Editorial

An Added Perspective on the 2009 SPARTAN and IGAS Report: An Innate Axial Myofascial Hypertonicity

The 2009 Joint Meeting of the Spondyloarthritis Research and Therapy Network (SPARTAN) and International Genetics of Ankylosing Spondylitis (IGAS) members was recently reported[1]. These comments offer a novel hypothesis to complement the progress reviewed in that report. Based upon the characteristic clinical and epidemiological features of ankylosing spondylitis (AS), a structural biomechanical contribution in causation is proposed, namely, an innate axial (spinal) myofascial hypertonicity[2,3]. Such a macro-diathesis would encompass biomechanical models already proposed at micro levels of tissue attachments (entheses) and related sites[4,5,6]. This commentary can only briefly outline biomechanical and clinical reasons for the proposed novel hypothesis in AS, as described[2,3,7]. The hypothesis also incorporates myofascial physiology[7,8] and tensegrity[9,10] mechanisms in the musculoskeletal system.

Consensus clinical features of AS[1,10,11,12,13] suggest that biomechanical influences may be operating at the level of both the body structure and tissue. Excessive physical force (L, fortis, strong) transmissions can be detrimental to both structures and enthesis sites[2,5,7]. The magnitudes of imposed (input) or internal (reactive) forces are influenced by the stiffness of a body or its component tissue attachments[5,7]. Force transmissions become amplified at sites of greater stiffness or resistance and concentrate at transition boundaries (entheses)[5,7]. Further, in mobile systems like the spine, with flexible links, the fusing (or stiffening) of component parts increases the stress concentrations in remaining connections[7]. Such physical principles are consistent with the progression of structural lesions in AS[1,11,12]. Typically, symptoms and structural pathology begin in the sacroiliac joints (SIJ), which bear the full load of the spine, and subsequently ascend up the vertebral column[11]. The spine and SIJ are complex, integrated, mobile, and load-bearing biomechanical structures[2].

As indicated in the SPARTAN and IGAS reviews[1], the onset age, sex, clinical, and pathological characteristics of AS are distinctive features, in addition to its strong genetic susceptibility. The causation of AS is complex and multifactorial[1]. The proposed novel hypothesis was inferred from those characteristic features[1,2,10,11,12,13], assuming that such expressions would reveal additional clues to underlying pathways.

Onset of AS is notable in adolescent and young adult ages, from age 15 to 35 years, in both sexes[1,10,11,12,13]. About two-thirds of onsets of AS occur in this distinctive range, the mean and median ages of onset being about 23 years[14]. Of note, physical maturation in adolescence and young adulthood naturally strengthens and stiffens the axial (postural and spinal) myofascia in both sexes[15]. Accordingly, patterns of age of onset in AS may in part reflect the natural developmental and maturational changes in axial stiffening[15] as well as the inherent disease severity risks[14]. Paralumbar muscles can be nearly twice as strong in men as in women, which is also consistent with the overall male preponderance of AS[1,11,12,13,16]. Females tend to have less syndesmophyte formation and severe spinal deformity than males[1,2,11,12,13], which may reflect their lesser natural spinal stiffness and strength. In addition, peripheral arthritis in juvenile and adult patients with AS predominates in the lower extremities[17]. That localization could result, in part, from increased impact stresses upon the lower extremities from the greater spinal stiffening[15].

Personal considerations of biomechanical pathways in AS had evolved over a period of 3 decades[13,16]. Such inferences had led to research and characterization of the subtle and little appreciated polymorphic trait of human resting myofascial tone (HRMT)[7,8,18]. Axial or postural HRMT is an innate polymorphic trait independent of the central nervous system that contributes vitally to postural stability in balanced equilibrium positions[7,8,18]. Increased paralumbar muscle stiffness in patients with early AS was first reported in 1951 by Forestier, *et al*[19], who described this finding as the "bowstring sign"[19]. That observation was subsequently confirmed by palpation and electromyography studies, as reviewed[20].

Insufficient compared to excessive innate axial HRMT was proposed as the expression of counter-opposing spinal disorders, i.e., adolescent idiopathic scoliosis (AIS) versus AS, respectively[21]. Those conditions have their respective polygenic determinants[21]. As well, genome-wide association studies in Caucasian patients have now been performed[1,22,23,24], which deserve critical comparison. Indeed, analytical methodology is now available to test if these disorders show inverse associations of single-nucleotide polymorphism alleles[24].

The Journal of Rheumatology 2011; 38:10; doi:10.3899/jrheum.110330

Monozygotic twin studies suggest that AS susceptibility has a 90% or slightly greater genetic inheritance and that HLA-B27 overall has almost half of the genetic association[1,22]. Thus, a comparable degree of association is left to all other non-HLA-B27 combined factors[1,22]. The HLA-B27 gene is found in about 90% of Caucasian patients with AS, and has a risk ratio of about 100-fold[22]. Yet the molecular mechanisms underlying the basis for such an association are not known[1,22]. Neither have the genetic determinants of HRMT polymorphism been determined[7,18] (PubMed search, 2011), although aging and gender have effects on contractile properties of human skeletal muscle and single fibers[25].

Of note, HLA-B27 is one of only 2 genetic markers observed to correlate significantly with colder climates in both hemispheres[26]. This finding and research on human non-exercise activity thermogenesis (NEAT)[27] suggested that the HLA-B27 gene was possibly related, in part, to cold climate adaptation and to greater intrinsic energy expenditures by skeletal muscles[10].

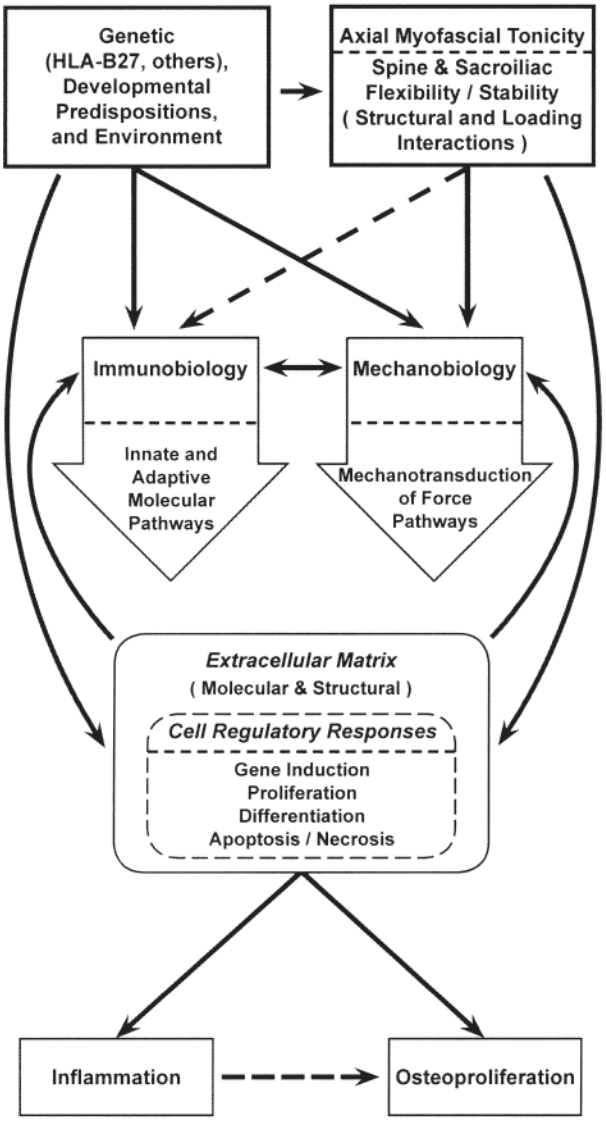

Figure 1. Theoretical pathways by which osteoproliferative reactions may proceed.

The course, severity, and progression of AS encompass a wide spectrum[11,12,13]. However, burnout (i.e., indefinite remission) rarely occurs[28]. The trajectory of spinal damage in AS may be individualized[29] and may already be determined at an early disease stage within the host[14]. Current research on genotype and phenotype markers of progression in AS is promising[1], as is current work in adolescent idiopathic scoliosis[23].

Anti-tumor necrosis factor therapy has shown significant benefits in reducing inflammation-related measures of AS, but the vertebral osteoproliferative lesions appear to be unabated[1]. Osteoproliferative lesions could be contributed by injury-related pathways, possibly from continuing consequences of excessive stress mechanisms[2,3,4,5,6]. A critical question is if axial myofascial hypertonicity in AS might precede the onset of pain (not stiffness) and inflammatory indicators? A prospective study design has been outlined to investigate this question among high-risk asymptomatic susceptible subjects and matched controls[7].

In early AS, MRI signal hyperintensities (lesions) are found in the spinal and SIJ bone marrow and at entheses on short inversion time inversion-recovery (STIR) images and on T2-weighted (water molecules) images[1]. In patients with AS, these lesions are usually referenced as inflammatory. However, studies of osteoarthritis[30] and sports-related injuries[31] show analogous hyperintensities, but are commonly described as bone marrow edema or edema-like lesions. Those MRI findings are mainly attributed to altered biomechanical/degenerative origins or excessive tissue stresses, rather than being inflammatory. Possible effects of excessive stresses or other biomechanical mechanisms[2,3,4,5,6] should be considered in the early MRI changes of AS that progress to osteoproliferative lesions.

This perspective is consistent with current concepts and progress reviewed in the SPARTAN and IGAS report[1,22]. Figure 1 illustrates our proposed added structural biomechanical component to the complex predisposition and course of AS that is novel and that deservies further critical examination. The current perspective of a possible innate mechanical diathesis in AS and the proposed schematic (Figure 1) may reveal theoretical pathways by which osteoproliferative reactions may proceed in this disorder, even though inflammatory mechanisms might be suppressed.

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Supported by the Department of Medicine and The MTM Foundation. Becky Hawkins is acknowledged for her invaluable technical assistance.

ACKNOWLEDGMENT

Kristina Prus, Brian Andonian, and Mary Jean Dzurisin contributed significantly in composing the schematic image.

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J Rheumatol 2011;38:2092–4; doi:10.3899/jrheum.110330