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Why is osteoarthritis an age-related disease?

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Although older age is the greatest risk factor for osteoarthritis (OA), OA is not an inevitable consequence of growing old. Radiographic changes of OA, particularly osteophytes, are common in the aged population, but symptoms of joint pain may be independent of radiographic severity in many older adults. Ageing changes in the musculoskeletal system increase the propensity to OA but the joints affected and the severity of disease are most closely related to other OA risk factors such as joint injury, obesity, genetics and anatomical factors that affect joint mechanics. The ageing changes in joint tissues that contribute to the development of OA include cell senescence that results in development of the senescent secretory phenotype and ageing changes in the matrix including formation of advanced glycation end-products that affect the mechanical properties of joint tissues. An improved mechanistic understanding of joint ageing will likely reveal new therapeutic targets to slow or halt disease progression. The ability to slow progression of OA in older adults will have enormous public health implications given the ageing of our population and the increase in other OA risk factors such as obesity.

Osteoarthritis (OA) is a classic age-related disorder. It is often described as a chronic degenerative disease and thought by many to be an inevitable consequence of growing old. In OA, degradation and loss of the articular cartilage is a central feature that is sometimes attributed to wear and tear. However, unlike an automobile tire that wears thin over time, the tissues affected by OA contain living cells that respond to mechanical stimulation and function to maintain joint homeostasis. Rather than OA being a simple consequence of joint ageing and repeated wear and tear, the current conceptual framework

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for the relationship between ageing and OA is that ageing of the musculoskeletal system increases the susceptibility to OA but alone does not cause it. Changes outside the joint (including sarcopenia and reduced proprioception) and within the joint (including cell and matrix changes in joint tissues) contribute to the development of OA, when other OA risk factors are also present (Fig. 1). The concept that ageing contributes to, but does not directly cause, OA is consistent with the multifactorial nature of OA and the knowledge that not all older adults develop OA and not all joints in the body are affected to the same degree. In this review, we discuss the relationship between ageing and the development of OA from both an epidemiological perspective and a biological perspective, with the goal of answering the question of why OA is an age-related disease.

Epidemiology of OA relevant to ageing

OA is the most common joint disorder in the world and one of the most common sources of pain and disability in the elderly [1,2]. While there remains considerable heterogeneity in defining OA among epidemiological studies, the evidence is conclusive that age remains the single greatest risk factor for the development of OA in susceptible joints. Radiographic changes, in particular, osteophytosis, are very common in the ageing population and, when used alone, may provide an overestimation of the true prevalence of symptomatic OA. Defining OA solely as joint pain occurring in an older adult without evidence for another form of arthritis is also inaccurate as there are many causes of non-articular pain, such as bursitis, that are common in older adults. In a study of 480 adults over the age of 65 years, who reported chronic knee pain, only about 50% had radiographic evidence of knee OA [3]. A recent systematic review [4] comparing the prevalence of knee pain and radiographic knee OA found considerable discordance between the two, adding further evidence to that already present that joint pain and severity of radiographic changes of OA do not correlate. However, Duncan et al. have shown through their work with the Knee Clinical Assessment Study cohort that, as the severity and persistence of knee pain increases, the degree of discordance between symptoms and radiography diminishes [5,6].

Due to the discrepancies between pain and radiographic evidence of OA, most current epidemiological studies define OA by a combination of clinical and radiographic criteria. The most-often used system for defining symptomatic OA is the American College of Rheumatology (ACR) OA criteria. The

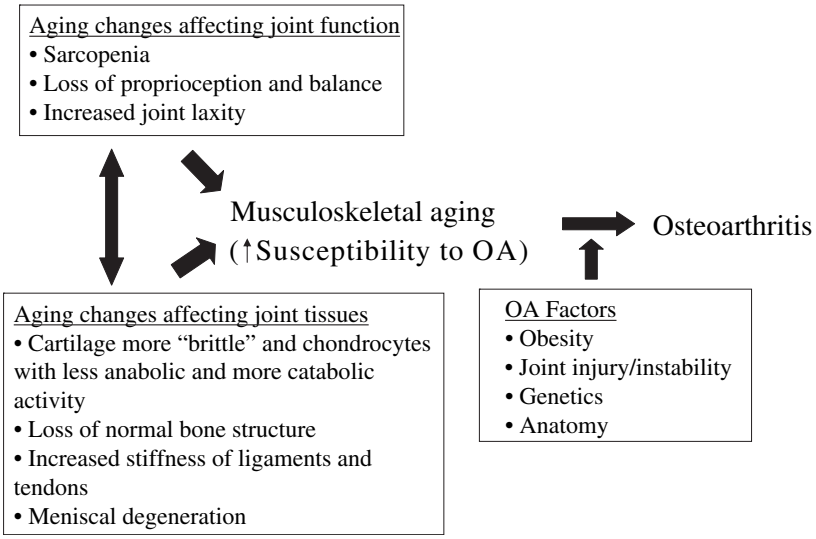

Fig. 1. Relationship between musculoskeletal aging and the development of osteoarthritis. Changes that affect joint structure and function with aging increase the susceptibility to developing osteoarthritis but additional factors (OA factors) are usually also present which lead to the development of symptomatic OA. Reproduced with permission from Hazzard's Geriatric Medicine and Gerontology, Sixth Edition, McGraw Hill Medical, 2009.