

What you should know about
pain



The innovative **Swiss** pharmaceutical company

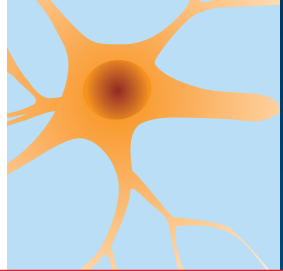
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Pain is a warning signal from our body



Pain sensors can detect a multitude of different stimuli



Pain and inflammation are often closely linked



Pain-relieving drugs can help reduce the symptoms of pain



Important

If you experience pain, the following points are important.

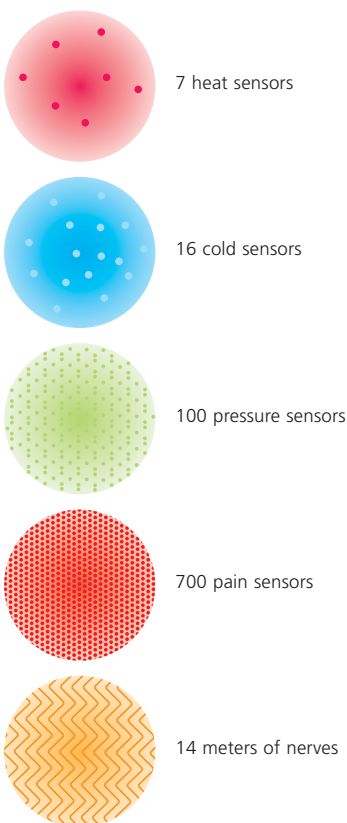
- Pain is a warning signal from your body – take it seriously and try to treat the cause of the pain.
- Pain-relieving drugs can help reduce the symptoms of pain but they do not cure the cause.
- Pain should be treated since untreated pain can become chronic.
- If pain persists a physician should investigate it. The same is true if the location of the severe pain cannot be pin-pointed or if other complaints are present at the same time.
- Drugs against pain can have severe side effects especially when taken over a longer period. They can even cause pain themselves. Ask your physician or pharmacist about their safe use.
- If possible, pregnant and breastfeeding women should not use pain-relieving drugs. Many drugs can cause severe problems for the child. If absolutely necessary paracetamol can be administered. This can also be used in low dosages for babies and small children (ask your doctor or pharmacist for more information).

Pain is a warning signal from our body

Feeling pain is a signal that something is wrong in our body. These signals should be taken seriously and the cause of the pain should be investigated in more detail.

Pain is what we feel when the sensitive endings of nerves are stimulated. Such nerve endings can be found in a great number in the skin and other parts of the body. These pain sensors can detect a multitude of different stimuli like heat, pressure or twisting. The signals that they give as a reaction vary as well. Every person perceives pain differently and psychological factors can influence the perception further. Pain is generally a warning sign that the body is in danger, overstrained or ill.

An area of skin this size contains on average

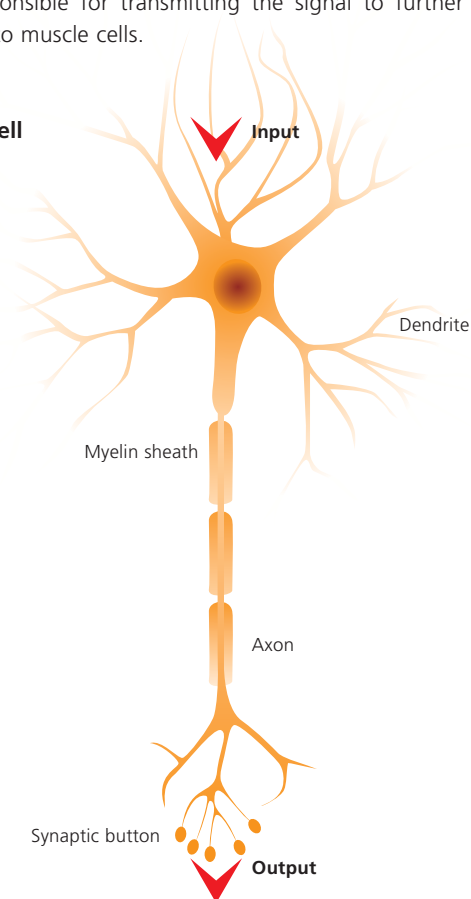


Pain detection, transmission and perception

To have a better understanding of what pain is we have to look at how our body detects pain and how this information is then transmitted and evaluated.

Nerve cells receive and transmit signals. Every nerve cell has an input and an output side. The little arms on the input side are called dendrites. These branch into free ends that are sensitive to stimulation. When a free end of a nerve cell such as this is stimulated it generates an electric signal. This signal is then transported down to the body of the nerve cell and then further through the axon. The axon is a longer branch and can be surrounded by a myelin sheath which accelerates the transmission of the electric signal. The axon works like a one way street, the signal can only be transmitted in one direction towards the output side. At the output end synaptic buttons are responsible for transmitting the signal to further nerve cells or to muscle cells.

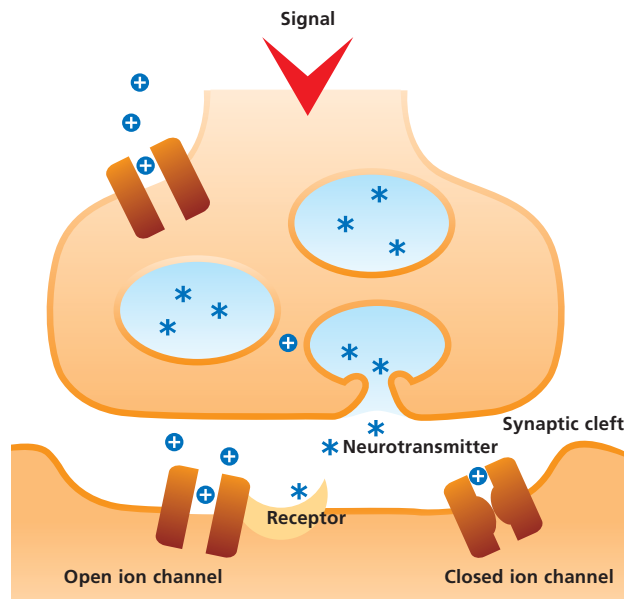
Nerve cell



Pain detection, transmission and perception

In the synaptic buttons the electric signal triggers the release of substances called neurotransmitters into the synaptic cleft. The neurotransmitter binds to receptors on the next nerve cell and causes the opening of ion channels. Ion channels are small holes that can be opened so that certain particles can pass through. Charged atoms, so called ions, flow through the channels into the cell. Because they are charged, an electric potential is built up and initiates the electric transmission of the signal.

Synapse

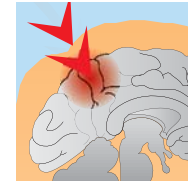


When the signal reaches the spinal cord it can be transmitted further to the brain, first to a central region called the thalamus and from there to the sensory regions of the cerebral cortex. Here the signals are translated into a perception of pain. The type and intensity of the signal decides if it is perceived as pain, just perceived as a touch or not at all.

In the spinal cord the signal can also cause a reflex. The signal is then passed on to other nerve cells called motor neurons that cause muscles to contract. In this way we can react to pain even before we have realised what kind of pain it is.

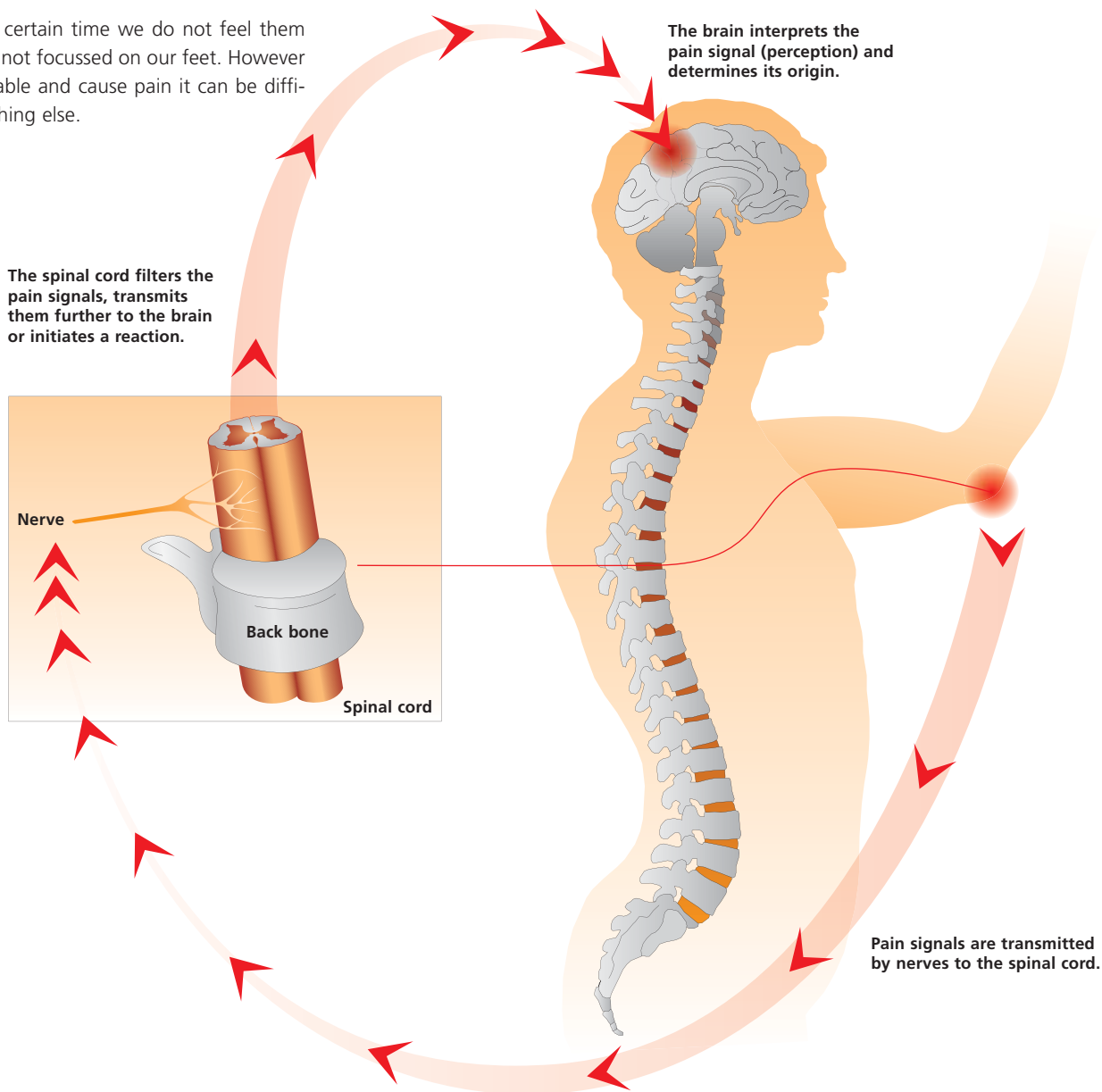
One example of this is touching a hot plate and retracting the hand even before consciously realising that it is hot.

Pain detection, transmission and perception



A huge amount of information is constantly being delivered from all the sensors in the body to the brain. Most of this information is filtered and never reaches our consciousness. Only in this way can we focus on what is important at the moment.

When wearing shoes for a certain time we do not feel them any more if our attention is not focussed on our feet. However if the shoes are uncomfortable and cause pain it can be difficult to concentrate on anything else.





Different kinds of pain

Pain comes in different intensities which can cause different sensations from stinging to burning or pounding. It often helps the diagnosis if the patient can locate the source of the pain and describe the type of pain.

Differentiation by location

- Somatic pain originates in the skin, muscles, joints, bones and connective tissues.
- Visceral pain originates in the internal organs and is caused for example by strain, spasm and inflammation.
- Neuropathic pain occurs when nerve cells are irritated or damaged.

Acute and chronic pain

- Acute pain has a restricted duration and disappears quickly, and can therefore be endured easier even at higher intensities.
- Chronic pain is either continuous (low back pain, tumour pain) or frequently recurring (migraine, angina), and is difficult to endure.

Psychogenic pain

- Not every pain is caused by irritated pain receptors. Psychological disturbances can also be expressed and described as pain. This perceived pain is clearly present and not just imagined.

Pain memory

If pain is not treated or not adequately treated the continuous pain signal that is transmitted to the brain can lead to a persistent change in the nerve fibres. The nerves become overly sensitive so that even the slightest touch or increased temperature is perceived as pain. Easy-to-treat acute pain can become hard-to-treat chronic pain.







Pain is strongly influenced by our perception. Every person reacts differently to pain. The situation can also influence our perception of pain. Fear for example can increase the perception of pain, distraction and human devotion can decrease it.





Pain intensity

Pain intensity cannot be measured because the perception of pain is individual. Therefore, to capture pain intensity, questionnaires are often used.

	0	1	2	3	4	5	6	7	8	9	10
Verbal descriptor scale	no pain		mild pain		moderate pain		moderate pain		severe pain		worst possible pain
Wong-Baker facial grimace scale											
Activity tolerance scale	no pain	can be ignored	interferes with tasks	interferes with concentration	interferes with basic needs	bed rest required					

With modern methods the activity of the different regions in the brain can be monitored. It is also possible to see if nerve cells are active. However it is not possible with even the most elaborate methods to measure how bad a patient feels with the pain.

The simplest method to quantify pain is using a so called visual analogue scale (VAS). The patient is asked to describe the pain intensity on a range from 0 to 10 where 0 is no pain and 10 is unbearable pain. This scale is often assisted by further descriptions of pain levels or pictograms.

For babies a variation of this scale is used, using the diagram of a child's face as an indication for the severity of its pain.

Other questionnaires also inquire about the location, and the exact sensation of the experienced pain. An exact description of the pain sensation can help to diagnose the disease.

Some situations or diseases might require a closer analysis. Different standardised questionnaires are available that help to assess the severity of a disease by its effect on the quality of life. Patients are asked if they can perform everyday activities like dressing, showering etc. on their own.

Pain and inflammation

Pain and inflammation are often closely linked and can induce a vicious circle as inflammation increases pain and pain stimulates the production of inflammation molecules.

To understand how pain and inflammation are linked we want to look at the following example. Touching a sharp object like a pin or a knife causes our body to react instinctively. The hand is retracted even before we are consciously aware of the situation. Immediately afterwards a sharp pain can be felt. Depending on the severity of the wound the heartbeat goes up as the body prepares a state of increased readiness to flee from a dangerous situation. This initial pain decreases within minutes to hours. The next day the wound has changed. The skin around the wound has turned red and sometimes feels warm. The sensation of pain has also changed. It is not the sharp initial pain but a more diffuse sensation of pain. However touching the unharmed, reddened skin around the wound just slightly might feel painful as well.

The reason for this change is the inflammatory process that has started. The pain caused by the wound has led the tissue surrounding it to start producing inflammation molecules. These molecules widen the small blood vessels. More blood is flowing into the tissue which is why the tissue turns red and might also feel warm. The inflammation molecules also increase the sensitivity of the nerve cells. Therefore even a gentle touch that would normally feel comfortable can suddenly feel painful in the affected area.

Because pain causes inflammation and inflammation increases pain treating pain often goes hand in hand with treating inflammation.





Treatment of pain

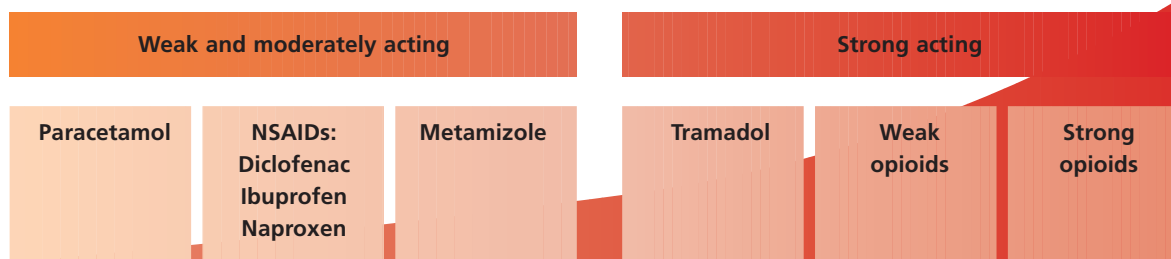
Because pain has different causes and intensities there is no optimal treatment for all painful conditions. Furthermore every patient reacts differently and therefore requires a personalised treatment of pain. The first goal however is to treat the cause of the pain.

Drug treatment

The widest used modality to treat pain is drugs. Different drugs or classes of drugs are used, depending on the intensity and origin of the pain.

Acetylsalicylate (Aspirin®) has a special position within the group of NSAIDs as it reduces blood clotting. It is therefore used in small doses in patients who have had a heart attack or stroke or who have a high cardiovascular risk to prevent the formation of blood clots. The side effect that can cause the stomach problems is here the desired effect. In the treatment of pain, acetylsalicylic acid has been widely replaced by the other NSAIDs with a lower risk of gastrointestinal side effects.

Pain



Drugs containing paracetamol are the first choice for the treatment of mild pain. Paracetamol has no marked effect on inflammation. It is gentle on the stomach but can cause serious side effects for the liver. Patients with known liver problems should seek advice from their physician before using these drugs. Concomitant intake of alcohol with paracetamol can be very dangerous and even fatal.

Many different molecules are in the class of non steroidal anti-inflammatory drugs (NSAIDs). The widest used contain diclofenac, ibuprofen and naproxen. All NSAIDs reduce pain and inflammation. NSAIDs can be harmful to the stomach and the intestine and may even cause bleeding. Patients suffering from gastric ulcers need to consult their physician before using these drugs.

Metamizole is a potent NSAID that is used in patients with more severe pain. However metamizole can cause blood problems like the reduction in white or red blood cells. Due to this additional risk its benefit must be weighed against the risk by the treating physician. Metamizole should only be taken as prescribed.

Tramadol is an especially weak opioid that seldom causes problems with breathing. However, it shares most of the undesirable effects of opioids like dizziness, nausea and sedation. Patients using drugs containing tramadol are not allowed to drive or use machinery. Like all opioids tramadol can cause dependencies and tolerance (reduction of efficacy over time). Tramadol is only indicated if NSAIDs are not effective enough and should only be used as indicated by the physician.



Treatment of pain

Weak and strong opioids all share the same undesirable effects they also cause dependency and tolerance. Opioids act by reducing the transfer of the nerve signal from one cell to the other. This is however not limited to pain signals but to other nerve impulses as well. Opioids can have life threatening undesirable effects like respiratory depression and a reduction of gastrointestinal activity. Opioids are controlled substances that are only used in special indications like immediately after surgery or for cancer pain.

For special kinds of pain certain specialised drugs are used

- For the treatment of migraine triptans are very effective, without the gastrointestinal side effects of NSAIDs and are therefore a good alternative for some patients. For severe migraine certain antiepileptic drugs might even be considered.
- For naturopathic pain certain antiepileptics and vitamin B often show better efficacy than classical drugs against pain.
- For musco-skeletal pain like low back pain spasmolytics that reduce muscle tension can help to reduce the pain.
- In severe rheumatic disease steroids like cortisone are used and act as very strong anti-inflammatory agents. To reduce the side effects of this treatment it is only done periodically, for example twice a year to reduce the peaks. Modified antibodies that capture inflammation markers were also shown to be very effective. However, they can also cause serious side effects and are therefore only used in severe cases.
- For very intense pain a local anaesthetic can also be used to temporarily block all nerve signals.

Non-drug treatment

Non-drug treatments can be used alone or in combination with drug treatments. As with drugs patients react differently to the various methods. The physician can only suggest different methods, the efficacy can be judged best by the patient. Sometimes it makes a lot of sense to try the different possibilities to see what has the best effect.

Physiotherapy helps to treat the cause of pain as muscles are trained and movements are optimised. Physiotherapy can also be used to reduce pain symptoms as it can help to relax (massage, warming, cooling).

Electrotherapy is based on the fact that nerve signals are transferred as electric signals. Targeted electric stimulation can help to balance the pain signalling system.

Hypnosis, biofeedback and relaxation techniques can help to change the perception of pain and increase the quality of life of patients with chronic pain.

For all treatments for pain, with and without drugs the effectiveness can ultimately be judged by the patient. Every patient has different needs and preferences and should discuss them with the physician. It is often helpful to try a different treatment if the current treatment does not bring the desired effect. The list of treatment options mentioned in this booklet is not complete. Your physician might provide further alternatives.

Caution

The drug that works miracles for your neighbour might not work for you – it might even be dangerous for you because you have different risk factors. Talk with your physician or pharmacist if you want to change your pain therapy.

Taking different drugs at the same time may increase the risk of undesirable effects. Do not change your medication and do not use drugs that you still have at home or that you bought without prescription without talking about it with your physician or pharmacist.

What is COX-2?

COX stands for cyclooxygenase. Cyclooxygenases are enzymes that facilitate chemical reactions. There are different versions of this enzyme in the body. While COX-1 predominantly produces molecules that reduce blood clotting, COX-2 predominantly produces molecules that increase inflammation.

NSAIDs reduce pain by inhibiting these cyclooxygenases and therefore reduce the production of inflammation molecules that increase pain. Some NSAIDs (like naproxen) nonselectively block COX-1 and COX-2 equally, others block one more than the other, and some selectively block COX-2 and have very little effect on COX-1 at therapeutic dosages. This latter class of selective NSAIDs like celecoxib are also called coxibs.

Rofecoxib (Vioxx®), a coxib was withdrawn from the market because an increased risk for cardiovascular events was found.

The reason for this increased risk is not completely understood. It is probably not only due to the COX-2 selectivity. An increased cardiovascular risk may occur with all NSAIDs.

If you have a high cardiovascular risk because you have already had a cardiovascular event like a heart attack or a stroke, or if you have risk factors like high cholesterol, hypertension etc. you should talk to your physician about the safe use of pain medication, even of the drugs you have purchased without prescription.

How can undesirable effects be avoided?

Every drug or treatment that has an effect can also cause undesirable effects. The physician carefully weighs the benefits against the potential risk of a treatment to minimize undesirable effects.

When choosing a certain drug for a patient the physician not only takes into account which drug might work best but also the probability of undesirable effects. The physician always has to balance the desired effects against the potential risk. This risk can be very different from one patient to the other depending on disease, age, sex, other risk factors and other concomitantly used drugs.

In some cases drugs are available in different formulations: as injectables, tablets, suppositories and topical forms like gels, patches or sprays. This allows the treatment to be tailored to specific needs.

For some undesirable effects an additional drug might be used to reduce the risk. For long term users of NSAIDs, gastroprotective drugs, so-called proton pump inhibitors, are often added to treatment. These drugs can reduce the risk of gastrointestinal bleeding caused by long-term NSAID usage.

You can help your physician to choose the right drug for you if you tell him about other drugs that you are using, even if you have bought them without a prescription. The physician needs to know your risk factors and preferences to choose the optimal therapy for you.



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