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Preface **xv**

David J. Hunter

Etiopathogenesis of Osteoarthritis **1**

Kenneth D. Brandt, Paul Dieppe, and Eric Radin

Because of the implications for prevention and treatment, how a clinician views osteoarthritis (OA) matters. We view OA as an attempt to contain a mechanical problem in the joint and as failed repair of damage caused by excessive mechanical stress on the joint. OA is organ failure of the synovial joint. Because of insufficient focus on reduction of the habitually loaded contact area of the joint and on aberrant loading, we believe that therapeutic efforts aimed at pathogenetic mechanisms in OA have been misdirected: neither the large role that a reduction of excessive levels of mechanical stress plays in promoting the healing response in OA nor the evidence that relief of joint pain and improvement in function, rather than the appearance of the articular surface, are the most important outcomes of the healing process have been sufficiently emphasized. Various mechanical abnormalities can trigger the processes involved in repair and attempts by the joint to contain the mechanical insult, but without a return to mechanical normality, attempts at healing will fail. In our view, drugs may be helpful symptomatically, but cannot accomplish this. In our view, as long as the joint remains in the same adverse mechanical environment that got it into trouble in the first place, it is unlikely that a drug that inhibits a specific enzyme or cytokine in the pathways of cartilage breakdown, or further stimulates the already increased synthesis of cartilage matrix molecules will solve the problem of OA. Also, because the subchondral bone is critically important in containing the mechanical abnormalities that damage the cartilage, emphasis on cartilage repair alone is likely to be futile. On the other hand, if the abnormal stresses on the joint are corrected, intervention with a structure-modifying drug may be superfluous.

Role of Bone in Osteoarthritis Pathogenesis **25**

Steven R. Goldring

Much of the attention in developing diagnostic tools and therapeutic interventions for the management of osteoarthritis (OA) has focused on the preservation or repair of articular cartilage. It is clear that all of the joint components, including the ligaments, tendons, capsule, synovial lining, and periarticular bone, undergo structural and functional alterations during the course of OA progression. This article focuses on the specific skeletal features of OA and the putative mechanisms involved in their pathogenesis.

The Role of the Meniscus in Osteoarthritis Genesis

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Martin Englund

The history of treating meniscal lesions has been characterized by firm belief in “radical” surgery, with serious long-term consequences for the individual and society. The menisci play a critical protective role for the knee joint through shock absorption and load distribution. Currently, the consensus in surgical treatment of meniscal tears is to preserve as much functional meniscal tissue as possible. Still, meniscal lesions are common, especially in the osteoarthritic knee. For health professionals, these lesions present a challenge in choosing the treatment that is best for the patient in both the short term and long term. A degenerative lesion, in the middle-aged or older patient, could suggest early-stage knee osteoarthritis and should be treated accordingly. Surgical resection of nonobstructive degenerate lesions may only remove evidence of the disorder while the osteoarthritis degradation proceeds. Well-designed randomized, controlled clinical trials are needed.

The Contribution of Genes to Osteoarthritis

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Ana M. Valdes and Timothy D. Spector

Osteoarthritis (OA) is the most prevalent form of arthritis in the elderly. A large body of evidence, including familial aggregation and classic twin studies, indicates that primary OA has a strong hereditary component that is likely polygenic in nature. Traits related to OA, such as longitudinal changes in cartilage volume and progression of radiographic features, are also under genetic control. In recent years several linkage analyses and candidate gene studies have been performed and unveiled some of the specific genes involved in disease risk, such as *FRZB* and *GDF5*. This article discusses the impact that future genome-wide association scans can have on our understanding of the pathogenesis of OA and on identifying individuals at high risk for developing severe OA.

The Measurement of Joint Mechanics and Their Role in Osteoarthritis Genesis and Progression

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David R. Wilson, Emily J. McWalter, and James D. Johnston

Mechanics play a role in the initiation, progression, and successful treatment of osteoarthritis. However, we don't yet know enough about which specific mechanical parameters are most important and what their impact is on the disease process to make comprehensive statements about how mechanics should be modified to prevent, slow, or arrest the disease process. The objectives of this review are (1) to summarize methods for assessing joint mechanics and their relative merits and limitations, (2) to describe current evidence for the role of mechanics in osteoarthritis initiation and progression, and (3) to describe some current treatment approaches that focus on modifying joint mechanics.

- The Symptoms of Osteoarthritis and the Genesis of Pain** 83
David J. Hunter, Jason J. McDougall, and Francis J. Keefe
- This article delineates the characteristic symptoms and signs associated with OA and how they can be used to make the clinical diagnosis. The predominant symptom in most patients is pain. The remainder of the article focuses on what we know causes pain in OA and contributes to its severity. Much has been learned over recent years; however, for the budding researcher much of this puzzle remains unexplored or inadequately understood.
- Osteoarthritis: Current Role of Imaging** 101
Ali Guermazi, Felix Eckstein, Marie-Pierre Hellio Le Graverand-Gastineau, Philip G. Conaghan, Deborah Burstein, Helen Keen, and Frank W. Roemer
- Osteoarthritis (OA) is the most prevalent joint disease; it is increasingly common in the aging population of Western society and has a major health economic impact. Despite surgery and symptom-oriented approaches there is no efficient treatment. Conventional radiography has played a role in the past in confirming diagnosis and demonstrating late bony changes and joint space narrowing. MRI has become the method of choice in large research endeavors and may become important for individualized treatment planning. This article focuses on radiography and MRI, with insight into other modalities, such as ultrasound, scintigraphy, and CT. Their role in OA diagnosis, follow-up, and research is discussed.
- The Management of Osteoarthritis: An Overview and Call to Appropriate Conservative Treatment** 127
David J. Hunter and Grace H. Lo
- This article presents a general outline for the management of the patient with osteoarthritis in the form of a narrative review considering diagnosis, investigation, and treatment. It is not a comprehensive discussion (subsequent articles on imaging, weight management, exercise, braces and orthotics, pharmacologic intervention, and surgery provide more detail); rather, it provides the clinician with an overview of what is available. Inevitably, there is much the interested clinician can do rather than practice nihilistic waiting. The authors encourage active clinician involvement and instilling self-management strategies in patients to further promote effective long-term treatment of this pervasive disease.
- Obesity and Osteoarthritis: Disease Genesis and Nonpharmacologic Weight Management** 145
Stephen P. Messier
- The mechanisms by which obesity affects osteoarthritis (OA) are of great concern to osteoarthritis researchers and clinicians who manage this disease. Inflammation and joint loads are pathways commonly believed to cause or to exacerbate the disease process. This article reviews the physiologic and mechanical consequences of obesity in older adults who have knee OA, the effects of long-term exercise and weight-loss interventions,

the most effective nonpharmacologic treatments for obesity, and the usefulness and feasibility of translating these results to clinical practice.

Muscle and Exercise in the Prevention and Management of Knee Osteoarthritis: an Internal Medicine Specialist's Guide

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Kim L. Bennell, Michael A. Hunt, Tim V. Wrigley, Boon-Whatt Lim, and Rana S. Hinman

This article outlines the influence of muscle activity on knee-joint loading, describes the deficits in muscle function observed in people with knee osteoarthritis, and summarizes available evidence pertaining to the role of muscle in the development and progression of knee osteoarthritis. The article focuses on whether muscle deficits can be modified in knee osteoarthritis and whether improvements in muscle function lead to improved symptoms and joint structure. This article concludes with a discussion of exercise prescription for muscle rehabilitation in knee osteoarthritis.

Knee Osteoarthritis: Primary Care Using Noninvasive Devices and Biomechanical Principles

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K. Douglas Gross and Howard Hillstrom

Osteoarthritis (OA) is an epidemic for which there is no known cure. There is enormous popular demand for noninvasive and nonpharmacologic therapies for OA, and there is a pressing need for primary care physicians to respond by updating their pattern of practice. Despite increasing concern about the capacity of our health care system to meet rising demands, routine primary care for knee OA has changed little over several decades. This article introduces physicians to many of the most important noninvasive devices used in the conservative management of symptomatic knee OA.

The Role of Analgesics and Intra-Articular Injections in Disease Management

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William F. Harvey and David J. Hunter

The most important goals of therapy in patients with osteoarthritis are pain management, improvement in function and disability, and, ultimately, disease modification. This review discusses the current pharmacologic regimens available to address these goals. Specific attention is paid to current trends and controversies related to pharmacologic management, including the use of oral, topical, and injectable agents.

Surgery for Osteoarthritis of the Knee

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John C. Richmond

The role of surgical treatment in osteoarthritis of the knee continues to evolve. The indications for arthroscopy have narrowed. Orthopedic surgeons continue to explore options less invasive than total knee replacement for isolated unicompartmental arthritis of the knee joint. In addition to arthroscopy, this article discusses the merits and drawbacks of and indications for osteotomy, interpositional arthroscopy, patellofemoral replacements, and emerging technologies for total knee replacements.

How Close are We to Having Structure-Modifying Drugs Available? 223

David J. Hunter and Marie-Pierre Hellio Le Graverand-Gastineau

This review describes the potential of disease-modifying osteoarthritis drugs (DMOADs), distinguishing between preventing, retarding, stopping, and reversing disease and what might be clinically meaningful. The authors also describe whether there is any evidence to suggest that one can modify disease, and whether the current tissue that is predominantly focused on, namely, cartilage, is an appropriate target. The methodologic approaches and other obstacles to demonstrating efficacy of these agents in clinical trials are considered. This discussion is a narrative review in a field that is rapidly evolving. It is hoped the reader appreciates the complexity of the field and the likely road ahead to DMOAD development.

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