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Are current available therapies disease-modifying in spondyloarthritis?

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Disease modification in spondyloarthritis should target the improvement of symptoms and preservation of function. Therefore, inhibition of structural damage caused by the disease processes appears essential. In spondyloarthritis, structural damage results mainly in progressive ankylosis of the spine and peripheral joint destruction. Currently available therapies for the treatment of spondyloarthritis appear effective at inhibiting tissue destruction but, with the exception of celecoxib, do not appear to affect new tissue formation leading to ankylosis. In this article, we discuss clinical and pathophysiological concepts of disease modification in spondyloarthritis, challenges in its evaluation, recent clinical data and new concepts that may help explain structural damage as well as the onset and progression of disease.

The concept of disease modification in arthritis

Major inflammatory joint diseases such as the spondyloarthritides (SpAs) and rheumatoid arthritis (RA) are chronic disorders. The immediate impact of inflammation (pain and loss of function) is complicated by the dimension of time. Any intervention in patients suffering from arthritis, therefore, aims to limit the short- and long-term consequences of disease. The concept of 'disease modification' refers to an improvement of symptoms in combination with changes in the course of the illness [1]. The

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former is perceived as the disease process and at the centre of the patient's immediate expectations and short-term interventions; the latter is reflected in the disease outcome and the main focus of the rheumatologist who defines a therapeutic strategy.

Drugs may be able to influence the disease process resulting in short-term control of the symptoms caused by inflammation (symptom-modifying drugs). They may also have an impact on the disease course and thereby the long-term outcome (disease-controlling or modifying drugs) [2]. Different instruments have been developed to assess disease activity (evaluating symptom control) and structural damage in SpA and RA but questionnaires and imaging methods do not seem to correlate very well. The combination of symptom control and prevention of permanent damage and disability results in an effect on function for which additional measurements exist. At any point in time during the disease, function is determined by a number of factors including inflammatory symptoms, disability caused by structural damage to the involved tissues and other consequences of the disease such as loss of muscle strength, general fitness, psychological impact and coping style (Fig. 1) [3,4]. The influence of each of these variables varies over time in individual patients. Disease modification results in improved function and is a complex issue for which many interventions exist.

However, this inclusive model is often narrowed down to the prevention of structural damage as a defining factor to categorise and evaluate the impact of drugs. Most investigations on drug interventions and their effects on long-term outcome of disease have been performed in patients with RA. Several drugs prevent structural damage, which is evaluated by radiographic methods and characterised by joint space narrowing and bone erosions. These drugs include chemical immune modulators such as methotrexate [5], and leflunomide [6] as well as biological cytokine or cell targeting approaches such as tumour necrosis factor (TNF) blocking agents [7–9], abatacept, a modulator of T-cell costimulatory signals [10] and tocilizumab, an interleukin (IL)-6 antagonist [11]. The acronym, DMARD (disease-modifying anti-rheumatic drug), is used to distinguish the chemicals within the first group as opposed to the biologics in the second group. However, the concept of DMARDs applies specifically to RA. It is less clear that structural modification is the *sine qua non* for disease modification in SpA [2] and the focus on structural damage is not undisputed [12]. Therefore, in this article, we look more specifically at clinical and pathophysiological concepts of disease modification in SpA in a broad context.

Current clinical concepts of disease modification in spondyloarthritis

The SpAs are a group of distinct diagnostic entities that share clinical, genetic and pathological characteristics. The disease cluster includes ankylosing spondylitis (AS), psoriatic arthritis (PsA), inflammatory bowel disease associated arthritis (IBD-SpA), reactive arthritis (ReA), juvenile and undifferentiated SpA. Axial disease with involvement of sacroiliac joints and spine, oligoarthritis frequently confined to the lower limbs, extra-articular enthesitis typically affecting the insertion of the Achilles' tendon and the fascia plantaris, and extra-articular manifestations such as psoriasis and IBD help to distinguish SpA from RA. These common traits are easily recognised and provide support for

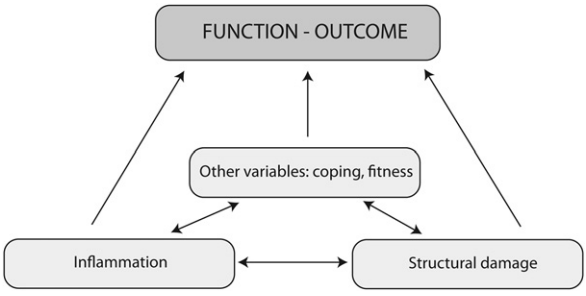

Figure 1. The concept of disease modification in arthritis in a broad perspective. Function and outcome are determined by inflammation causing symptoms but also by structural damage and other patient-specific variables such as coping and fitness.