

# On the Horizon From the ORS

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## Osteoarthritis and Metabolic Syndrome

The consensus definition of osteoarthritis (OA) is summarized as follows: OA is a chronic joint disease that is a result of mechanical and biologic events. Mechanical events uncouple the degradation and synthesis of cartilage and subchondral bone. Ultimately, morphologic, biochemical, molecular, and biomechanical changes occur with variable degrees of inflammation without systemic effects.<sup>1</sup> The stereotypical patient is a woman with central obesity, chronic pain, and multiple medical problems. As recently as 2006, it was suggested that 19% of overweight and obese patients with severe knee pain occurring over a 3-year period could potentially avoid progression by a one-category shift downward in body mass index (BMI).<sup>2</sup>

During the past decade, metabolic syndrome (MetS) has been defined as the co-occurrence of cardiovascular risk factors that include insulin resistance, obesity, atherogenic dyslipidemia, and hypertension. These factors share mediators, mechanisms, and pathways.<sup>3</sup> During the past 4 years, investigators have noted that OA is not always a mechanical and aging disease but may be linked with MetS.<sup>4</sup> Rates of MetS and knee OA increase with age in females but not in males.<sup>5</sup> The total number of MetS elements is inversely related to medial joint space width in men and women and to medial joint space area in women, and it is positively related to osteophyte area.<sup>6</sup> The overlap between BMI and waist-to-hip ratio is greater in women than men and may be useful in defining the prevalence of MetS in women but not men.<sup>7</sup> Females have greater se-

rum and synovial fluid levels of leptin than do males. Female sex and waist circumference are predictors of a greater synovial fluid leptin level, independent of age, BMI, and presence of diabetes. In the relationship between the metabolic effects of adipose tissue and OA, waist circumference may be a more accurate measure of body habitus than BMI.<sup>8</sup>

Major joint surgeons see a wide range of pain perception prior to management. Generally, psychological factors were thought to predominate. However, investigators have found that, after adjustment for insulin resistance, inflammation, and pain-related comorbidities, central obesity predicted higher total pain index scores than did those measures and nearly doubled the risk of chronic pain.<sup>9</sup> Other research has shown that activated white adipose tissue increases the synthesis of proinflammatory cytokines, such as interleukin (IL)-6, IL-1, IL-8, IL-18, and tumor necrosis factor (TNF)- $\alpha$ , and of adipokines capable of promoting synovial inflammation. Additionally, proinflammatory cytokines stimulate adipocytes to synthesize neuropeptides, such as substance P and nerve growth factor. The combined metabolic and pain response effect may be important in future therapy.<sup>10</sup> Patient function following joint arthroplasty surgery, particularly hip surgery, is negatively affected by MetS, perhaps secondary to the systemic proinflammatory state. This knowledge should be used when counseling patients before surgery.<sup>11</sup> C-reactive protein (CRP) level, a measure of the system's inflammatory state, was asso-

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ciated with knee OA in an age-adjusted analysis. However, CRP level was not associated with incidence of knee or hip OA when possible confounding factors were taken into account.<sup>12</sup>

The significance of synovium and bone is apparent in the relationship of MetS to OA when OA is regarded as organ failure. Synovitis is often seen in advancing knee OA. It is significantly associated with the Kellgren Lawrence grade on radiographs and with the total volume of bone marrow lesions seen on MRI. Investigators are therefore scoring synovitis on contrast-enhanced MRIs.<sup>13</sup> In a study of asymptomatic middle-aged women, elevated serum cholesterol and triglyceride levels were associated with bone marrow lesion on MRI over 2 years.<sup>14</sup> More research will likely determine whether reducing serum lipids decreases symptomatic knee OA.

For patients with lower limb OA, the role of the orthopaedic surgeon is changing. Patients should be aware of the importance of nutritional counseling with more than weight loss in mind. Knowledgeable dietitians can teach which foods affect lipids and blood pressure. The identification of patients who are at risk for increased inflammation and pain can have a notable effect on the management of this debilitating disease. Dietitians also can be influential in defining other factors, such as

low levels of selenium, that lead to increased cartilage degeneration<sup>15</sup> and vitamin D deficiency, which is associated with several chronic conditions, such as osteoporosis, OA, MetS, fibromyalgia, and chronic fatigue syndrome.<sup>16</sup>

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