

treatment effect is typically 2 years. Only small changes can be assessed over this period, normally about 1–2 mSASSS units. It is hard to define that this is clinically relevant. The most important for treatment is to show that there is inhibition of structural progression in comparison to untreated patients, especially as axial SpA is a lifelong disease and 1 unit over 30 years still leads to severe ankylosis of the spine.

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SP0044

#### WHAT DO WE LEARN FROM RCTS ON THE TREATMENT EFFECT ON STRUCTURAL PROGRESSION IN AXSPA?

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The introduction of tumour necrosis factor inhibitors (TNFis) about 20 years ago has led to the hope of disease modification of ankylosing spondylitis, since biologics showed for the first time a decrease of inflammatory activity on MRI, with the latter being theoretically also directly linked to new bone formation. However, the first open-label extensions of randomized-controlled trials with a treatment duration of 2 years failed to show any positive effect on the radiographic progression in AS patients when compared to historical cohorts that had not been exposed to biologics. Nevertheless, later data indicated that this lack of influence on radiographic progression might have been due to many different reasons that were not taken into account in these first analyses, such as the radiographic status of patients at baseline, CRP levels or insufficient duration of follow-up. Furthermore, most recent data from MRI studies also indicated that the most important link to influence radiographic progression with biologics might not be the suppression of inflammation but the protection of bone to show tissue metaplasia to post-inflammatory findings, while early suppression of inflammation might be the key to even completely inhibit radiographic progression in AS patients.

Indeed, most recent cohort data have been able to demonstrate an association between TNF-blocker treatment and reduced risk of spinal structural progression (e.g. formation of syndesmophytes). Furthermore, early escalation of treatment from NSAIDs to biologics and long-term treatment with biologics have also independently been able to show positive effects on radiographic progression in patients with AS. Finally, also newer biologics such as IL-17A inhibitors have also provided promising results in terms of overall low radiographic progression rates as measured by validated scoring systems.

Currently, first head-to-head trials of different biologics are underway to examine any possible differences between the available compounds with a primary outcome of their effect on spinal radiographic progression.

It remains to be shown whether and how these results will also become clinically relevant in terms of decrease or even inhibition of spinal mobility restrictions, in order to be able to postulate a 'real' disease modifying effect of biologic treatment in axial spondyloarthritis.

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### Reproductive issues in rheumatology

SP0045

#### OESTROGENS, IMMUNE RESPONSE AND AUTOIMMUNE DISEASES

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Sex hormones are implicated in the immune response, with estrogens as enhancers at least of the humoral immunity and androgens and progesterone (and glucocorticoids) as natural immune-suppressors. Several physiological, pathological and therapeutic conditions may change the serum oestrogen milieu including the menstrual cycle, pregnancy, postpartum period, menopause, elderly, chronic stress, altered circadian rhythms, inflammatory cytokines, use of glucocorticoids, oral contraceptives, and steroid hormonal replacements. Cortisol and melatonin circadian rhythms are altered, at least in rheumatoid arthritis (RA), and partially involve also sex hormone circadian synthesis and levels. Abnormal regulation of aromatase activity (i.e. increased activity) by inflammatory cytokines production (i.e. TNF-alpha, IL-1, IL-6) may partially explain the abnormalities of peripheral oestrogen synthesis in RA (i.e. increased availability of 17-beta estradiol and possible metabolites in synovial fluids) and in systemic lupus erythematosus (SLE). In the synovial fluids of RA patients the increased oestrogen concentration are observed in both sexes and are more specifically characterised

by the hydroxylated forms, in particular 16alpha-hydroxyestrone, that is a mitogenic and cell proliferative endogenous hormone. Local effects of sex hormones in autoimmune rheumatic diseases seems to consist mainly in modulation of cell proliferation.

Epidemiological evidence indicates that during the fertile age women are more often affected by rheumatic diseases than men, particularly autoimmune diseases. As a matter of fact, rheumatic disorders with autoimmune involvement such as RA or SLE, result from the combination of several predisposing factors, that include the relationships between epitopes of the trigger agent (i.e. virus), the status of the stress response system including the hypothalamic-pituitary-adrenocortical axis (HPA) and mainly the effects of the gonadal hormones (hypothalamic-pituitary-gonadal axis – HPG).

The pre- or post-menopausal serum sex hormonal status is a further factor influencing the rate of rheumatic diseases. It is therefore important, whenever possible, to evaluate epidemiologic data broken down into age (for example 10 year age band) and sex-specific group before making inferences. Obviously, sex hormones seem to play an important role as modulators of both disease onset and perpetuation and show circadian rhythms together with cortisol.

Sex hormones are implicated in the immune response, with estrogens as enhancers at least of the humoral immunity and androgens and progesterone (and glucocorticoids) as natural immune-suppressors. Low concentrations of gonadal and adrenal androgens [testosterone (T)/dihydrotestosterone (DHT), dehydroepiandrosterone (DHEA) and its sulphate (DHEAS), respectively] levels, as well as reduced androgens/estrogens ratio, have been detected in serum and body fluids (i.e. blood, synovial fluid (SF), smears, salivary) of male and female RA patients, as well as in SLE, supporting the possible pathogenic role for the decreased levels of the immune-suppressive androgens. However, respect to serum levels of estrogens, interestingly they are not significantly changed which is in strict contrast to androgen levels in RA patients (reduced).

As a matter of fact, sex hormones can exert also local actions (paracrine) in the tissues in which they are formed or enter the circulation and both T and 17-beta estradiol seem to exert dose and time-dependent effects on cell growth and apoptosis. These effects, as well as important influences on gene promoter of Th1/Th2 cytokines and the recently discovered increased SF oestrogen concentrations, might suggest new interesting roles for estrogens at least in RA. Finally estrogens exert important epigenetic actions on cell proliferation. Estrogens act as key factors in cellular proliferation and differentiation as well as cancer development and progression (prostate). The expression of oestrogen receptor (ER)-β appears to be lost during prostate cancer progression through hypermethylation mechanism. Epigenetic drugs such as 5-aza-2'-deoxycytidine (5-AZAC) and Trichostatin A (TSA) showed efficacy in restoring ERβ expression in prostate cancer cells. These observations highlights that the strategy of merging epigenetic and hormonal therapies might be beneficial also in inflammatory/autoimmune diseases (synovial tissue)

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SP0046

#### WHAT WE NEED TO CONSIDER IN PHYSICIAN-PATIENT COMMUNICATION ON SEXUAL PROBLEMS IN DIFFERENT RHEUMATIC CONDITIONS

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Quality of life (QOL) is often reduced in patients with chronic diseases. Sexual activity and enjoyment constitute an important aspect of QOL. Sexuality is a neglected area of QOL in patients with rheumatic disease.

Sexual problems among patients are common and often increase with disease duration. Both disease related factors and the psychological response to chronic disease can impair sexual functioning. General disease symptoms like pain, fatigue, disease activity, and impaired physical function contribute to reduced sexual activity in both genders. However, psychological factors like depression, anxiety, negative body image and low self-esteem play an important role. Sexual dysfunction can create frustration and distress, and if chronic increase anxiety and depression, and damage interpersonal relationships.