

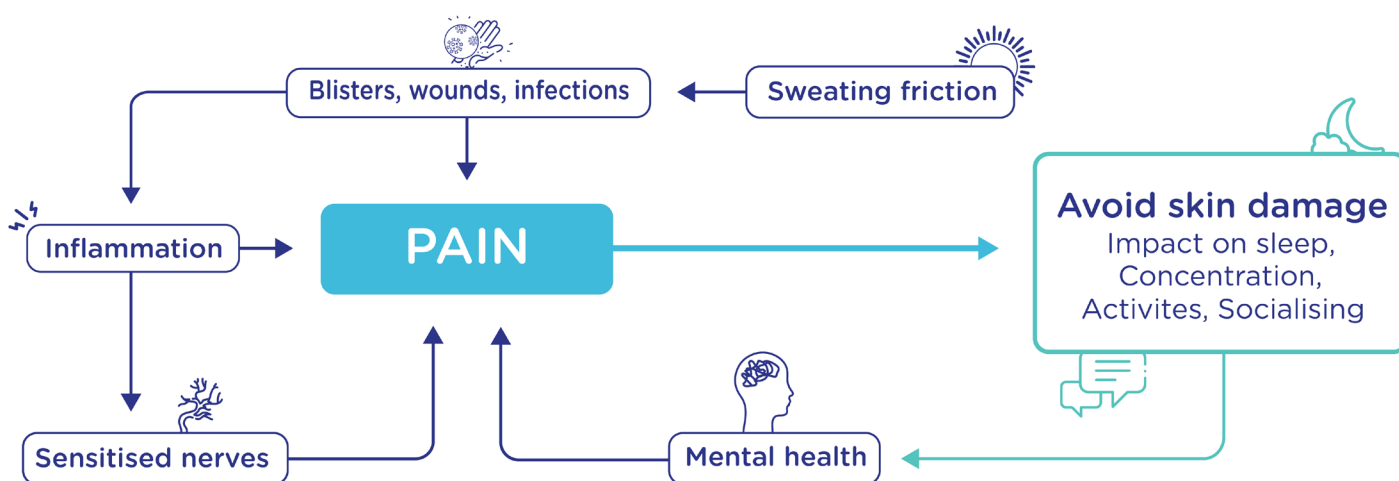
The science behind EB pain and itch

With thanks to Dr Syed Ammar Husain, Internal Medicine Trainee, UK

Some of the most difficult challenges of living with epidermolysis bullosa (EB) come from pain and itch, symptoms that affect many aspects of life. These can be due to blisters, wounds and the healing process but can persist even when skin appears healed due to changes in the nervous system. Understanding the science behind pain and itch can help make sense of why they happen, how they are connected and what can be done to manage them.

What is pain?

Pain is an unpleasant sensory and emotional experience associated with damage to the body. It may not be proportional to the amount of damage that is happening and can occur even without any damage at all, for example when the nervous system has become sensitised. It is subjective because people can feel and report sensations differently but, by any measure, pain is an unpleasant but vital alarm system that warns our body of harm. A natural response to pain is to attempt to stop whatever action is causing it and remember and avoid the cause in future. Memory of pain and anticipation of pain are part of how pain protects the body.

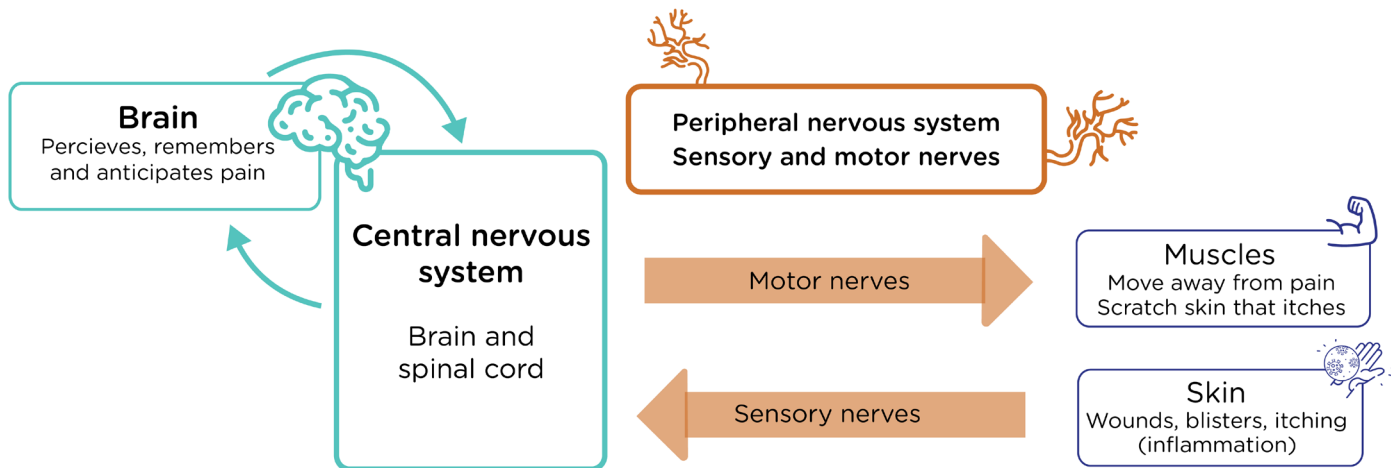


What is the nervous system?

The nervous system is made up of the central nervous system (CNS), which is the brain and spinal cord, and the nerves that spread from the CNS throughout the body, called the peripheral nervous system. It is responsible for detecting sensations through sensory nerves and directing actions through motor nerves. The nerve cells that make up the nervous system look very different to skin cells under the microscope. They can be as long as a metre in length to carry signals from toes or fingertips but are too thin to see with the naked eye.

One end, the receptor, reacts to chemical changes in the skin and creates an electrical charge that travels along the long thin 'axon' to the central nervous system. Nerve cells bundle together to form nerve fibres, like small roads joining motorways, that are big enough to be seen without a microscope.

There are millions of sensory nerve endings in the skin that send messages to the spinal cord and brain. The spinal cord can 'bounce back' a reflex action like moving away from something hot, by signalling to muscles through motor nerves without any more complex processing. The brain carries out the more complex thinking, remembering, anticipating, imagining, and conscious awareness of sensations including feelings of pain. Because of the brain's involvement, pain has a 'physical' and 'emotional' side with tiredness and worry often making pain feel worse.



How does pain happen?

Pain can feel sharp, dull, burning, aching, stabbing or throbbing, and different types of sensory nerve cells have been shown to be responsible for these different experiences of pain.

Pain can affect a person's emotional state, just as their emotional state can affect their brain's perception of pain. Being in pain can be exhausting and cause low mood or depression. Tiredness and depression can make pain feel worse.

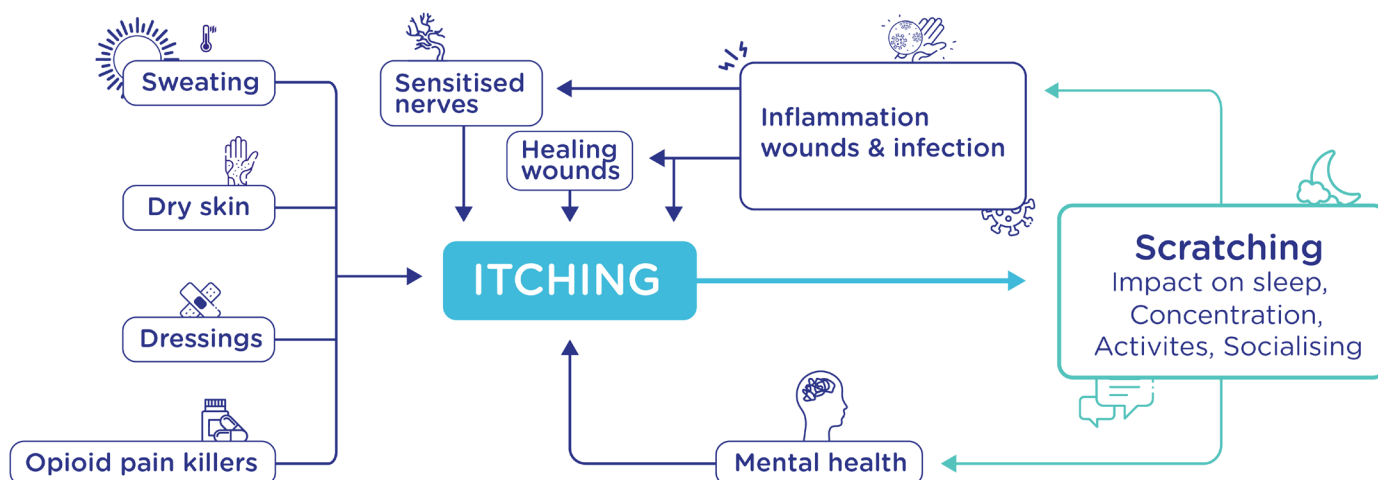
What is itch?

Itch, also known as 'pruritus', is the strong, unwanted sensation that makes a person feel they want to rub or scratch the skin. It is an alarm system like pain that can warn the brain that the body is under attack from insects, parasites, something small that might be about to bite, or if a harmful substance is starting to cause damage to the skin. A natural response is to wipe, flick, rub, scrub or scratch. Just like pain, itch can also affect sleep, mood, concentration, and quality of life.

How does itch happen?

Some sensory nerves near the surface of the skin are responsible for feelings of itchiness. They can react to immune proteins such as histamine, that are released from immune cells and keratinocytes (skin cells in the top layer of the skin) in response to tiny skin breaks or chemical irritants by sending electrical messages through the spinal cord to the brain.

The brain interprets this as itch and a person can, to some extent, decide whether to ignore the feeling or start scratching. Scratching typically gives a brief relief to the sensation. It momentarily interrupts the itch message, but can also cause minor damage to the skin, which can trigger more itch and lead to a vicious cycle.



Pain and itch are due to different nerves:

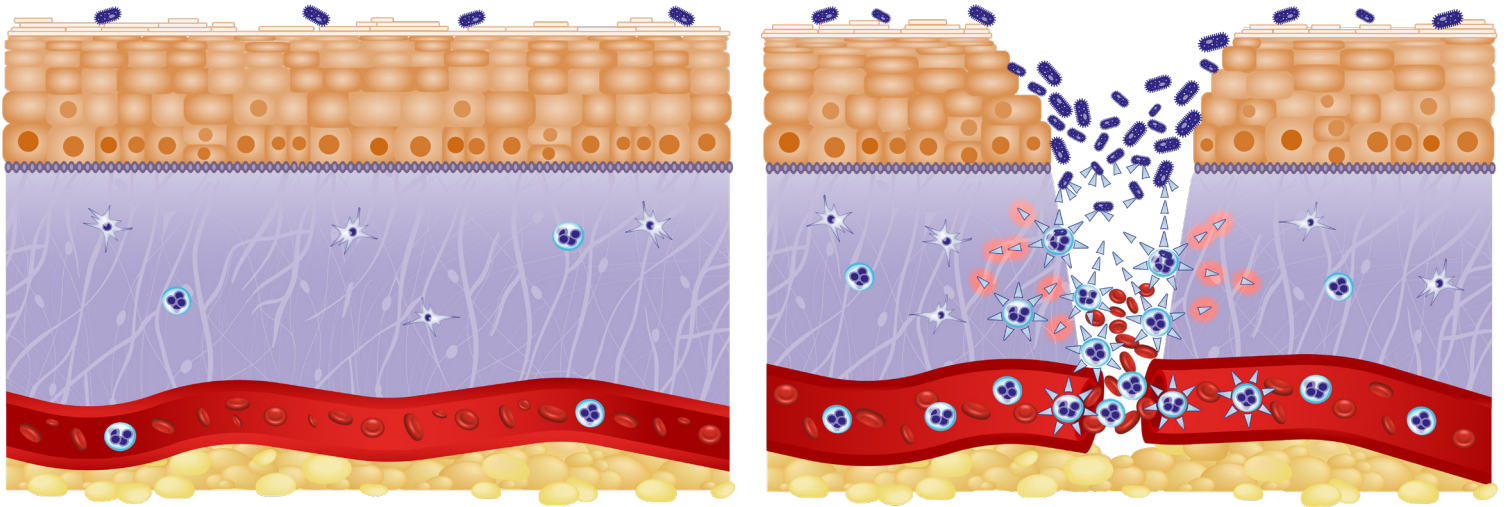
- Pain can be felt when skin is damaged and pain sensing nerves send signals to the brain (nociceptive).
- Itch can be felt when itch sensing nerves in the skin respond to slight damage such as scratches, tightness from healing wounds or dry skin, substances or medications that irritate the skin, or light touches from insects, hair or clothing (pruriceptive).
- Pain and itch can be felt when skin is healthy but there is damage to the nerves themselves, so they send signals to the brain without damage to the skin (neuropathic). If the sensory nerves are 'sensitised' by frequent skin damage, they can signal pain in response to touch that isn't harmful, like clothes rubbing against skin, or temperatures that aren't too hot or cold (nociplastic).
- Pain and itch can be felt without any damage at all to skin or sensory nerves when emotional or psychological factors cause the brain to perceive pain or itch (psychogenic).

Inflammation causes pain and itching:

Inflammation is an immune system process that the body uses in response to damage or infection. It involves skin cells and cells of the immune system and the proteins these cells make when they are damaged. Some of these proteins, such as prostaglandins, interleukins, bradykinin and histamine can make the sensory nerves in the skin more likely to send their pain or itch messages to the brain. Itching can cause skin damage leading to more inflammation and more itch and pain. When the skin is damaged, bacteria can grow quickly on an open wound. The immune system fights the bacteria with inflammation, but this causes extra pain.

Chronic, ongoing inflammation can make the sensory nerves in the skin and nerves in the central nervous system more sensitive, so they signal itch and pain more readily. This means that conditions such as EB, that involve persistent pain and itch, can sensitise the nervous system so that pain and itching continue even when wounds are healed. Although, inflammation can cause ongoing pain and itch, this is also part of the human body's normal healing and defence process to fight infection or any irritation.

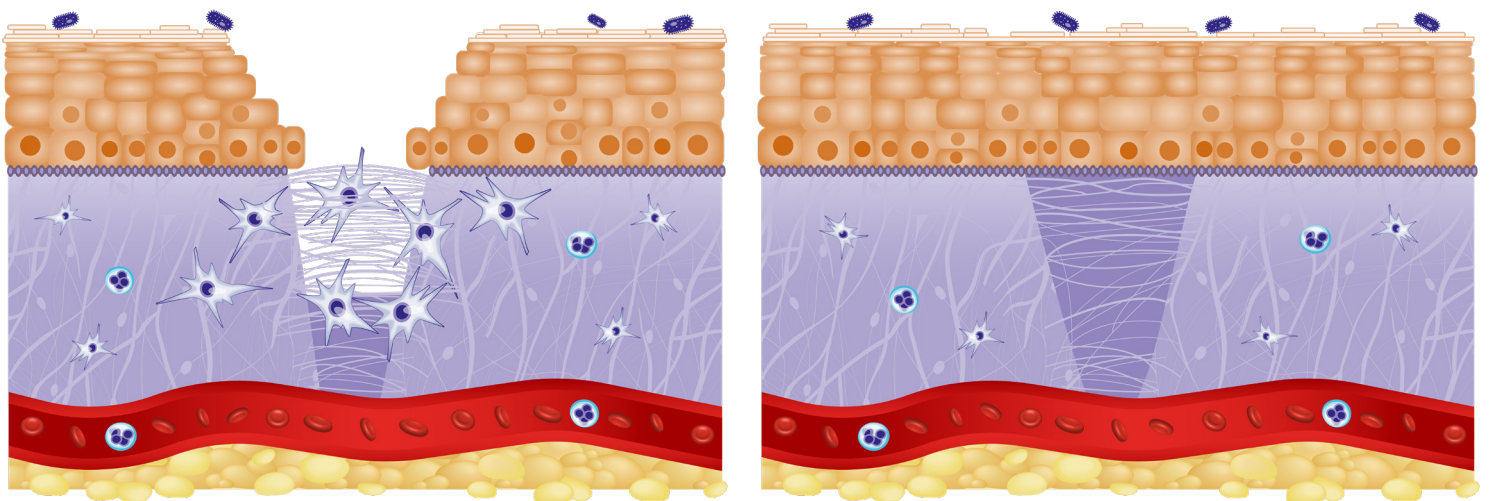
When healthy skin is damaged, cells release proteins as part of the inflammation process that can fight bacteria but also add to pain and itching:



Healing wounds can itch:

As a wound is healed by new skin forming, it is normal for it to feel dry or tight and itchy. Scabs can itch and the new nerve cells regrowing in the damaged area can be more sensitive. The itch experienced by people living with EB is often a mix of this normal prurceptive/cutaneous itch from skin injury, inflammation and healing, along with neuropathic itch from nerves that have been sensitised by so much itching. This means that the itching can continue for longer than would be expected and be triggered more easily in the skin of people living with EB.

During the process of skin healing, new nerves can be more sensitive to itch





Sweat can contribute

Sweating is part of the body's way of maintaining its temperature. Humans work best at a very specific temperature range, and all sorts of things can go wrong at higher (fever) or lower (hypothermia) temperatures. Any external heat source can warm up the body from the outside – the warmth from fires, radiators or the sun can be felt on the skin. When muscles work, they generate heat inside the body, so shivering is a method the body uses to warm up from the inside. Layers of air between clothes and the skin, trap heat and clothes can be very useful to keep the body at a comfortable temperature. When the body starts to overheat, a spray of water on the skin can help it to cool down very effectively because the water takes away some heat when it evaporates. Sweat is the body's natural way of providing this cooling. However, the dampness of sweaty skin can make it sticky. When sweaty skin rubs against itself it can become sore or itchy. Sweat isn't just water; it contains other substances that can be deposited on the skin as the water evaporates which may also cause itching. Sweat can be trapped under the skin and cause an itchy rash called 'heat rash' or 'prickly heat'.

'Acute' or 'chronic':

'Acute' and 'chronic' are words used to describe medical conditions and symptoms. Something that is acute, appears suddenly and gets better while something chronic is long-lasting. Some EB wounds appear rapidly then heal but EB itself is a life-long chronic condition. While some 'acute' wounds happen in response to damage then heal, others are 'chronic' wounds that remain open and unhealed for much longer. Pain and itch can also be acute, in response to damage, or chronic and last longer than the injury when a long-term condition affects the functioning of the nervous system.

The frequent, acute, wounding of the skin in EB as well as chronic wounds that heal very slowly can mean people living with EB experience frequent acute pain and itch, and also chronic pain and itch as the nervous system is affected by so much stimulation.

Pain and itch in EB

Pain and itch are among the most common symptoms experienced by people living with EB. Pain and itching at night can make it difficult to sleep leading to sleep deprivation and difficulties concentrating. Both pain and itch can negatively affect the mental health of those experiencing them and that of their loved ones and carers who witness these symptoms and support their wound care.

Treating pain and itch

The experiences of pain and itch both involve the nervous system linking the skin and the brain. They can happen together and can make each other worse. The skin can be protected with moisturisers (emollients) and non-adhesive dressings, and the body can be kept cool with fans or air conditioning. A cold pack on the skin can reduce inflammation and have a numbing effect by decreasing the signals the sensory nerves in the skin send to the brain. Loose-fitting cotton clothing and carefully chosen footwear can minimise sweating to help avoid blisters and wounds forming.

Pain and itching can be managed to some degree with different medicines. Any medicine should only be used under the guidance of a GP (general practice doctor), dermatologist (skin specialist doctor) or an EB specialist healthcare professional.

- painkillers (analgesics) such as paracetamol or opioids (morphine-based drugs) can reduce the brain's perception of pain.
- non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and antihistamines can reduce the inflammation that causes pain and itch.
- corticosteroids can be applied directly to the skin (topical) to reduce inflammation.
- antiseptics and prescribed antibiotics can reduce the bacteria that grow on wounds that make them more painful and slow down their healing.
- a prescription gel containing extracts from birch trees called Filsuvez can be prescribed for DEB and JEB to speed up wound healing.

The sensitisation of the nervous system can be made worse by stress, lack of sleep and anxiety. Cognitive behavioural therapy (CBT) and methods such as guided breathing and mindfulness can have a positive impact on this aspect.

EB is a complex condition, and it can be extremely challenging to manage these symptoms. Specialist EB dermatologists (skin doctors) and nurses can help, and DEBRA exists to support everyone affected by EB.