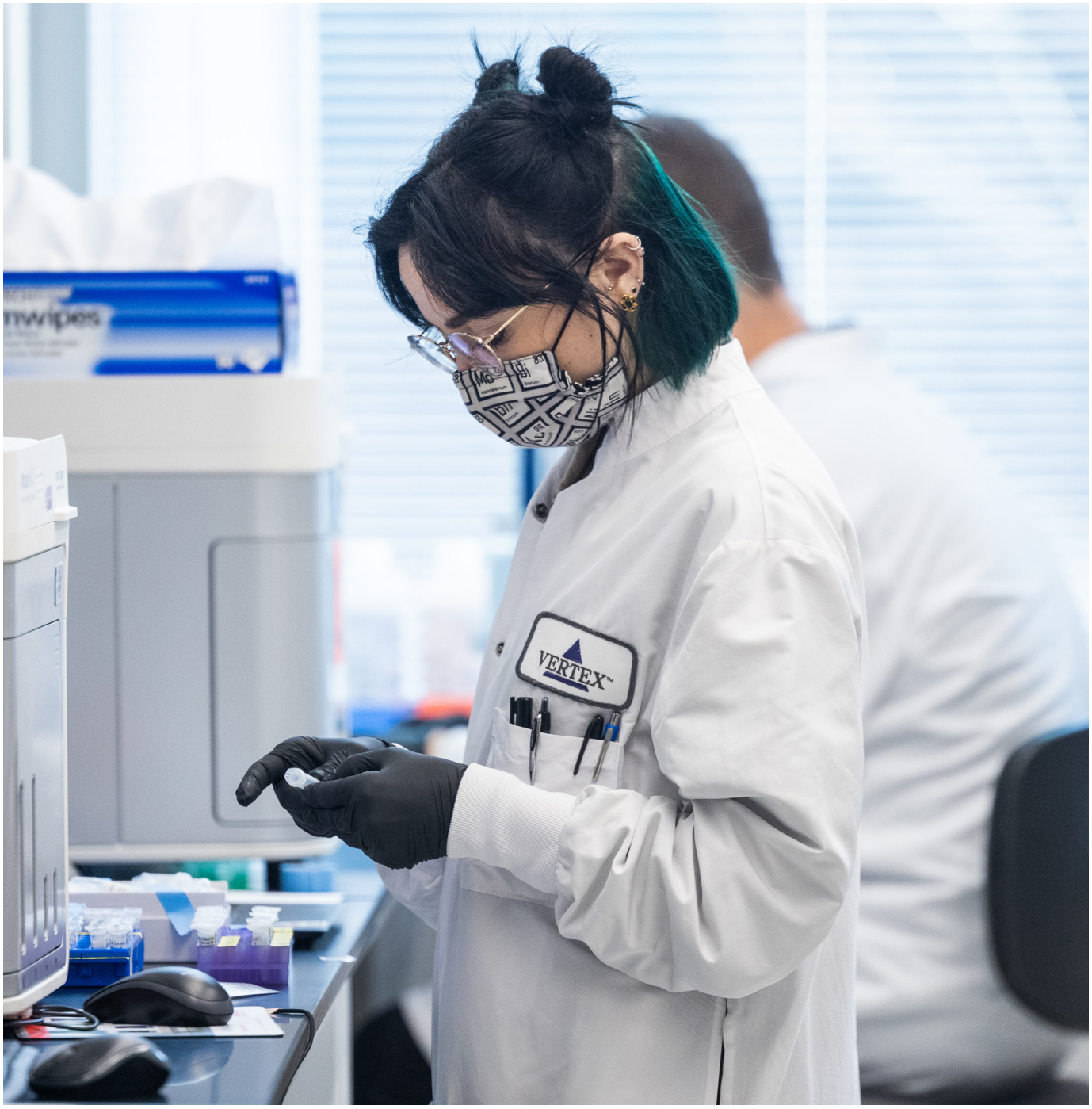
Disease Education: Pain



About Pain

Severe pain is a debilitating disorder that affects millions of people around the world. Pain is defined as an unpleasant sensory experience associated with actual or potential tissue damage, and it can develop from a variety of physiological, pathophysiological and psychological conditions. There are many different types of pain. Common types include acute, chronic neuropathic (caused by damage or dysfunction of the nervous system) and chronic musculoskeletal pain (where there is damage to the muscle, joint or bone). Some common causes of pain include injuries, surgical procedures, arthritis and neuropathies, to name a few. Poorly managed pain can lead to a significant decrease in quality of life and is often associated with complications such as sleep interruption, immobility, inability to work and major depression.

Pain types are classified based on various attributes including its duration, cause and qualitative experience.

Duration

Generally, pain duration is described as *acute* if it is short-lived or *chronic* if it persists longer than 3 months. Acute pain is a familiar experience for most people. It is the immediate unpleasant response to an injury such as a stubbed toe or a minor burn, or more seriously, a broken bone. Acute pain typically resolves when the underlying injury heals. In contrast, chronic pain persists for months to years.

Underlying cause

The underlying cause of pain generally involves an injury or damage to the body and broadly falls into two categories: nociceptive and neuropathic. Pain caused by injury or damage to tissues including skin, muscle, joints, bone or internal organs is often called *nociceptive pain* because it is due to signals from sensory neurons that specialize in the detection of painful stimuli – called nociceptors (or pain receptors). Pain caused by damage or dysfunction of the nervous system (nerves, spinal cord, brain) is termed *neuropathic pain* because it is due to a pathology of the neurons (cells of the nervous system).

Qualitative experience

Whether acute or chronic, nociceptive or neuropathic, the perception of pain can vary widely in terms of both qualitative descriptors of the experience and its intensity. Descriptors include familiar sensations like burning, throbbing, stinging or stabbing pains. Intensity can range from mild to severe.

These and other factors are considered when a patient is assessed, diagnosed and treated for pain. While there are additional ways to further classify and categorize pain, this toolkit focuses on providing background information on the areas of pain that Vertex is focused on: **acute pain** and **chronic peripheral neuropathic pain**.

Pain impacts millions of people around the world and is one of the most common reasons that patients see a doctor. The prevalence of pain exerts substantial burden on individuals, employers, healthcare systems and society in general.

The Underlying Cause

Acute pain

Acute pain occurs suddenly and is caused by something specific, such as an injury or a surgical operation. Acute pain is detected by specialized pain-sensing neurons, called nociceptors. It's often characterized as "sharp," "throbbing," "burning" or "stabbing." Common causes of acute pain include:

Surgery

Labor & childbirth

Dental work

Burns or cuts

Broken bones

These events may cause acute pain for up to several weeks. While acute pain may dissipate over time as the body heals, unrelieved acute pain can disrupt daily activities and may transition to chronic pain.

Chronic peripheral neuropathic pain

Peripheral neuropathic pain is a type of neuropathic pain caused by damage to the peripheral nerves. These nerves are located outside of the brain and spinal cord and are responsible for detecting and transmitting sensory signals to the brain. People with peripheral neuropathy generally describe the pain as "stabbing," "burning," "shooting" or "tingling." Peripheral neuropathy can develop from a variety of conditions. Common examples include:

- Diabetes
- Viral infections, including post-herpetic neuralgia
- Certain kinds of cancer and the chemotherapy used to treat it
- Failure of nerves to heal after surgeries (post-surgical neuropathic pain)
- Damage to nerves due to compression, as in certain neck and back pain
- Small fiber neuropathy/idiopathic (unexplained)

Acute pain affects more than 100 million people in the US each year

According to the US Institute of Medicine, 80% of patients who undergo surgery report postoperative pain, with 88% of these patients reporting moderate to severe pain levels.

It is estimated that approximately 10% of the US population suffer from chronic neuropathic pain

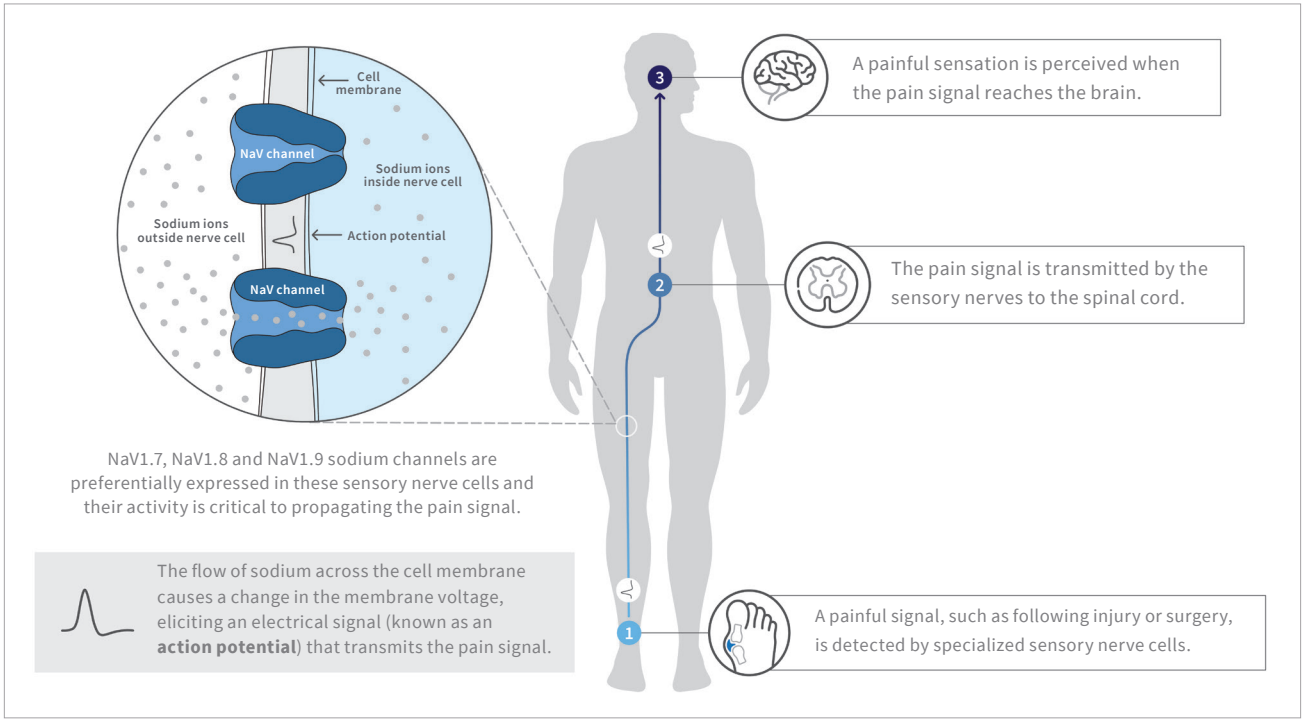
Approximately 90% of chronic pain patients are actively seeking new treatment methods for pain. The effects of neuropathy can be debilitating, and people living with neuropathic pain may experience frequent and severe sleep disturbances, anxiety and depression leading to decreased quality of life.

Our Nervous System and Pain

The nervous system is responsible for how the body senses, transmits and interprets pain. Pain is usually initially detected by specialized sensory nerve cells in our body called nociceptors. The pain signal is then transmitted through these sensory nerves to the spinal cord. At the spinal cord, the signal is transferred to neurons in the spinal cord that carry the signal to the brain where the signal is processed and perceived as pain.

The role of voltage-gated sodium channels in transmission of pain signals

Voltage-gated sodium (NaV) channels play an important role in transmission of electrical signals in the nervous system and muscles throughout the body. There are nine different types of NaV channels. Some types of NaV channels, like NaV1.7 and 1.8 are preferentially expressed on sensory nerves and their activity is critical to propagating pain signals from peripheral sensory neurons to the central nervous system. Mutations in NaV1.7 and NaV1.8 have been shown to affect human sensitivity to pain, and therefore are genetically validated targets for pain.



The Patient Experience

Assessment and diagnosis

Pain can result from many types of conditions. It is one of the most common symptoms that causes people to go to a doctor. Pain is often assessed on a zero to 10 scale, with zero being no pain and 10 being the worst imaginable pain. Medical evaluations focus on both the source of the pain and the impact of the pain. During an evaluation, a health care professional will typically start with a physical exam and ask detailed questions about the pain and its impact on the person's life. Other tests may include blood and imaging tests.

Treatment

The management of pain is influenced by whether the pain is acute or chronic, nociceptive or neuropathic, and its severity. Chronic neuropathic pain is often treated with anti-seizure medications or antidepressants. Opioids are generally prescribed for acute nociceptive pain but may not be suitable for chronic use. Anti-inflammatory drugs can be used for both acute and chronic pain, but their use can be limited due to side effects. Pain medications are often combined together and the dosages adjusted, which can make pain management complex. Beyond these approaches, there are limited options for medications and there haven't been any major innovations in pain treatment for decades.

FAQ

What is the underlying cause of acute pain?

Acute pain occurs suddenly and is caused by something specific, such as an injury or a surgical operation. Some common causes of pain include surgery, broken bones, dental work, burns or cuts and labor and childbirth. While acute pain may dissipate over time as the body heals, unrelieved acute pain can disrupt daily activities and may transition to chronic pain.

What is the underlying cause of neuropathic pain?

Neuropathic pain is caused by damage to the nervous system. Peripheral neuropathic pain is a type of neuropathic pain caused by damage to the peripheral nerves, which are located outside of the brain and spinal cord. Peripheral neuropathy can develop from a variety of conditions, including diabetes, certain viral infections and other processes or events that can damage peripheral nerves.

How does the nervous system produce a pain response?

The nervous system is responsible for how the body senses, transmits and interprets pain. Pain is usually initially detected by specialized sensory nerve cells in our body called nociceptors. The pain signal is then transmitted through these sensory nerves to the spinal cord. At the spinal cord, the signal is transferred to neurons in the spinal cord that carry the signal to the brain where the signal is processed and perceived as pain.

What are voltage-gated sodium (NaV) channels?

Voltage-gated sodium (NaV) channels are transmembrane proteins that conduct the flow of sodium ions down an electrochemical gradient through cell membranes. NaV channels are required for the function of electrically excitable cells, such as neurons and muscles, throughout the body. Some NaV channels, such as NaV 1.7 and 1.8, are present in sensory nerves and play an important role in transmitting pain signals.

What are the current treatments for pain?

Chronic neuropathic pain is often treated with anti-seizure medications or antidepressants. Opioids are generally prescribed for acute nociceptive pain but may not be suitable for chronic use. Anti-inflammatory drugs can be used for both acute and chronic pain, but their use can be limited due to side effects. There are currently no approved medicines that target specific NaV channels to treat pain.