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# Types of pain. The flare up, a new entity?

## Tipos de dolor. El dolor reagudizado *(flare up)*, ¿una nueva entidad?

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ABSTRACT:

We can classify pain based on different conditions, such as its origin, temporality or pathophysiology. These classifications are interrelated with each other, allowing a global vision. Depending on its temporality, the pain can be acute as a normal, physiological response, whose duration does not exceed six months; chronic: one that persists after six months beyond the expected recovery or repair time; breakthrough pain understood as the acute exacerbation of pain that is rapid in onset, short in duration, and occurs spontaneously or in relation to an event despite the existence of stabilized and controlled baseline pain in patients with cancer pain; or a flare-up, exacerbation, explained as a period of temporary intense pain, which is more intense than chronic non-cancer pain. According to its pathophysiology, we classify it as nociceptive, that which arises from real or threatened damage to non-neuronal tissue; neuropathic, caused by injury or disease of the somatosensory nervous system; or nociplastic: impaired nociception despite no clear evidence of actual or threatened tissue damage. According to its etiology, we base ourselves on the seven types of pain of the ICD-11 classification.

RESUMEN:

Podemos clasificar el dolor en función de diferentes condiciones, tales como su origen, temporalidad o fisiopatología. Estas clasificaciones están interrelacionadas entre sí, permitiendo una visión global. Según su temporalidad el dolor puede ser agudo como respuesta normal, fisiológica, cuya duración no va más allá de los seis meses; crónico que es aquel que tras seis meses persiste superando el tiempo de recuperación o reparación esperados; dolor irruptivo, entendido como la exacerbación aguda del dolor de rápida aparición, corta duración y que ocurre de forma espontánea o en relación a un evento a pesar de existir un dolor basal estabilizado y controlado en pacientes con dolor oncológico; o una reagudización, exacerbación o brote, explicado como un periodo de dolor intenso temporal, que es más intenso que el dolor crónico no oncológico. Según su fisiopatología lo clasificamos en: nociceptivo, aquel que surge de un daño real o amenazado sobre el tejido no neuronal; neuropático, causado por una lesión o enfermedad del sistema nervioso somatosensorial; o nociplástico, nocicepción alterada a pesar de que no hay evidencia clara de daño tisular real o amenazado. Según su etiología nos basamos en los siete tipos de dolor de la clasificación CIE-11.

## Definition

In 2020, the International Association for the Study of Pain (IASP) reformulated the definition of pain through a group of experts and public exposure open to allegations. The need to cover situations previously not reflected in the definition and the search for recognition of chronic pain as a disease per se, make this definition a more inclusive concept. Among the conflicting points that the 1979 definition had were: The impossibility of identifying pain in patients with communication difficulties such as neonates or the elderly, even animals. The exclusion of a cognitive and social dimension. The need to give a perspective of illness rather than symptom. Issue included in the 11th edition of the International Classification of Diseases (ICD-11), which recognizes chronic pain as a disease in itself.

The current definition of pain according to the IASP is: “an unpleasant sensory and emotional experience associated or similar to that associated with actual or potential tissue damage.” Furthermore, the IASP emphasizes its definition with six key notes:

The biopsychosocial model of pain is understood as a personal experience influenced to varying degrees by biological, psychological and social factors.

Pain and nociception are not the same concept. Pain cannot be inferred exclusively from the activity of sensory neurons. Through their life experience, individuals learn the concept of pain. Respect for the personal story about the experience of pain.

Although pain often serves an adaptive function, it can have adverse effects on social and psychological function and well-being. Verbal description is only one of several behaviors to express pain; The inability to communicate does not negate the ability of a human or animal to experience pain.

## Pain classification

We can classify pain based on different conditions, such as its origin, temporality or pathophysiology. These classifications are interrelated with each other, allowing a global vision. Each of

the classifications will help us better understand pain, identify it in each patient and be able to propose a therapeutic attitude adapted to individual circumstances.

## Classification according to temporality

1. **Acute pain:** it is a normal, physiological and predictable response of the body to a physical, chemical or traumatic attack. It lasts depending on the healing or repair process and its duration is no longer than 3-6 months. It constitutes a physiological alarm response, since it warns us of a deterioration or danger to our integrity, allowing us to focus our attention on developing avoidance or protection mechanisms.
2. **Chronic pain:** pain whose persistence exceeds 3-6 months from its onset, which has the following characteristics:
   a) It exceeds the time of tissue repair or resolution of the problem that started it.
   b) It is secondary to pathophysiological changes that occur in our somatosensory system.
   c) It constitutes a disease in itself.
3. **Breakthrough pain:** acute exacerbation of pain of rapid onset, short duration and of moderate or high intensity, which occurs spontaneously or in relation to a predictable or unpredictable event despite the existence of stabilized and controlled baseline pain (Figure 1). patients with cancer pain. We can classify breakthrough pain into:
   a) Incidental breakthrough pain: related to an activity, gesture or procedure (sneezing, washing, postural changes, etc.). In most cases, these are predictable pains, so we can take measures to prevent or cushion them. When they are unpredictable, such as having a bad gesture, we cannot anticipate.
   b) Idiopathic breakthrough pain: without known cause, related to cancer pain in a progressive process. Sudden appearance.
   c) Breakthrough pain related to end of dose: before or around the next analgesic dose. It usually appears gradually and lasts longer than the previous ones.

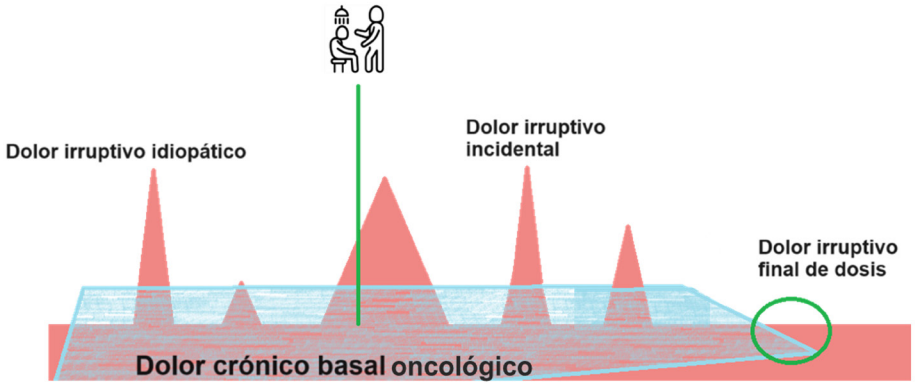


**Figure 1. Representation of the different breakthrough pains. The use of a prolonged-release step III drug as a treatment model for chronic baseline cancer pain is represented in blue.**

Breakthrough pain is directly related to cancer pain since there is no significant evidence of its presence in non-cancer pain in the available literature.

4. **Flare up:** it is a period of temporary intense pain, which is more intense than chronic non-cancer pain. Exacerbations can last hours or days, with no identifiable pattern and very little warning. Outbreaks can be either somatic or neuropathic pain.
   When we talk about chronic non-cancer pain, despite effective treatment for pain management, exacerbations are possible. Among the different exacerbations that can occur, we must differentiate (Figure 2):
   a) Exacerbation due to therapeutic exhaustion: when the basic treatment begins to have less effect, an increase in pain may appear. Its appearance is usually more gradual, beginning at the end of the dose. In such a case, the patient may benefit from a dose increase or rotation.
   b) Exacerbation due to new pain: This is pain in a new location or new symptom. It must be studied to identify the cause.
   c) Exacerbation due to flare or exacerbation: generally an increase in the intensity of your chronic pain, of variable duration, in the same location and with the

same characteristics. Although its pattern is difficult to identify, we must analyze whether there are triggers such as increases in activity, stress, climate changes, family or work challenges, etc.

The presence of flare-ups or exacerbations is common in chronic non-oncological pain, which, although limited, must be taken into account when considering optimal long-term treatment. Having a therapeutic plan that includes both the basic treatment (based on prolonged release drugs) and one aimed at exacerbations (where rapid releases are required), means for the patient to face their pain with more confidence, being aware that the Outbreaks are part of the evolutionary process of your disease (Figure 2).

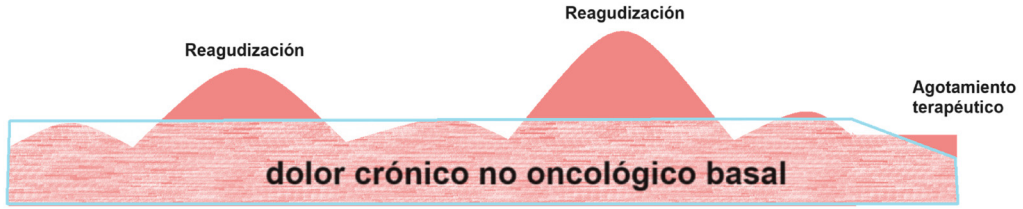


**Figure 2. Representation of chronic non-oncological pain in the form of a "roller coaster", where there are controlled oscillations with basal medication (in blue) and uncontrolled exacerbations or outbreaks, requiring treatment.**

Flare-ups, unlike breakthrough pain, do not appear suddenly as peaks of pain, but rather less abruptly and with longer durations.

## Classification according to its pathophysiology

Depending on the injury and the pathophysiological pathway that leads to the perception of pain, we must divide pain into:

1. **Nociceptive:** pain that arises from actual or threatened damage to non-neuronal tissue and owes its activation to nociceptors. It is understood as a normal response to a stimulus produced by tissue damage or injury, such as trauma or infection. It contrasts with the abnormal function that occurs in neuropathic pain. We can differentiate two types:
   a) Somatic pain: coming from the musculoskeletal system, as well as the meninges or bone marrow, in short from any non-visceral structure. It is the most common cause of chronic pain.
   b) Visceral pain: comes from the internal organs. For its diagnosis, it must be taken into account that many organs do not generate pain (liver, kidneys, lungs, etc.), that it can appear due to non-harmful stimuli and that it can trigger vegetative and reflex motor responses. It is a diffuse pain, poorly localized and sometimes accompanied by referred pain.
2. **Neuropathic:** pain caused by an injury or disease of the somatosensory nervous system. This is a clinical description and not a diagnosis, which requires a demonstrable injury or illness that meets the established requirements. There are two types:
   a) Peripheral neuropathic pain: somatosensory involvement caused by an injury or disease at a peripheral level, such as diabetic neuropathy or radiculopathy due to nerve compression.
   b) Central neuropathic pain: pain caused by an injury or disease of the central somatosensory nervous system. Pathologies such as multiple sclerosis or spinal cord injury can present this type of pain.
3. **Nociplastic pain:** it is an altered nociception despite there being no clear evidence of actual or threatened tissue damage causing activation of peripheral nociceptors or evidence of disease or injury to the somatosensory system causing the pain. It may appear accompanying nociceptive pain. Central sensitization can be defined as the central involvement of a peripheral process and has a duration or intensity that is not directly related to the peripheral damage presented, whether nociceptive or neuropathic.

There is the possibility that different types of pain coexist in a patient depending on the type of disease that causes it, in which case we will say that they present mixed type pain (Table I).

## Classification according to etiology

Classically, pain is defined from an etiological point of view in two large groups: cancer pain and non-cancer pain. This binary model does not make clear important aspects when evaluating the ultimate origin of the painful process, the mechanisms that have been carried out for its appearance and the possible consequences and expectations, since it leaves the group of chronic non-oncological pain (CDNO ) as a very heterogeneous group.

The World Health Organization (WHO), in collaboration with the IASP, has developed in response to the shortcomings of the International Classification of Diseases (ICD) in its ICD-10 version, a new and pragmatic classification of chronic pain for its version ICD-11. The objective was to have a useful classification system for the different levels of patient care, from primary care to units specialized in pain treatment, taking into account all kinds of specialties that could use it. This classification is based on perceived location, etiology, affected anatomical structure, or idiopathic condition. These disorders are divided into 7 groups:

1. **Chronic primary pain:** it is the appearance of pain in one or more anatomical regions, lasting more than 3 months and that is associated with significant emotional distress or functional disability and that cannot be better explained by another chronic pain condition. Within this group are: generalized back pain, fibromyalgia or irritable bowel syndrome.
2. **Chronic cancer pain:** includes pain caused by the cancer itself (the primary tumor or metastases) and by its treatment. This pain will be divided into visceral, musculoskeletal and neuropathic, and will also be described as continuous or intermittent (episodic, breakthrough).
3. **Chronic post-surgical and post-traumatic pain:** persistent pain beyond normal healing, for at least 3 months after the event. This is a diagnosis of exclusion, since other causes such as infection or recurrent malignancy must be considered.
4. **Chronic neuropathic pain:** Caused by an injury or disease of the somatosensory nervous system. It can be spontaneous or evoked (allodynia and hyperalgesia). Its diagnosis requires a history of a nervous system lesion and a plausible neuroanatomical distribution. It must present positive or negative sensory signs compatible with the injured structure. It will be classified as peripheral or central.
5. **Chronic headache and orofacial pain:** Within this group we find primary (idiopathic), secondary (symptomatic) headaches and orofacial pain, such as cranial neuralgia. To belong to this group, pain must occur on at least 50% of days for at least 3 months. Orofacial pain includes temporomandibular disorders, orofacial presentation of primary headaches, neuralgia such as trigeminal pain, persistent idiopathic orofacial pain or burning mouth syndrome.
6. **Chronic visceral pain:** persistent or recurrent pain of internal organs. It is usually perceived in the somatic tissues of the body wall of areas that receive the same sensory innervation as the offending organ (referred visceral pain). It is subdivided into: persistent inflammation, vascular, obstruction and distention, traction and compression, or combined.
7. **Chronic musculoskeletal pain:** arises as part of a pathological process related to bones, joints, muscles

**Table I.**

| | Nociceptive | Neuropathic | Nociplastic |
|---|---|---|---|
| **Concept** | Nociceptive activation due to non-neuronal damage | Lesion or disease of the somatosensory system | No evidence of actual or threatened tissue damage or somatosensory involvement |
| **Pathophysiology** | Normal response to the stimulus produced by damage or injury | Nerve compression, direct damage, or disease affecting the peripheral or central system | Altered perception in central processing |
| **Clinical** | Proportional, limited to the affected area Mechanical pattern. Antalgic posture | Positive symptoms: dysesthesia, paresthesia, allodynia, and hyperalgesia Negative symptoms: hypoesthesia, anesthesia | Disproportionate to the stimulus and unpredictable Sensitive areas to palpation |
| **Treatment response** | Responds to NSAIDs and opioids | Poor response to NSAIDs Responds to GABAergic drugs and norepinephrine and serotonin reuptake inhibitors Topical treatments such as capsaicin or lidocaine | Usually does not respond to prescribed treatments |

or related soft tissues. It is limited to nociceptive pain and does not include pain perceived on these structures that does not arise from them. The entities included are characterized by persistent inflammation such as infections, autoimmune or metabolic diseases (arthritis), or structural changes (osteoarthrosis).

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