Osteoarthritis (OA) results from interaction among a number of complex biologic processes, both degradative and reparative. There is a growing trend to view the joint as an entire organ and primary OA as a disease of this organ. OA can be classified as primary or secondary. The secondary form of OA, for the most part, involves, a structurally or biomechanically faulty joint, with superimposed risk factors that affect the intensity and distribution of loading forces across the joint surfaces. However, for most patients who suffer from this disease, inflammatory components are present to a variable degree. This chapter focuses on research advances in the understanding of the major etiopathogenic factors contributing to OA, with emphasis on the cellular biology, molecular mechanisms, and biochemistry of joint tissues as well as the role played by relevant inflammatory and growth factors. A section on new diagnostic tools and therapeutic advances is also included.