Cartilage degeneration, Osteoarthritis and patients' suffering : where are we?

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Despite the socioeconomic burden imposed by osteoarthritis(OA), the etiology remains unclear. Because OA has been considered primarily a disease of articular cartilage, most researchers have focused on the pathophysiology of articular cartilage degradation. Aging decreases the ability of chondrocytes to maintain and restore articular cartilage. Oxidative stress, advanced glycation end products, and reduced anabolic response to growth hormone have been postulated as the most prominent mechanisms linking aging and OA. A protective effect of estrogen replacement therapy(ERT) on the incidence and prevalence of OA has been reported. In vitro, estrogen has synergistic effect on cartilage matrix synthesis when co-treated with insulin-like growth factor(IGF). Mechanical factors associated with wear and tear on the joint have been the most important factors found in association with site-specific OA. Indian hedgehog, MAP kinase, and basic fibroblast growth factor were reported to play an important role as mediators for shear and compression stress related cartilage degradation. Lacunar emptying as a typical feature of OA cartilage has led to the assumption that cell death is a central feature in OA cartilage degeneration. There is an intriguing possibility that chondrocyte death and matrix loss form a vicious cycle, the progression of one having detrimental effects on the other. Recently, the mechanism of pain generation in OA is gaining interest. It is widely reported that the severity of radiographic OA is not related with the degree or the

presence of pain. Some investigators suggest that our inability to effectively manage OA pharmacologically is the result of overemphasis on articular cartilage and on the inflammatory phase of OA. In a recent animal study of gunea pig OA, no significant correlation between the severity of joint degeneration and nociception was noted, corroborating the clinical observation that pain is a poor predictor of OA severity. A study using monoiodoacetate induced rat OA model revealed that neuropathic pain mechanism plays a role in the process of pain in this model. In addition, a protective role of endogenous opioid system in OA has also been reported. In evolutionary terms, local inhibition of pain would allow the individual with OA to continue normal life despite mild tissue damage and would impart an advantage for survival.