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Editorial

The labyrinth of pain and the need for fostering basic research

El laberinto del dolor y la necesidad de impulsar la investigación básica

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The International Association for the Study of Pain (IASP), defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [1,2]. Chronic pain is considered as a disease and a public health problem worldwide. Pain is the most frequent reason for medical visits, in particular among the elderly, with significant repercussions for the quality of life of the people who suffer from it. According to the aphorism by Hippocrates, medicine does not always cure, but it must try to provide relief – from what – from pain. The World Health Organization predicts that deaths due to cancer (the second leading cause of death in the world) will double by 2030; and every year there are 5.5 million people with end-stage cancer in whom pain management is inadequate [3].

In this new century in the United States, Congress declared the country's purpose of designating the first decade as the "10 years of pain research and control"[4]. Assessing pain as a vital sign (the fifth vital sign) and establishing a management protocol has been the motto of current times worldwide [5]. However, are the mechanisms underlying acute pain similar to those underlying chronic pain? Is the pathogenesis of pain fully understood? Do factors like genetics, the environment, culture, personality and the plasticity of the nervous system per se influence pain intensity and progression? Unfortunately, these and many other questions are still unanswered and these cunundrums are expected to be solved through cell, genetic and molecular biology research conducted in animal models (mice), despite the deceitful and misguided controversy of banning animal studies [6]. In this respect, some legislations, like the European, are clear in rejecting experiments with primates, with very specific exceptions such as prevention, diagnostic or treatment studies on life-threatening diseases that cannot otherwise be conducted in humans [7].

Mammals are equipped with a powerful system to fight pain, i.e., the endogenous opioid system consisting of beta-endorphins, met-leu-enkephalins and dynorphins that act as

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neurotransmitters and neuromodulators on 3 classes of receptors – mu, delta and kappa –producing an analgesic effect. Medical science has developed and used molecules that intervene at these sites of action with highly effective effects (opioids) [8]. Nonetheless, pain control is not always possible, because there other types of receptors and ion channels that affect and alter neuronal status, leading to continuing or irreversible damage; in other circumstances, afferent nociceptive stimuli travel along aberrant nervous pathways [9] which do not respond to analgesics or NSAIDs used routinely but to other specific biological therapies or even therapeutic options that have shown certain positive effects such as transcutaneous electrical nerve stimulation, acupuncture, antidepressants, anticonvulsants, etc. [10–12]. Some of the ion channels, like the TRPV1, have been identified in nociceptive neurons where, upon activation, they release neuropeptides and neurotransmitters, creating action potentials through the central nervous system fibers until they reach the brain where they are perceived as painful stimuli. In the periphery, they may release pro-inflammatory compounds which sensitize other neurons, making them prone to respond to physical, thermal or chemical stimuli that may be blocked using anti-inflammatory agents or local anesthetics [13].

Despite the large number of expert pain professionals working in this area, the management of chronic pain has only been possible through a comprehensive multi-disciplinary approach, used only in a small number of institutions that have understood the efficacy and cost-effectiveness of this type of strategy. There is a need to set up specialized units for the treatment of pain as the main pillars for the implementation of clinical and basic pain research programs and policies. Molecular biology has been a tool of basic science in its attempt at understanding the multiple mechanisms of nociceptive and neuropathic origin. On the other hand, clinicians have learnt that there is no single way to relief pain and, as long as there are no other alternatives, the trend will continue to be that of implementing multimodal and multidisciplinary management.

Modifications to the cell's genetic material (microsomal DNA-RNA) [14], as well as nutritional, chemical and even social and cultural influences, may alter genetic expression with pro- or anti-nociceptive effects. However, research on the genetic manipulation that may result in the understanding and management of pain is in the phase of animal experimentation [15,16].

Scientific societies have the commitment and obligation to discuss, share and make recommendations on the needs and requirements of the health sector for including the care and management of pain. Moreover, they must foster and encourage research policies as well as the implementation of scientific advances in clinical practice centers, both public and private. Developed countries where research is a priority driver of economic and social development have recognized the huge value of molecular biology for understanding the genetic, epigenetic and pharmacogenomic determination and variation of pain. These are activities that might contribute to personalized prescriptions and have a greater individual impact, rendering medical practice safer and more effective while reducing side effects and enhancing prompt pain control [17–19]. Readers are encouraged to read the report entitled "Unidad de Tratamiento del Dolor. Estándares y recomendaciones de calidad y seguridad" [2].

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