

## Osteoarthritis Etiology: Pain as a Basis of Local Therapy

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**Abstract:** The article describes the etiology of pain occurrence, namely, structures in which it initially occurs and ultimately leads to the progression of symptoms. It describes the mechanism of interaction between the central and peripheral nervous system in the formation of a vicious circle and chronic pain. As the result of literature sources analysis the author concluded that, there are multiple sources of pain in case of osteoarthritis, but they all originate directly in or around the joint. This is the main reason to use the local therapy in the treatment of osteoarthritis. In the case of local impact on the source of pain the best and fastest result is achieved, in comparison with the standard therapy.

**Key words:** Osteoarthritis • Topical Treatment • Pain • Vicious Circle Of Pain • Pathological Pain • Neurogenic Inflammation

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### INTRODUCTION

Pain associated with musculoskeletal disorders, in varying degrees, affects up to 20% of the adult population of the planet [1, 2]. About 30% of the adult population in the U.S. suffers from joint pain, limited mobility or swelling [3]. According to C.G. Helmick (2008), in the U.S. 46.4 million people are experiencing joint pain, representing 21% of the total population of the country [4].

The main clinical sign of osteoarthritis is a joint pain and the pain is due to the pathological changes in articular cartilage [5]. Accordingly to him, neurophysiological substrate of joint pain is always the synovium, which plays the role in the regulation of neurotrophic functions and processes of life support of joint tissue. The pain is directly involved in the provision of the trophic links of articular cartilage; it is richly supplied with nerve fibers and nociceptors, blood and lymphatic vessels. Subchondral bone, periosteum, ligaments, joints, muscles and joint capsule are also richly innervated sources of nociception in osteoarthritis [6, 7]. Articular cartilage itself, by virtue of its anatomical and physiological features (lacks innervation) and cannot be the cause of pain [8].

Other causes of pain are associated with the formation of osteophytes [9], subchondral bone trabeculae microdamage [10], bone ischemia and increased intraosseous pressure [11]. Studies of blood flow and intraosseous pressure in areas of bone, adjoined to the damaged joint with osteoarthritis, appear to violate the vascular clearance of the bones and prove that there is an increase of intraosseous pressure [12, 13].

In case of osteoarthritis synovium hypertrophies, fibrosis appears, synoviocytes are activated, resulting in forming of the lymphocytic infiltrate [14]. Also synovium trauma is occurring caused by osteophytes. Synovitis is often goes along with osteoarthritis leading to structural changes in joint tissues and correlates with the intensity of pain [15, 16].

As a result of the above events, evolved algogens (prostaglandins, kinins, histamine, serotonin, nitric oxide and others) [17] irritate receptors located in tissues that make up the joint (modal A-delta-nociceptors, polymodal C-nociceptors, "sleeping" nociceptors) and destroy the cartilage [18, 19]. Impulses from these receptors are transmitted to the posterior horn of the spinal cord. The axons of sensory cells of the posterior horn form the spinothalamic way that conveys pain

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afferentation to thalamus and from them-to different parts of the brain (nuclei of the thalamus and the somatosensory cerebral cortex). Single pain center does not exist [20].

The strength of pain is regulated by endogenous analgesic systems. These are a non-opioid and opioid systems and also a descending pain inhibition path through which falling impulses are sent from the central nervous system in the rear horn of the spinal cord.

Long course of such disease as osteoarthritis leads to chronic pain that gradually loses its protective function, which is inherent to physiological pain. Pathological pain is developing, which differs by losing the signal value and does not have an activating effect on the mechanisms of elimination of the algogenic factor. It is also accompanied with clinical and behavioral reactions [21].

Zones of primary and secondary hyperalgesia begin to form. Primary hyperalgesia develops in the tissues of the affected joint, Secondary-can spread to healthy tissues. At the heart of the development of primary hyperalgesia is a phenomenon of peripheral sensitization (damage of the sensitivity of nociceptors to the actions of the damaging stimulus.) Secondary hyperalgesia is the result of central sensitization (increased excitability, primarily with the nociceptive neurons in the posterior horns of the spinal cord).

Sensitization of nociceptors is the result of the action of algogens coming from blood plasma and released from damaged tissue and also in C-fibers and from peripheral terminals-C-nociceptors. The latter in great numbers are presented in the joint capsule, ligaments, meniscus, the periosteum and subchondral bone sites [22, 23].

C-nociceptors' neuropeptides have proinflammatory effects. Cleared the activation of C-nociceptors, leading to the development of "neurogenic inflammation", causing vasodilation and increase vessels' permeability. In addition, they promote the release of mast cells and white blood prostaglandins, cytokines, biogenic amines, which, in turn, affect the free nerve endings of nociceptors, increasing their excitability and thus closing vicious circle.

Also in the aggravation of nociceptive pain a reflective muscle tension plays an important role. The increase in the excitability of nociceptive neurons in the structures of the central nervous system leads to a reflex activation of the anterior horn motor neurons of the spinal cord segments and tonic contraction of muscles. Their long-term stress impairs blood flow to muscle tissue. As the result, processes as hypoxia and acidosis are developing; an allocation of arachidonic acid and biogenic amines begins. These inflammatory mediators act

on nociceptors again, sensitizing them. Loci of painful muscle joints appears which further increases the flow of afferent nociceptive impulses to the posterior horn of the spinal cord and other divisions of the central nervous system. Muscular component contributes to the vicious circle of pain in case of osteoarthritis [24-27].

Synovitis-an important symptom of articular inflammation in case of osteoarthritis. Pain in this case usually becomes permanent and is associated with long-term sensitization of nociceptors during inflammation of synovial membrane. The severity of synovitis correlates in this situation with the severity of pain, but not with the degree of cartilage destruction. The presence and intensity of synovitis correlates with the radiographic stage of the gonarthrosis [28]. Dense thickenings of the joint margins (osteophytes) are often well palpable, can be painful and are the important differential diagnostic feature of osteoarthritis.

In addition, IL-1 is involved in the process of inflammation in osteoarthritis, which stimulates the synthesis and the secretion of many cartilage destroying ferments, including latent collagenase, latent stromelysin, latent gelatinase and tissue plasminogen activator [29].

Based on the foregoing, at the same time a set of inflammatory processes are running in the affected joint (inflammation due to osteoarthritis, neurogenic inflammation, inflammation in muscle tissues, tendons, ligaments), which determine the sources of pain.

Particular attention in understanding of the pathogenesis of pain in case of osteoarthritis should be given to the role of prostaglandins. They accompany almost all pathological processes associated with the mechanism of pain in osteoarthritis. And that is the main rationale for local anti-inflammatory therapy directly in the affected joint.

V.I. Mazurov (2008) identifies several specific types of pain in case of osteoarthritis [30]:

Mechanical pain-occurs in case of the load on joints, takes time in the evenings, subsiding after a night's rest. They are associated with a gradual increase in pressure on the bone; in this case bony beams bend and put pressure on the spongy bone receptors.

Starting pain-occurs in the presence of reactive synovitis at the beginning of walk (or load), then quickly fade and are renewed after the ongoing exercise. Starting pain may occur during the process of damaged cartilages rubbing against each other, on the surface of which cartilage detritus falls (fragments of necrotic cartilage). During the first steps this detritus is pushed into the joint cavity and the pain stops [31].

Pain, associated with tendobursitis and peri-arthritis, occurs only during movement, which involves the affected tendon and also in case of certain positions of a joint during movement.

Pain, associated with venous hyperemia and blood stasis in the subchondral bone on the background of an intraosseous hypertension, usually occurs at night, is dull in nature and disappears in the morning while walking.

Reflex pain-is due to reactive synovitis, which leads to reflex spasm of surrounding muscles and hypoxia.

Reference pain-is associated with involvement of the joint capsule in inflammatory and degenerative process, which leads to compression of the nerve endings and appearance of pain, which increases with movement (increased tension of capsules). They may appear in the area of unaffected joint, for example, in case of damaged hip joint can be felt in the knee joint (reflex irradiation of pain).

“Siege pain”-occurs during the periodic "jamming" of the joint as a result of infringement of sequestration of cartilage (articular "mouse") between the joint surfaces. This is usually a sudden sharp pain, blocking movement in the joint, which just as suddenly disappears at a certain position of the epiphyses, creating conditions to slide "mouse" from the articular surface.

Pain associated with irritation of the synovial membrane osteophytes.

S.M. Noskov (2007) gives other types of pain case of osteoarthritis, which are associated with concomitant venous disorders [32].

According to many authors, in case of osteoarthritis patients experience a psycho-emotional component of pain [33-35] and pain behavior [36].

Other important clinical expressions are closely related to the pathological process of inflammation and pain case of osteoarthritis, that is the stiffness in the affected joint after the rest (not to exceed, however, 30 min), varying degrees of joint mobility in the performance of individual movements, a sense of instability in the affected joint and functional limitations up to reduced disability.

That is why pain-one of the most important clinical expressions of osteoarthritis [37].

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