Osteoarthritis in 2010

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Owing to the rapidly aging world population, osteoarthritis (OA) is becoming a more significant public health issue. Most people over 60 years of age will have some form of OA and approximately half will experience symptoms. Although significant progress has been made in providing short-term relief of pain from OA, the major unmet need is for pharmacological agents that are able to stop or reverse the progression of the joint structural damage. Recent innovations in the pharmaceutical drug discovery environment have generated new chemical entities with the potential to become disease-modifying OA drugs (DMOADs). However, appropriate clinical trials will have to be designed to demonstrate the favorable benefit:risk ratio of any new compound prior to approval from a regulatory agency for labeling as a DMOAD.

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Till Uhlig and colleagues assess the burden of OA from patient and societal perspectives [1]. This disease has potentially devastating effects on health-related quality of life and will represent an increase in the economic burden of healthcare in the future. This article serves as a strong introduction to this issue as it reminds us that both pharmacological and nonpharmacological treatment modalities are important, and that the choice of therapy must take into account evidence of effectiveness and particular disease risk factors in an individual.

Animal models of OA have been extensively used to gain insight into the disease process and to explore new potential therapeutic targets. The review presented by Jean-Pierre Pelletier and collaborators, which focuses on some animal models, summarizes the work done with these models to explore the disease-modifying capability of a number of OA drugs and agents [2]. There has been extensive development of preclinical models of OA targeting structural changes in the different tissues of the joint, which has brought forth new and valuable information that has translated into more new promising treatments for clinical development, including DMOADs, bringing novel therapeutic options to patients suffering from OA.

The importance of the role played by new imaging technologies in the diagnosis and assessment of OA structural changes is summarized by Stephanie Tanamas *et al.* [3]. In the last decade, a number of new sensitive and reliable technologies, such as MRI, have been developed, providing useful information not only on the cross-sectional aspect and longitudinal changes of structural changes of the different joint tissues, but also on the risk factors associated with the progression of the disease. MRI technology has also recently been shown to be a promising tool in multicentre knee OA DMOAD trials, as it has been proven more sensitive than x-rays at establishing the effectiveness of drug treatment. There is a strong belief within the scientific community that MRI will, in the near future, replace radiographs in the assessment of musculoskeletal diseases and, more specifically, of OA. Other imaging technologies, such as ultrasound and CT scans, are also undergoing interesting developments in the musculoskeletal field and will likely provide new applications.

Daniel Lajeunesse, and Roxana Monemdjou and colleagues shift the paradigm of OA, which has focused mainly on the articular cartilage, to the disease concept of a whole-organ failure that includes other joint tissues such as bone [4]

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and synovial membrane [5], respectively. Their reviews concentrate on the involvement of these tissues in the pathophysiology and progression of OA. The review by Daniel Lajeunesse focuses on strong scientific evidence that underscores the key role played by the subchondral bone in OA, for which the exact causes leading to this tissue remodeling still remain to be ascertained. He explores the pathways involved in this tissue remodeling in OA, describing the mechanisms that are likely to be responsible for such alteration. A better understanding of the cross-talking between bone and articular cartilage will undoubtedly open new doors for the management of OA. For their part, Roxana Monemdjou and colleagues look at the critical role of synovitis as an active component in the pathogenesis of OA and cartilage degradation. More specifically, they address the complex factor/mediator network involved in this disease tissue. They conclude that the understanding of the precise interplay of these factors/mediators is essential for the effective treatment of OA.

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Besides pharmacological and surgical therapies, nonpharmacological therapies including, but not restricted to, education and self management, regular telephone contact, referral to a physical therapist, aerobic, muscle strengthening and water-based exercises, weight reduction, working aids, knee brasses, footwear and insoles, thermal modalities, transcutaneous electrical nerve stimulation, or acupuncture are of primary importance in the management of OA. Olivier Bruyère and collaborators review basic and current concepts of nonpharmacological management of OA, with a special focus on exercise intervention [6]. Unfortunately, in the daily management of OA, these noninvasive, usually harmless, therapeutic approaches are neglected, hence depriving the patient of interesting and highly efficient therapeutic options.

Jorge Roman-Blas *et al.* assess the role of glucosamine sulfate (GS) in the management of knee OA [7]. After reviewing the mechanisms of action of GS in OA, including the evolving concept that GS does not act through stimulation of proteoglycans or cartilage matrix components, but instead through the inhibition of catabolic enzymes responsible for cartilage degradation, they address the controversy regarding the efficacy of GS with respect to symptomatic improvement of OA. Also explained are how several potential confounders, including the use of prescription medicines versus over-the-counter pills or food supplements, or the use of GS versus glucosamine hydrochloride, may have relevance when attempting to interpret the seemingly contradictory results of different clinical trials.

A better understanding of the etiopathophysiological role of cytokines in the pathophysiology of arthritic disorders has been instrumental in the development of new therapies for arthritis. A number of biological agents targeting cytokines and some immunological processes have been developed for the treatment of musculoskeletal diseases. This field has experienced explosive development in the last decade, with most of the new therapeutic agents available focusing on the treatment of inflammatory arthritis used in rheumatoid arthritis. As reviewed by Xavier Chevalier and colleagues, some clinical studies have explored the usefulness of a number of anticytokine agents for the treatment of OA [8]. Although the results are too preliminary to draw any conclusions at this time, new and promising results have been obtained. Further investigation is needed to explore the potential of biological agents, both for the treatment of disease symptoms as well as their DMOAD effects. The point made by Xavier Chevalier *et al.* regarding the benefit:risk ratio of biological treatment in OA is a major one that needs to be addressed thoroughly.

Much progress has been made in recent years in the understanding of the pathophysiology of OA. Moreover, there have been important advancements in identifying new therapeutic targets and developing DMOAD agents that can be tested in clinical trials. There is hope that some of these new agents will soon be available to successfully treat patients suffering from this extremely debilitating disease.

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