

Pain as a disease: an overview

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Abstract: The acknowledgment of pain as a pathologic entity in its own right remains debated. Notwithstanding the data showing the burden of pain as a disease, an ultimate recognition of the pathologic nature of this condition is lacking. In this study, we analyze the notion of pain as a disease through an historical overview of its several conceptualizations and report the main evidence supporting this notion. We believe that a clear definition of pain as a disease is necessary, especially considering the enormous global burden of this condition. Indeed, the recognition of pain as a definite pathologic state is crucial to raise awareness about this neglected global health problem and to promote the exploration of new specific therapeutic approaches.

Keywords: pain, disease, chronic pain, classification

Introduction

The attempt to understand pain represents one of the oldest challenges in the history of medicine. Pain has a valuable role in medical action, as the symptom par excellence and, therefore, as a precious and meaningful tool. An important step forward in the scientific characterization of pain has been taken with the Sherrington's definition of the phenomenon as "the psychical adjunct of an imperative, protective reflex" and the description of its neurophysiological aspects.¹ Nevertheless, it is only with the discovery of abnormal pains that the phenomenon and its role start to be directly addressed in medicine, that is, when traditional interpretation of pain as a symptom of disease starts to weaken. As stated by John J Bonica, the founding father of pain medicine, in 1953, pain "in its late phases, when it becomes intractable, it no longer serves a useful purpose and then becomes, through its mental and physical effects, a destructive force".² Thus, in these circumstances, the peculiar nature of pain is revealed in its complexity, particularly because of the double value of the phenomenon, that is, pain is biologically a protective tool, but it can also lose its adaptive function and becomes a pathologic condition severely impacting quality of life.

The development of a universally accepted definition of pain and related concepts was indicated by John J Bonica as one of the main goals of the then rising International Association for the Study of Pain (IASP).³ Among the first proposals of the association there were, indeed, the definition of pain and the classification of chronic pain syndromes. These first efforts have contributed to stimulate a worldwide debate on pain terms and classification, which continues today.⁴

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If there is a general agreement nowadays on the definition of pain, the recognition of pain as a disease remains debated. Based on their duration, different types of pain are currently classified as chronic pain, whose commonly accepted definition is “that pain which persists past the normal time of healing”.³ However, although this definition has historically been helpful to distinguish between pain as a symptom of an underlying disease and more complex long-lasting pain states, this definition does not identify this condition as a distinct disease state.

In this paper, we report an overview of the several conceptualizations of pain as a disease since the pioneering work of John J Bonica in the 50s, in order to retrace the history of this notion and of its interpretations (Table 1). We aim to provide a breeding ground for reflection on the concept of pain as a disease and to encourage the identification of a new meaningful definition for this complex condition.

Pain as a disease: the impact of the problem

The European Federation of IASP Chapters Declaration on pain presented at the first Global Day against Pain claims that “chronic and recurrent pain is a specific health care problem, a disease in its own right.”⁵ This view, today extensively divulged at the institutional level by the main scientific pain societies, is still debated in the scientific community. The core question is whether chronic pain, recognized as different from pain as a symptom, can be considered as a disease in its own right.

According to the Merriam-Webster medical dictionary, disease is “an impairment of the normal state of the living animal or plant body or one of its parts that interrupts or modifies the performance of the vital functions (...)”.⁶ In addition, the definition states that a disease is usually characterized by specific signs and symptoms, and it is a response to environmental factors, infective agents, defects of the organism, or a combination of these factors. Three main aspects characterizing a disease are, therefore, 1) the presence of an impairment of the normal functions, 2) the presence of a specific symptomatology, and 3) a distinct etiopathogenesis.

Chronic pain has been notoriously defined as the pain that lasts longer than the usual course of an acute injury or disease or the pain that recurs for months or years.¹⁰ The value of this definition is its ability to describe all the conditions that can be defined as chronic pain even if it does not refer to the impairment brought about by the pain, the presence of specific symptoms, and the supposed etiologic framework. This is also because chronic pain is a term employed to

Table 1 Pain as a disease: first usage of the term, features, and supporting evidences

	Bonica, 1953 ²	Bonica, 1990 ⁹	Raffaelli, 1992 ¹	Cousins, 1999 ²³	Siddall and Cousins, 2004 ²⁴	Niv and Devor, 2004 ⁵	Melzack, 2005 ²⁹	Cousins, 2007 ⁵⁰	Tracey and Bushnell, 2009 ³⁰	Dubois et al., 2009 ³²
Term	Pathologic pain	Chronic pain	Pain as a disease	Chronic pain	Persistent pain	Chronic pain	Chronic pain	Persistent pain	Chronic pain	Maldynia
Features	Pain deviating from the physiologic norm	Pain persisting beyond the usual healing course of an acute injury or disease, or the pain recurring at intervals for months or years	Dysfunction of the endogenous nociceptive system	Persisting pain causing physical effects involving the nervous system	Persistent pain entailing changes expressed in a specific constellation of symptoms	Autonomous disease with own symptoms and a specific tissue physiopathology	The output of the body-self neuromatrix activating perceptual, homeostatic, and behavioral programs after injury, pathology, or chronic stress	A self-perpetuating condition which may be due to biologic, psychological, and environmental factors	A condition characterized by a disordered nervous system	A neurologic condition characterized by pathologic changes in the nervous system
Evidences	Hypothesis grounded on clinical evidences	Clinical evidences	Hypothesis grounded on a theoretical idea and clinical evidences	Clinical cases and experimental studies	Literature review	Clinical and experimental evidences	Experimental and clinical evidences	Literature review	Literature review	Literature review

Abbreviation: AAPM, American Academy of Pain Medicine.

define several diverse conditions whose common feature is the presence of persistent pain.

According to a 2014 study on the global burden of chronic pain, at least 10% of the world's population is affected by a chronic pain condition and every year, an additional 1 in 10 people develops chronic pain.⁷ Even if these data are confirmed also for the low-income and middle-income countries, the unequal distribution of risk factors and pain management options leads the most disadvantaged to bear higher burdens of persistent pain and less effective treatment.⁸ A 2012 study of the National Institutes of Health's National Center for Complementary and Integrative Health shows that nearly 50 million American adults have chronic or severe pain;⁹ according to the American Academy of Pain Medicine, in the USA, pain affects more Americans than diabetes, heart disease, and cancer combined.¹⁰ The data from Europe present similar results: the 2006 enquiry on the prevalence of chronic pain shows that 19% of adult Europeans are affected by this condition, seriously compromising their quality of life.¹¹

Chronic pain is a disabling condition. As reported by Turk et al, "chronic pain affects every aspect of a patient's life, contributing to a loss of both physical and emotional function, affecting a patient's levels of activity (ability to work at home and job and engage in social and recreational pursuits);"¹² furthermore, the authors remark the economic consequences of this condition for the sufferers, as a result of the health care expenses and the potential decrease in financial income. A recent analysis of the morbidity and disability data from The Global Burden of Disease highlights "the high prominence of pain, and diseases associated with pain, as a global cause of disability in both the developed and developing countries", with chronic low back pain as the single greatest cause of years lost due to disability.¹³ Chronic pain negatively impacts the quality of life also because of the unmet needs of pain management: a 2008 survey on the quality of life of chronic pain sufferers shows high percentages of chronic pain patients suffering from issues related to their mental health, employment status, sleep, and personal relationships.¹⁴

Beside the huge impact of chronic pain on the quality of life, another relevant issue is the relation between pain and mortality: a 2009 work cohort record linkage study suggests that severe chronic pain is associated with increased risk of mortality, independent of sociodemographic factors.¹⁵

Notwithstanding the amount of data currently available accounting for the pathologic character of pain, a full acknowledgment of pain as a disease is still lacking. One of the major obstacles in this regard is the lack of an ultimate

etiologic description of chronic pain supporting a view of pain as a disease instead of a syndrome; as a matter of fact, the majority of chronic pain conditions are defined on the basis of their pathologic manifestation. The nosologic endeavor is, therefore, thwarted by the absence of an etiological description allowing to group together diverse conditions primarily characterized by the presence of persistent pain. This situation entails the fact that chronic pain as a disease is mainly a clinical definition, a diagnosis a posteriori, made when the clinician recognizes the presence of a pathologic process primarily characterized by pain.³

In the last half of the century, there have been several attempts to identify the pathologic nature of chronic pain by looking at the different features that might define this condition as a disease in its own right, but none of them has brought an ultimate recognition of pain as a disease.

Pain as a disease: a debated concept

The roots of the conception of pain as a disease have to be retraced in the work of the pioneers of pain medicine, the medical branch established in the USA in the 60s with the aim of creating a specific discipline for the study and the management of pain. The leader of this movement, John J Bonica, was also the author of the first medical textbook entirely devoted to pain, *The Management of Pain*, first issued in 1953. In this work, Bonica distinguishes between normal and abnormal pain on the basis of time and physiology: pain becomes pathologic when, if persisting, loses its biologic damage signaling function and, with its devastating psychophysiologic consequences, becomes a destructive force hard to manage with traditional therapeutic means. Thus, in his perspective, this so-called intractable pain has to be considered as a pathologic entity requiring a specific therapeutic approach.

Further progresses toward the acknowledgment of the specific nature of persistent pain were made in the 80s, although this recognition was still based only on the difference in terms of behavioral manifestations between this condition and acute pain. Indeed, in two 1981 studies, Sternbach¹⁶ and Pilowski¹⁷ remark that chronic pain, that is, the pain persisting after the healing of the injury, is totally different from acute pain because of its pathologic psychobehavioral manifestations. As highlighted by Doleys, in those years chronic pain was seen as "a set of behaviors or responses to some type of insult or injury that exceeded expectations and extended beyond the normal healing time (...). Thus, chronic pain was that which was 'left over' after the 'real' disease resolved."¹⁸

A crucial step forward in the definition of pain as a disease was taken in the 90s, when chronic pain was first defined as an autonomous entity, not only in opposition to acute pain. In the 1990 edition of *The Management of Pain*, Bonica devotes an entire chapter to chronic pain and defines it as the pain “which persists a month beyond the usual course of an acute disease or reasonable time for an injury to heal, or pain that recurs at intervals for months or years”.¹⁹ The acknowledgment of the specificity of chronic pain, already indicated in the 1986 first edition of the classification of chronic pain syndromes by the IASP Subcommittee on Taxonomy,²⁰ becomes a central subject of widespread international debate. At the Second Congress of the Italian Society of Pain Clinicians held in 1992, Raffaelli put forward the idea that there could not be a system so complex as the endogenous pain system, consisting of several receptors involved, at the neurophysiological level, in the integrative pain modulation, without a pathologic counterpart. According to this view, although the underlying mechanisms are still unknown, pain should be recognized as an autonomous pathology, that is, a “chronic pain status” characterized by the sole and imperative presence of the pain requiring a therapeutic response.²¹ In 1995, Raffaelli reinforced this view by organizing with the ISAL (Istituto di Scienze Algologiche) School a symposium entitled “Pain as a disease. Neurophysiological and clinical aspects”.²²

The change in the view of chronic pain that occurred in the 90s was so dramatic that in 1999, Michael Cousins stated that “chronic pain will be regarded as the disease of the 21st century.”²³ In a 2004 work, Siddall and Cousins further strengthened this view by claiming that chronic pain is a disease with its own pathology, symptoms, and signs, based on the pathophysiological changes brought about by pain itself.²⁴

In the 21st century, the identification of pain as a disease in its own right is supported by further reflections by pain medicine experts. In his 2004 Bonica lecture, John D Loeser recalls *Encyclopedia Britannica*’s definition of disease as “an impairment of the normal state of an organism that interrupts or modifies its vital functions” and concludes that since “chronic pain certainly does modify functioning, in many different ways”, it has to be recognized as a disease in its own right.²⁵

The efforts in providing specific biologic characterization of pain as a disease continues in the 21st century, when crucial studies reveal the pathologic features associated with persistent pain, especially at the nervous system level.^{26–28} In his 2004 lecture at the Congress of the World Institute of Pain, Ronald Melzack described chronic pain syndromes to

be caused as a result of “neural mechanisms gone awry”.²⁹ In the last decade, significant progresses in this field have been made, also thanks to the noteworthy contribution from neuroimaging studies. Compelling evidence of functional, structural, and chemical changes occurring in the brain in association with chronic pain were reported in a 2009 review by Tracey and Bushnell.³⁰ In the authors’ view, these findings support the idea that chronic pain should be put “in the realm of a disease state” as a condition characterized by a disordered nervous system.³¹ In the same year, the American Academy of Pain Medicine put forward a Position Paper recommending to distinguish between two categories of pain and proposing a new terminology for pain: *eudynia* and *maldynia*, literally good pain and bad pain.³² While the first one refers to pain as “a symptom of an underlying pathological disorder, either an illness or an injury”, *maldynia* denotes instead “‘pathological pain’, referring to pain as a neuropathological disorder or disease process that occurs due to changes at cellular and molecular levels”.

Today, it is recognized that persistent pain entails a pathologic reorganization of the neural system.³³ This process can be due to several factors, such as a genetic predisposition,^{34–36} central sensitization mechanisms,³⁷ and many other factors, which are at the core of the study of the etiology of pathologic pain conditions.³⁸ However, despite the progress in the understanding of the neuropathological changes associated with persistent pain, achieved especially thanks to the contribution of neuroimaging studies, two main questions remain open: 1) Do neuroimaging studies define chronic pain as a disease?^{39–40} 2) Is the definition of chronic pain as a brain disease useful, especially in the clinical practice?⁴¹ Cohen et al challenge the view of pain as a disease, by claiming that scientific findings showing pathologic changes associated with persistent pain are not sufficient to define pain as a disease.⁴² According to the authors, there are no “‘characteristic’ clinical features apart from the complaint of pain” which “constitute the ‘disease’ of pain” and the sole presence of pathologic symptoms is not enough to define pain as a disease which, on an explanatory ground, does not tell us a lot. However, beyond controversies on the definition of pain as a disease, we agree with the authors that the primary issue to be addressed in the debate is: how defining pain as a disease would improve our approach to this condition?

Conclusion

Today, it is acknowledged that there is an essential difference between pain as a symptom and chronic pain. The scientific community has also recognized the specificity of

this condition on the basis of the identification of several associated pathologic modifications, but the recognition of pain as a disease in its own right remains debated, principally owing to the lack of an ultimate scientific description of this pathologic condition. Nevertheless, we believe that the acknowledgment of pain as a disease, and its clear definition and classification, should be intensively pursued. In 2015, the IASP Task Force for the classification of chronic pain proposed a new categorization of pathologic pain conditions for the 11th Revision of the International Classification of Diseases (ICD-11).⁴³ This work aims at filling the gap in the World Health Organization's ICD by presenting a "classification system that is applicable in primary care and in clinical settings for specialized pain management". As remarked by the authors, "the lack of adequate coding in the ICD makes the acquisition of accurate epidemiological data related to chronic pain difficult, prevents adequate billing for health care expenses related to pain treatment, and hinders the development and implementation of new therapies." Thus, the lack of a proper definition of this condition hampers adequate investigations,⁴⁴ which could lead to a more accurate estimation of the burden of pathologic pain.⁴⁵ This situation entails the denial of the pain sufferers' right to be recognized as ill and even affects their ability to identify themselves as ill⁴⁶ and to receive adequate health care support; this would also entail a reduction of the number of inappropriate diagnostic procedures aimed at finding "the cause of pain". Moreover, the fact that today pain is not recognized as a public health care priority⁴⁷ hinders scientific research on pain, including its risk factors and comorbidities.⁴⁸

Thus, a vicious circle is created: without a definition of pain as a disease, despite the scientific knowledge already available on the pathologic mechanisms underlying this condition and the socioeconomic burden of chronic pain, pain does not gain the attention it deserves and is not adequately studied in order to consolidate definitively its recognition as a disease in its own right. Therefore, we believe that proposals aimed at improving the definition of pain as a disease which might result in a primary pain diagnosis and an adequate classification of its clinical forms should be embraced and encouraged.⁴⁹

Significance

This work contributes to the debate on the acknowledgment of chronic pain as a disease, presenting an historical overview of the definitions of this entity in the scientific literature. By recalling the reflections on this entity and its main features since Bonica's first analysis, we aim at providing a wider

perspective to the international debate aimed at recognizing pain as a disease in itself.

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Author contributions

WR and EA designed, drafted, and revised the manuscript. Both authors approved the final version of the article and take full responsibility for its content.

Disclosure

The authors report no conflicts of interest in this work.

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