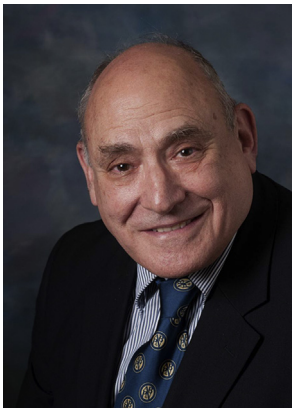
Editor-in-Chief's Note

Associations About Arthritis



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This issue is wholly devoted to the topic of subclinical or early-stage rheumatoid arthritis (RA). While he was transitioning from his role as our Topic Editor for Endocrinology, Diabetes, and other Endocrine Disorders, Dr. John G. Ryan took on additional responsibilities in the area of new content development for *Clinical Therapeutics*. His first project was to team up with our Topic Editor for Rheumatology, Dr. Tommy Cheung, to form an international working group to discuss early-stage RA, with an emphasis on the clinical burden, natural history, nomenclature, and prediction of RA, and opportunities for the prevention of clinically manifested inflammatory arthritis. Given the broad scope of this effort, Dr. Kevin Deane joined them as a Guest Editor. Our Senior Science Editor, Dr. Stefanie Bronson, directed, harmonized, and provided her editorial skills to ensure a coherent collection. I will not describe the composition of the group or how it functioned. This will appear in the editorial by the team's leaders.[1] Following this editorial will be the contributions of the group's members.[2–16] Although it may seem strange to link a diabetes specialist with two rheumatologists, it made complete sense to me when I learned that approximately 42% of patients with diabetes have comorbid arthritis and about 25% of persons classified as prediabetic have comorbid arthritis.[17] Autoimmunity and inflammation may account for the association between RA and type 1 diabetes mellitus, and excessive weight may explain the comorbidity of type 2 diabetes mellitus (T2DM) with osteoarthritis (OA).[18]

My own awareness of arthritis began during my adolescence. My father had both T2DM and arthritis. What mostly bothered him was lower back pain. Periodically, he would use a contraption that to me seemed to be right out of a torture chamber—an elaborate system of ropes, pulleys, weights, and a black leather chin strap—all attached to both ends of a metal bedframe. Until I asked, I had no idea that this was called *traction*. Some years later, he lost weight, which helped with both his back pain and his T2DM.

In the May 2018 issue of *Clinical Therapeutics*, I briefly described my own experience with arthritic pain in my hands; my clinical picture fits more with OA than RA.[19] My laboratory tests are not consistent with RA. My erythrocyte sedimentation rate is not elevated and my C-reactive protein values are normal. I do not have elevated rheumatoid factor autoantibodies; I have never been tested for anti–cyclic citrullinated peptide antibodies. Because of the brevity of my Note, I did not discuss the involvement of other joints. Since my 20s, I have experienced episodic transient pain in my big toe on my right foot, along with swelling; and in my left ankle just above the heel, along with tenderness. In the past 2 years, I developed intermittent pain in my right sternoclavicular joint, along with tenderness; and in my left shoulder at the insertion of my triceps tendons, along with tenderness. Pain in these latter joints is generally not present in the absence of movement. In addition, I have bone spurs in both hip joints and had a right hip replacement because of a loss of joint space. Episodic pain almost always occurs following a viral infection. I was once told I have reactive arthritis. My suspicion is that I have both OA and reactive arthritis. I believe reactive arthritis accounts for my multifocal transient episodes, while OA accounts for my hip and hand problems, including osteophytes. I am almost always able to benefit from ibuprophen. My uric acid levels have never been never elevated. The episode in my mid-20s involved a painful foot (in the arch and heel) and in the ipsilateral ankle along with urethritis; both lasted for about a week. My physician called it Reiter syndrome, but he was puzzled because there was no evidence of a chlamydia infection. It is important to note that Reiter syndrome usually occurs in men and women between the ages of 20 and 40 years.[20]

Currently, reactive arthritis and Reiter syndrome are both subsumed in the category of spondyloarthritis (SpA).[21] The latter name implies aseptic inflammatory arthritis of the spinal processes; other joints, and ligaments and tendons where they attach to bone (aka entheses), may be involved. The worldwide prevalence of SpA is about 0.20%, with no region reporting more than slightly above 1%.[22,23] SpA accounts for a small fraction of all cases of arthropathy. OA is the most common arthropathy in the United States, with knee OA prevalence estimates of 10% and 13% in men and women over age 60 years, respectively.[24] Women are more prone than men to both OA and RA; I could not find similar data on SpA.

In light of the working group's efforts to further understand early-stage RA, I wondered whether the presence of SpA in early adulthood was a risk factor for either OA or RA. From what I have learned, it clearly is not. Reactive arthritis and other forms of SpA are entities completely separate from RA and OA, although there is no reason to suggest that any of these conditions are mutually exclusive. The histocompatibility complex antigen HLA-B27 is involved in the activation of several proinflammatory mechanisms, and its presence is highly associated with SpA.[25] HLA-B27 is not meaningfully associated with RA or OA. The presence of HLA-B27 in seropositive RA patients appears to be relatively low (5.6%)[26] However, when it is present in RA patients, one study linked it to a greater likelihood of sacroiliitis, low back pain and morning stiffness, and early involvement of the radiocarpal joints.[27]

RA is usually a debilitating disease. RA often severely impairs quality of life. Reactive arthritis and Reiter syndrome are transient, and although they are troubling and may cause considerable pain, they do not have the progressive, life-modifying effects associated with RA. In addition to progressively destructive changes in joints, RA can lead to complications in other parts of the body, such as pericarditis, lung problems (eg, pleural effusions or pulmonary hypertension), or Sjögren syndrome.

The efforts of this working group to raise awareness of RA and to explore methods for early detection and intervention should catalyze the medical and scientific communities to increase their efforts to find better ways to treat and perhaps even prevent RA and its complications.

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