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Abstracts

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INV 1
INTERPLAY BETWEEN PATHOGENIC EFFECTOR TH17 AND REGULATORY T CELLS IN AUTOIMMUNITY AND TISSUE INFLAMMATION

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Upon activation, T cells undergo distinct developmental pathways, attaining specialized properties and effector functions. T-helper (TH) cells are traditionally thought to differentiate into TH1 and TH2 cell subsets. TH1 cells are necessary to clear intracellular pathogens and TH2 cells are important for clearing extracellular organisms. Recently, a subset of interleukin (IL)-17-producing cells (TH17) distinct from TH1 or TH2 cells has been described and shown to have a crucial role in the induction of autoimmune tissue injury including Rheumatoid Arthritis (RA). In contrast, CD4+CD25+, Fox-P3+ regulatory T cells (Tregs) inhibit autoimmunity and protect against tissue injury. TGF-b1 is a critical differentiation factor for the generation of T-regs and using Foxp3-GFP “knock-in” mice we show that IL-6, an acute phase protein induced during inflammation, completely inhibits the generation of Foxp3+ T-reg cells induced by TGF-b1. On the other hand, we demonstrate that IL-23 is not the differentiation factor for the generation Th-IL-17 cells, instead IL-6 and TGF-b1 induces differentiation of pathogenic Th-IL-17 T cells from naïve T cells. Th17 cells produce maximal amounts of IL-21 that further amplifies the Th17 differentiation by acting together with TGF-b1. Consistent with these observations, immunization of inducible TGF-b1 transgenic mice with myelin antigens in complete Freund’s adjuvant induces a severe and lethal experimental autoimmune encephalomyelitis (EAE) with massive production of IL-17.

Our data suggests a reciprocal relationship in the generation of pathogenic (Th-IL-17) T cells that induce autoimmunity and regulatory (Foxp3+) T cells that inhibit autoimmune tissue injury.

INV 2
THE APPLIED ANATOMY OF ENTHESES IN RELATION TO THE PATHOGENESIS OF SPONDYLOARTHRITIS

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Entheses are inherently regions at risk of mechanical damage and evidence of degeneration is characteristic of numerous attachment sites studied by the author in dissecting room cadavers. The anatomy of entheses reflects the need to dissipate stress concentration near the anchor site. Thus, many insertions that are known targets in spondyloarthritis (SpA) are characterized by fibrocartilage at the bony interface. Uncalcified fibrocartilage creates a gradual change in mechanical properties between soft tendon/ligament and hard bone, and the calcified fibrocartilage/bone interface contributes to anchorage and provides resistance against shear. Insertional angle changes that accompany joint movement are minimized by pulleys and retinacula, and stress is dissipated onto the area adjacent to the enthesis by the formation of ‘enthesis organs’ and the fact that many tendons/ligaments have fascial expansions. Enthesis organs typically occur at sites where the immediately adjacent tendon/ligament presses on the bone and their existence emphasizes the importance of viewing entheseopathies as potentially multifocal pathologies. A key component of a classic enthesis organ such as that of the Achilles tendon is a bursa. Its presence means that a highly vascular and pro-inflammatory, synovium (that may be independent of that of any synovial joint) is juxtaposed to what in a healthy enthesis, is a poorly vascularised and essentially anti-inflammatory dense connective tissue. The term ‘synovio-entheseal complex’ has been coined to emphasize the importance of recognizing local joint-specific factors in relation to SpA. It is possible that mechanical damage at entheses in genetically-susceptible individuals (and in the presence of appropriate microbes) could trigger the inflammatory changes characteristic of SpA. On the bone side of entheses, stress is dissipated via a network of trabeculae that characterize spongy bone. The mechanical integration of these spicules as part of the enthesis itself, provides a basis for understanding why osteitis and enthesitis are frequently linked.
Within the Assessments in Spondyloarthritis (ASAS) detailed in the presentation, the development and validation process of the ASDAS will be instances better as compared to the BASDAI and always better as compared to change over time. The performance of the 4 ASDAS scores are similar and in most ease activity, sensitivity to change and discrimination between groups based on disease activity measures such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). About 30-40% show an increase in function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI). Applying the Assessment in Spondyloarthritis International Society (ASAS) outcome criteria usually more than 60% reach ASAS 20 and more than 40% the ASAS40 criteria, while 20-30% even achieve ASAS partial remission. Furthermore, AS patients treated with TNF blockers report an improved quality of life and reach higher productivity scores.

In contrast to the rather dramatic improvement of clinical and imaging parameters reflecting inflammation, structural damage, which manifests in AS mostly as growing syndesmophytes and ankylosis seems not to be inhibited by anti-TNF therapy. However, regarding these studies there are some unresolved methodological issues such as the inability to assess the thoracic spine by standard radiography, the study design (comparison only with historical cohorts) and the low sensitivity of the current used mSASSS scoring method, the best currently available tool to quantify radiographic changes in AS. Furthermore, the degree of damage that has been reported to occur in AS is not impressive over 2 years with less than 1 (mean) new syndesmophytes developing in the whole spine.

Reasons for the possible lack of an influence of anti-TNF therapy on syndesmophyte formation are that (i) inflammation and new bone formation are, at least in part, uncoupled in AS, and/or (ii) that anti-TNF therapy by inhibiting osteoclast and promoting osteoblast activity even triggers ankylosing processes by interfering with the wnt and/or the RANKL pathway. This may be different for NSAIDs which, by inhibition of COX-2, may affect bone healing, prevent heterotopic ossification and even decelerate pathologic bone growth in AS.

Clearly, this situation is different in rheumatoid arthritis (RA) and pioriatic arthritis where structural damage has been regarded as the most important outcome parameter and where all anti-TNF agents were shown to inhibit radiographic progression characterized by erosions. The situation in AS is likely to be different since new bone formation (in contrast to bone destruction) is the main factor to influence the structure of affected patients. New bone formation might be prevented in AS when inflammation is suppressed before erosive structural damage has occurred. However, any ongoing new bone formation as part of partly possibly physiological repair mechanism may just not be stopped by blocking TNF.

The cornerstone of treatment are physical therapy and drug therapy with non-steroidal anti-inflammatory agents (NSAIDs). The pros and cons of these agents in the therapy of AS have recently been discussed. Patients in whom the disease activity cannot be adequately controlled by conventional means require and may be treated with biologic agents targeting TNF-α. As many as 40% of the ASAS patients in Belgian rheumatological offices were reported to be in need for anti-TNF therapy if recent international recommendations were followed. Anti-TNF therapy with currently 3 approved agents, infliximab, etanercept and adalimumab, has clearly been shown to improve signs and symptoms, function and spinal mobility on both a short-term and a long-term basis of until now up to 5 years, as recently reported. In general, about half of the patients gain about 50% improvement of disease activity as assessed by the Bath Ankylosing Spondylitis Activity Index (BASDAI), about 30-40% show an increase in function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI).

The diagnosis and classification of axial SpA in patients without definite radiographic sacroiliitis has been a challenge in the past. Moreover, none of the available criteria contain magnetic resonance imaging (MRI) which proved to be highly important in early sacroilitis.

Materials and Methods: Within the Assessments in Spondyloarthritis (ASAS) International Society candidate criteria for axial SpA were developed by means of paper patients who were assessed by 20 ASAS experts. In a second step, an international validation study was conducted: consecutive patients were included if they suffered from chronic back pain of unknown origin and had an age at onset <45 years. Using a standardized case report form, the clinical, laboratory, and imaging information was documented. The final clinical diagnosis by the local rheumatologist served as gold standard.

Results: A total of 650 patients fulfilling the entry criteria was included in the study. The ASAS candidate criteria for axial SpA performed well in terms of sensitivity and specificity. The specificity could be improved even further upon minor changes. The resulting ASAS classification criteria for axial SpA are fulfilled if either definite sacroiliitis on radiographs or MRI is present together with one clinical SpA feature (imaging part, specificity 97%) or if HLA-B27 plus two further clinical SpA features are present (clinical part, specificity 84%).

Conclusion: In a joint effort, the ASAS group has generated new classification criteria for axial SpA which for the first time have incorporated MRI of the sacroiliac joints. Depending on the purpose the new ASAS classification criteria can be used in a flexible way with either a rather balanced sensitivity and specificity for the whole set of criteria or with a very high specificity of 97% for the imaging part of the criteria which requires definite sacroilitis.
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GWAS IN INFLAMMATORY BOWEL DISEASE: MULTIPLE HITS,

The era of the genomewide association study may not crack all genes or all disease associations like the genetic association depends on the extent and functional significance of the genetic polymorphisms present. The small effect sizes do impact on the utility of the genetic studies as diagnostic or prognostic tests. However even in these early days of such research, examples do exist where genetic findings are clearly of value in diagnosis, particularly in AS. The era of the genomewide association study may not crack all genes or all diseases, but its impact will affect us all.

INV 9
GWAS IN INFLAMMATORY BOWEL DISEASE: MULTIPLE HITS, OVERLAPPING PATHWAYS

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The last 2 years has seen an explosion in interest in complex disease genetics. The new technology of genome-wide association scanning (GWAS) is being applied across a range of diseases and traits, and nowhere more successfully than in Crohn’s disease (CD). Individual scans have identified a total of 10 validated CD-associated genes and loci, and a recent meta-analysis by our international consortium has identified and replicated 20 more. In particular the interleukin 23 pathway has been highlighted by multiple hits, as has the process of autophagy. GWAS has also identified a number of loci common to more than one disease. It is thus beginning to shed light on the aetiological relationships between Crohn’s disease and ulcerative colitis as well as analysing spondylitis. Details of these overlaps and the lessons learned will be discussed.
INV 12

ASSESSMENT OF FUNCTION AND SPINAL MOBILITY IN SpA

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Several instruments for assessment of function in SpA have been developed but increasingly consensus favours the use of the BASFI based on feasibility and responsiveness to change. The approach to the assessment of function in SpA is undergoing re-appraisal to conform to the framework of the World Health Organization International Classification of Functioning and Disability. A brief ICF Core Set has now been proposed that includes a total of 19 second-level categories: 6 on body functions; 4 on body structures; 7 on activities and participation; 2 on environmental factors. Domains not previously addressed in function instruments include sleep, emotional functions, family relations, and driving. Advances in spinal mobility evaluation have addressed the importance of standardization of assessment and have shown which measures are reliable. Data from phase III clinical trials indicates that lateral lumbar flexion and cervical rotation are most responsive and discriminate best between treatment groups. Cervical rotation using a goniometer has now been added to the core set of mobility measures recommended by ASAS. The responsiveness of the BASMI composite is limited when scored nominally (0, 1, 2) but improves significantly with a 0-10 scoring method or when based on continuous data, with a linear assessment-to-score conversion in the range 0-10, as in the linear BASMI. The responsiveness of the EDASMI is improved when cervical rotation is measured using the goniometer rather than a tape-based approach. Recent adaptations to the assessment of spinal mobility show that this domain is highly responsive to anti-TNF therapy.

INV 13

THE SIGNIFICANCE OF THE ICF FOR RHEUMATIC DISEASES

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A patient’s diagnosis alone provides limited information. It tells little about what patients can do, what their prognosis is, what they need, etc. Because functioning is a central dimension in working with patients with rheumatic diseases, concepts, classifications, and measurements of functioning and health are important to clinical practice, research, and teaching in this field (1). The approval of the International Classification of Functioning, Disability and Health (ICF) by the World Health Assembly in May 2001 can be considered a landmark event in establishing a new era of patient-oriented clinical practice, research, and teaching (2,3). The ICF offers information about how people live with their health conditions. It is based on an integrative bio-psychosocial model of functioning, disability, and health. Domains not previously addressed in function instruments include sleep, emotional functions, family relations, and driving. Advances in spinal mobility evaluation have addressed the importance of standardization of assessment and have shown which measures are reliable. Data from phase III clinical trials indicates that lateral lumbar flexion and cervical rotation are most responsive and discriminate best between treatment groups. Cervical rotation using a goniometer has now been added to the core set of mobility measures recommended by ASAS. The responsiveness of the BASMI composite is limited when scored nominally (0, 1, 2) but improves significantly with a 0-10 scoring method or when based on continuous data, with a linear assessment-to-score conversion in the range 0-10, as in the linear BASMI. The responsiveness of the EDASMI is improved when cervical rotation is measured using the goniometer rather than a tape-based approach. Recent adaptations to the assessment of spinal mobility show that this domain is highly responsive to anti-TNF therapy.

INV 14

DEVELOPMENT OF THE ICF CORE SET FOR AS

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To assess health outcome in ankylosing spondylitis (AS), experts selected the ASAS/OMERACT core set of domains and instruments to measure them. These domains represent the minimum to be assessed in clinical trials or for record keeping. The ICF Core Set, on the other hand, aims represent the comprehensive view on the impact of the disease on functioning and health. Moreover, it includes not only the perspective of experts, but also the perspective of patients. Recently, the ICF Core Set for AS has been defined, following a standard approach that also enables to compare impact of functioning. Altogether 79 categories were included in the Large ICF Core Set with 23 categories representing body functions, 19 body structures, 24 activities and participation, and 13 environmental factors. In addition, ‘posture’ was identified as an impairment but could not be linked to the ICF. Comparison of the ICF Core Set of domains with the ASAS/OMERACT outcome domains makes clear which aspects of functioning and health will be missed when restricting outcome assessment to the minimal approach. Also when including other disease specific instruments in the comparison, several aspects of the impact of health are not represented by any disease specific instrument. The ICF Core Set for AS broadens our view on functioning and health and poses challenges to improve existing instruments or develop new instruments to more comprehensively describe and measure the impact of AS.

INV 15

INTRODUCTION: INFLAMMATION AND NEW BONE FORMATION IN ANKYLOSING SPONDYLITIS

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Based on histological, immunohistological and MRI studies it is evident that ankylosing spondylitis starts with inflammation in the sacroiliac joints and spine at the cartilage/bone interface. Symptoms such as pain, morning stiffness and fatigue are caused by inflammation. However, long-term outcome and disability is predominantly determined by new bone formation and ankylosis of the spine. Function is determined by both inflammation and ankylosis. Inflammation is the major determinant for function early in the disease while ankylosis is the more relevant component later on. The question of how inflammation and new bone formation are linked is of major importance for understanding part of the pathogenesis and for the development of optimal treatment strategies in AS. We have recently proposed that inflammation causes erosive structural damage first (1). Fibrous repair tissue will then subsequently be ossified, a process which is even stimulated when inflammation is suppressed, either spontaneously or by treatment, because inflammatory cytokines such as TNF-alpha inhibit the wnt-pathway of new bone formation. Once structural damage has occurred further ossification of the fibrous repair tissue cannot be inhibited by TNF-blockade. On this background it is not surprising that growth of syndesmophytes have been observed in AS patients treated successfully, as judged by improvement of signs and symptoms, with TNF-blockers. Thus, it is the crucial question for the near future whether new bone formation can be prevented when inflammation is suppressed early enough before structural damage has occurred or whether new bone formation can occur completely independent from inflammation. In the first case early diagnosis and early therapy of inflammation would be the optimal treatment strategy while therapeutic intervention would have to target both inflammation and new bone formation in the latter case.

References:
INV 16
WHAT DRIVES THE INFLAMMATION IN SpA?
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Over the past years, it has become clear that TNF is a key player in the pathogenesis of spondyloarthritis but the mechanisms by which this occurs are only partially known.

Particularly, the cellular targets sufficient to mediate the articular and extra-articular manifestations of spondyloarthritis remained to be defined, as well as the cellular constituents capable of modulating this TNF driven inflammation. Recently, we reported a peculiar role for mesenchymal cells in a mouse model of spondyloarthritis, characterized by enhanced TNF mRNA stability, resulting in Crohn’s like ileitis as well as peripheral arthritis. Hence, TNF-R1 expression on mesenchymal cells was sufficient to mediate combined gut and joint pathologies in this model of murine spondyloarthritis. However, it remained unclear whether regulatory T cell subsets could modulate this inflammation. More recently, we uncovered that a particular regulatory T cell lineage, invariant NKT (iNKT) cells, are natural regulators of TNF driven inflammation by modulating maturation and differentiation of antigen presenting cells in a pathway that is strictly dependent upon TNF. Altogether, these observations provide new insights in the regulatory as well as the effector mechanisms of spondyloarthritis.

INV 17
ANIMAL MODELS OF ENTHESISIS AND ANKYLOSIS
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Ankylosing enthesitis is a hallmark feature of the human spondyloarthritides (SpA). The enthesis defines an anatomical zone in which tendons, ligaments and capsules insert into the bone. Entheses can be part of the joint organ but are also recognized as extra-articular disease locations. New cartilage and bone formation originating from the entheseal sites are typical for SpA both in the axial and the peripheral skeleton. Ankylosis causes loss of function leading to disability. Spontaneous arthritis in aging male DBA/1 mice is triggered by grouping male skeletons. Ankylosis causes loss of function leading to disability.

Presence of fibrocartilage could determine the sites, which are prone to enhanced bone proliferation. However, these sites are also present in peripheral joints and thus differences in the distribution of the disease may not or only partially explain the different patterns of joint remodelling among RA and AS.

INV 18
LINKS BETWEEN INFLAMMATION AND NEW BONE FORMATION
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Structural damage in ankylosing spondylitis is essentially different from rheumatoid arthritis. Whereas both diseases share trabecular bone loss leading to major osteoporosis, the local changes along joints and intervertebral spaces (in case of AS) are contrary. In RA, progressive destruction of bone is observed leading to local bone erosion, which is thought to be a direct consequence from inflammation mediated osteoclast formation and tissue destruction. A large proportion of local bone damage starts at the outer side of the joint based on chronic synovitis and resorption of cortical bone at the periosteal sites. In contrast, AS is characterized by bone proliferation and the deposition of mineralized tissue along periosteal sites close to joints or intervertebral spaces. Thus, AS is characterized by a dissociation of trabecular and cortical bone changes - with a negative balance in the former one and a positive balance in the latter one. Understanding of periosteal bone proliferation in AS is essential to explain the clinical picture of disease. Although it is currently not entirely clear whether syndesmophyte formation has a pivotal role in patients’ symptoms. In fact, the efficacy of TNF blocking agents to control signs and symptoms of AS but syndesmophyte formation suggest a different picture. Still, these lesions warrant attention because they reflect the progressive disease process in AS. Despite there is no final explanation, why AS leads to periosteal bone proliferation and RA does not, there are several hypotheses which could explain these differences. (i) Joint remodelling in RA and AS occurs at different sites, RA preferentially at at peripheral joints, AS at axial joints and intervertebral spaces. (ii) Differences among structural remodelling in RA and AS could be based on entirely different molecules, which are turned on during joint inflammation. (iii) There is a profound difference between RA and AS with respect to the origin of inflammation.

RA is synovial driven inflammation, whereas AS is predominantly osteitis, evident by an inflammation of the bone marrow as observed in MRI scans. In fact, the link between osseous and subsequent formation of syndesmophytes at the same sites becomes more and more evident. (iii) RA and AS have a profoundly different kinetics of disease, with RA resembling a chronic inflammatory disease process, which is characterized by a continuous synovitis, whereas AS is a more flare like disease process with phases of lower disease activity. These phases of lower activity could thus enable a regenerative response leading to osteophyte formation. (iv) Differences among structural remodelling in RA and AS could be based on entirely different molecules.

Understanding of the mechanisms, which lead to syndesmophyte formation in AS are essential for a better understanding of the disease process. We are currently in a phase, where we begin to understand the molecules driving osteophyte formation and this knowledge will also give us a better insight into the disease process of AS.

INV 19
EARLY DIAGNOSIS AND THERAPY IN SpA – THE MAASTRICHT EXPERIENCE
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The concept of spondyloarthritis (SpA) has gained importance in the light of the availability of effective clinical treatments including the TNF-blocking drugs. If axial SpA is considered an early form of AS – and there is some argument to underscore that thesis - it may be possible to shorten the delay between the onset of complaints and the diagnosis of AS with 5 to 10 years on average. It is therefore mandatory that the disease is recognised before definite radiographic changes of the sacroiliac joints have occurred, and several sets of criteria and algorithms have been proposed for early diagnosis and classification. The Maastricht Early Spondyloarthritis Cohort (ESPAC) has been established to investigate the concept of early diagnosis, and its consequences with regard to long term outcome. Magnetic resonance imaging (MRI) of the SI joints, performed over time, has a prominent place in this cohort.

In this lecture, the cohort will be described, as well as the performance of several criteria sets with regard to early diagnosis. Additionally, the role of MRI in making a diagnosis of SpA will be highlighted.
INV 20
REFERRAL PATTERNS FOR EARLY AXIAL SPONDYLOARTHROPATHIES, AND SELECTION CRITERIA FOR AND RESPONSE TO ANTI-TNF THERAPY

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Introduction: Early axial SpA is the attributable cause of back pain in about 5% of chronic back pain patients. The identification and referral to rheumatologists of these patients remains a challenge in primary care. The ASAS recommendations on initiation of anti-TNF therapy in ankylosing spondylitis have proven useful in daily practice. Nonetheless, certain patient characteristics may allow to predict the response to anti-TNF agents.

Materials and Methods: A standardized local referral programme was initiated to test the feasibility of screening for axial SpA. Patients with chronic back pain and age at onset below 45 years of age could be referred to rheumatology if in addition either inflammatory back pain (IBP) was present or HLA-B27 was positive. The potential of patient characteristics to predict a good clinical response (BASDAI 50) was tested in clinical trials with anti-TNF agents.

Results: The local referral programme turned out to be highly effective. Among 350 referred chronic back pain patients 43% had axial SpA, either ankylosing spondylitis or non-radiographic axial SpA. The symptom duration of the latter group was 4 years, and about 30% had a duration of less than 1 year. Both, IBP and HLA-B27 performed well as screening instruments, however, the rate of positive diagnoses (i.e. axial SpA) was expectedly higher in HLA-B27 positive patients than in patients who were referred because of IBP. Significant predictors of a good response to anti-TNF agents in axial SpA were younger age/shorter disease duration, elevated CRP, better functional status, positivity for HLA-B27 and extended inflammation on MRI.

Conclusion: Screening for axial SpA using standardized referral programmes is feasible and highly effective. Certain patient characteristics may help to estimate which patient with axial SpA is likely to achieve a great clinical benefit from anti-TNF therapy.

INV 21
EARLY STUDIES OF SpA: THE LEEDS EXPERIENCE

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Inflammatory back pain (IBP) perceived in the sacroiliac joint (SIJ) region is often the earliest harbinger for the development of axial SpA including AS. Radiographic changes of sacroiliitis are uncommon in early disease and may take several years to develop. In a clinical and imaging study, 54 patients with IBP of recent onset were investigated. Baseline MRI showed that 85% had bone marrow oedema (BMO) at the SIJs and lumbar spine consistent with active disease. BMO was also found in 40% of subjects in a control group with mechanical back pain and asymptomatic volunteers, however its severity differed between the groups with severe inflammation (grade 2 and 3) found solely in the inflammatory group but not in the controls and associated with HLA-B27. Follow-up MRI at one year showed that subclinical disease (persistence of BMO) was present in the majority of patients (73.5%) despite clinical improvement and was associated with HLA-B27. Radiographic follow-up of this cohort at 8 years identified predictors of poor prognosis with severity of MRI sacroiliitis (BMO grade 3) at baseline and HLA B27 showing a high specificity for the future development of AS (LR=8.0).

In a parallel study, 40 patients within 3 years of onset of symptoms and identified as having a high risk of developing AS (all HLA B27 positive, with IBP1 and SIJ BMO on MRI) were randomised to 4 infusions of infliximab or placebo with MRI as having a high risk of developing AS (all HLA B27 positive, with IBP1 and SIJ BMO on MRI). Results showed that infliximab was effective in suppressing inflammation on MRI.

Conclusion: Screening for axial SpA using standardized referral programmes is feasible and highly effective. Certain patient characteristics may help to estimate which patient with axial SpA is likely to achieve a great clinical benefit from anti-TNF therapy.

INV 22
JUVENILE ONSET SPONDYLOARTHRITIS: WHAT IS THE PROGNOSIS AND ROLE OF ANTI-TNF THERAPY?

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Juvenile-onset spondyloarthritides (SpA) comprise a group of HLA-B27 associated disorders characterized by peripheral arthritis and enthesitis. At onset, most cases correspond to undifferentiated SpA, but within the following 10 years, ~75% of the patients may develop sacroiliac joint and spinal symptoms and the diagnosis of ankylosing spondylitis (AS) should then be considered.

The frequency of juvenile-onset SpA (including psoriatic arthritis) may surpass that of juvenile rheumatoid arthritis. On the long term, the probability of remission five years after onset is only 17%; nearly 60% – particularly those with disease activity for >5 years – had moderate to severe functional limitations by ten years despite remission in 47%. In children with enthesitis related arthritis, CHAQ scores are higher than those of children with oliga or polyarticular JA and their physical functioning lower; their physical health is poorer and bodily pain higher. In contrast, it has been also reported low level disability, including sexual activities after a mean of 27 years disease duration. Compared with adults, juvenile-onset AS required more hip replacements and more patients were in functional classes III and IV and their mean BASFI score was higher.

The therapeutic approach of juvenile-onset SpA is only aimed to reduce disease activity. Yet, case-series of juvenile-onset SpA treated with infliximab and etanercept have reported excellent results with no significant adverse events. Our double-blind, 12-week, infliximab vs placebo trial have shown superior clinical efficacy with infliximab in controlling the signs and symptoms of active juvenile-onset SpA. The 52-week-extension phase showed infliximab sustained efficacy, safety, and tolerability.

Infliximab and perhaps other TNF-α blockers are the best alternative for treating juvenile-onset SpA. Because TNF-α blockers were indicated for arthritis and enthesitis – the earliest manifestations of juvenile-onset SpA – it is expected that this therapy would prevent late structural damage, particularly spinal.

INV 23
THE ROLE OF INFECTION IN SpA

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Infection plays a role as a triggering event in reactive arthritis (ReA) ReA is triggered by Chlamydia trachomatis, Yersinia, Salmonella, Shigella and Campylobacter in about 10-14% of the infected subjects. Ureaplasma urealyticum and Mycoplasma hominis, Clostridium difficile, Escherichia coli O157:H7, even Helicobacter pylori have also been suggested as triggering microbes.

Does persistent infection lead to chronic SpA? About 10-20% of patients with enteric triggered ReA have a prolonged course, which is more common in Chlamydia ReA. Persistent or recurrent urogenital infection or chronic gut inflammation are good candidates for chronicity. There is evidence of persisting microbial antigens in synovium, gut, or lymph nodes. Persisting microbial structures (cell-wall deficient bacteria and bacterial biofilms) may also contribute to chronicity. Psoriatic arthritis (PsA) patients have streptococcal infections, but also chronic viral infections (e.g. hepatitis C and HIV) more frequently compared with subjects with psoriasis.

Do infections cause ankylosing spondylitis (AS)? Acute ReA (especially in HLA-B27+), can proceed to chronic SpA and about 20-40% of patients have AS 10-20 years later. Klebsiella has been proposed to be involved in SpA and in AS, especially in association with peripheral arthritis. Klebsiella belongs to normal gut flora, thus linking AS with gut. AS occurs in between 5 and 10% of patients with inflammatory bowel disease (IBD), those positive for HLA-B27 having a especially high risk. Although IBD cannot be seen as a bacterial infection, stimulation of the immune system by local gut bacteria because of mucosal lesions may contribute to this synergistic relationship. Asymptomatic or uncomplicated enteric or urogenital infection have been linked to the development of AS. Thus an infection might be able to trigger pathogenic mechanisms which later manifest itself as ‘primary AS’. Probably in most, if not all, of the AS patients a bacterial trigger is essential in the pathogenesis.
as early as one week after immunization, well before the onset of joint disease, and by intravital microscopy and confirmed by histology. The eye inflammation begins in the antigenic G1 domain) with aggrecan in DDA adjuvant induces an anterior uveitis as detectable by Western blotting. Patient studies indicate that IL-23 receptor polymorphisms predispose to recurrent, acute anterior uveitis, even in patients who do not have clinical evidence for spondyloarthritis. Further studies in these relatives may yield important data on the early pathogenic events in Crohn’s disease.

Materials and Methods: Data was obtained from the authors files.

Results: Studies involving asymptomatic first degree relatives of patients with Crohn’s disease (n=151) and AS (n=124) in Iceland show that between 40 and 50% have intestinal inflammation (judged by a faecal calprotectin test). Variance components analyses suggest that the inheritance pattern of this inflammation is affected by a similar and major additive gene in both groups of relatives. The importance of this inflammation was assessed in the relatives of AS patients where HLA B27 status, faecal calprotectin levels and CT abnormalities of the sacroiliac joints were correlated.

Conclusion: These findings suggest that one or more undiscovered genetic variants may underlie the risk of both AS and Crohn’s disease and that the intestinal inflammation plays a pathogenic role in AS. Further studies in these relatives may yield important data on the early pathogenic events in Crohn’s disease.
**INV 28**

**CYTOKINES AS TARGETS IN INFLAMMATORY RHEUMATIC DISEASES**

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Despite the successful development of a variety of novel therapeutic agents, unmet clinical needs exist in the treatment of inflammatory arthritis and spondyloarthropa-thy. Therapeutic intervention should address inflammation, articular damage, co-morbidity and functional decline, all attendant to uncontrolled inflammatory proc-esses. Several data now suggest that the kinetics of intervention are important – in principal earlier intervention leads to improved outcome regardless of the therapeu-tic agent employed. This is evident in comparing primary with subsequent DMARD interventions and in particular in comparing the clinical responses to TNF blockade in early versus later disease cohorts. Pathologic studies of synovial biology have not revealed particularly striking phenotypic differences in appearances over time– there are however limitations in the extent and rigor of sequential analyses in individual patients’ biopsies and in the functional nature of such studies by neces-sity. This raises important issues in the design of optimal management strategies. (i) Upon clinical presentation, the inflammatory response should be limited rapidly to minimise the onset of damage to tissues that could provide an environment condu-cive to chronicity. There may be cytokines (in addition to TNF) that are effective as targets in this respect by virtue of their broad roles at early stages of inflammatory responses. (ii) Cytokines (e.g. IL-12, IL-23, IL-35) that regulate critical T cell, den-trritic cell and B cell interactions remain relatively poorly understood in the context of inflammatory synovitis but may facilitate interventions that can promote toler-ance induction. Moreover, novel cytokine activities such as IL-33 are emerging that implicate other cellular lineages in the inflammatory synovial responses e.g. mast cells. Similarly the pathways that lie upstream of cytokine release are not being recognized and offer targeting potential in their own right. (iii) A variety of models now exist that facilitate analysis of such possibilities in particular in vivo. These will in turn instruct appropriate target selection – we should not at this stage assume that the same targets will be valid across the kinetics of an immune response and therefore a disease state.

**INV 29**

**POSSIBLE NEW AGENTS TO TREAT ANKYLOSING SPONDYLITIS AND OTHER SPONDYLOARTHRITIDES**

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The introduction of TNF-blockers for the treatment of patients with active ankylos-ing spondylitis (AS) over the last 5-10 years has meant a major breakthrough in the management of this chronic inflammatory disease. How early AS patients should be treated with a TNF-blocker, whether the remission rate can be increased or whether even a drug free remission can be achieved if treated early enough and whether ear-ly therapy can prevent long-term structural damage are open and important ques-tions which have to be addressed and solved in the near future. NSAIDs are potent anti-inflammatory agents which are still the first line of treatment. Recent evidence even indicates that NSAIADs might inhibit the growth of syndesmophytes, possibly through a prostaglandin-mediated inhibition of osteoblasts. Thus, the exact role of the two established therapies for AS, TNF-blockers and NSAIDs, in treatment strat-egies has still to be determined. Nonetheless, it has become clear by clinical experi-ence but also through many studies which have been performed with the two kind of drugs over the last years that not all patients show a major response if treated. Future research will focus on new agents which can inhibit inflammation in patients who are TNF-failures but also in direct comparison to TNF-blockers and on drugs which can inhibit new bone formation. An ideal drug for the treatment of AS would suppress inflammation and prevent new bone formation. Based on experience in animal models, on the treatment of other chronic inflammatory diseases and on histological and functional studies in AS treatment directed at the following targets are currently already tested or should be tested in the near future: B cells (rituxi-mab), T cells (abatacept), IL-6R, IL-17, IL-23, regulatory T cell (Treg). Regarding new bone formation several molecules of the wnt pathways could be targeted such as ‘bone morphogenetic proteins’ (BMP). Obviously, a better understanding of the pathogenesis will allow to investigate further targeted therapies.

**INV 30**

**BIOLOGY AND ROLE IN AUTOIMMUNITY OF TRIMMING AMINOPEPTIDASES**

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Peptide ligands for MHC class I molecules are produced through the action of one or several intracellular proteases. Initial antigen degradation by cytosolic protea-some complexes is frequently followed by aminopeptidase mediated trimming. Trim-ming can occur in the cytosol, before peptide transport into the endoplasmic reticu-lum (ER) by the transporters associated with antigen processing (TAP). However, available evidence suggests that trimming after TAP transport, by aminopeptidases of the ER, plays a larger role in HLA class I antigen processing. In human cells, two related ER aminopeptidases with complementary specificities, ERAp1 and ERAp2, have been shown to trim epitope precursors. The two enzymes can form dimeric complexes, with a possible effect on enzyme activity and/or specificity. Analysis of mice deficient for ERAp1, the only known ER trimming peptidease in that species, demonstrated that formation of a substantial percentage of pMHC complexes requires peptide trimming in the ER. Cell surface MHC class I mole-cules in these mice display reduced stability, presumably because of a dearth of optimal peptides in the ER, and of MHC class I loading with N-terminally extended peptides, ERApAko mice mount only slightly altered T cell responses to several viruses, demonstrating that peptide trimming is not essential for priming of anti- viral CD8+ T cells. However, ERApAko antigen presenting cells are highly immuno-nugenic in ERApAdeficient mice and elicit vigorous T and B cell responses. It is therefore conceivable that local changes in expression of human ERAP enzymes, as well as altered ERAp specificity due to coding sequence polymorphism, might render affected tissues immunogenic, and underlie the recently reported association of ERAP polymorphism with ankylosing spondylitis.

**INV 31**

**THE BIOLOGICAL AND PATHOGENETIC ROLE OF HLA-B27-BOUND PEPTIDES: TOWARDS A GLOBAL PERSPECTIVE**

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The basis for the association of HLA-B27 with ankylosing spondylitis (AS) and chronically evolving reactive arthritis remains unknown. Several hypotheses, each one emphasizing the pathogenetic potential of a particular feature of HLA-B27, attempt to explain the mechanism of these diseases and the differential association of B27 subtypes to AS. Stable transfection of bacterial protein constructs into hu-man cells was used to demonstrate that HLA-B27 presents endogenously processed peptides from thearthritogenic bacteria Chlamydia trachomatis with a high level of sequence identity to self-derived HLA-B27 ligands and other human protein se-quences. This finding provides molecular support for a pathogenetic role of HLA-B27 based on mimicry between foreign and self-B27 epitopes. Folding and other biological features do not correlate with the differential association of HLA-B27 subtypes to AS. As an alternative to single-feature based mechanisms, HLA-B27 can be analyzed from a more global perspective of its biology, emphasizing the inter-dependency of multiple molecular features and the influence of other disease-modifying genes. From this viewpoint, peptide binding emerges as the cornerstone of HLA-B27 biology and pathogenetic role, as it determines not only the antigenic features of the molecule, but also its folding and stability.
Animal models have provided important insights into molecular mechanisms of pathogenesis in inflammatory arthritis diseases. Rodents that overexpress the MHC class I molecule HLA-B27, a major predisposing factor for ankylosing spondylitis (AS) and other human spondyloarthritides (SpA), have been shown to develop spontaneous SpA-like disease. Although these animals do not provide a precise phenocopy of AS, they have been useful for defining the cellular requirements for disease, and further dissection of pathogenic mechanisms is likely to provide insights into the precise role of HLA-B27.

In my presentation I will review the handling of and mishandling of peptides by HLA-B27 in animal models of SpA. Peptides, along with β2m, constitute the cargo that MHC class I molecules deliver to the cell surface for display to CD8+ T cells. Peptides play a crucial role in self, non-self discrimination, and in marking cells for destruction when infected with certain microorganisms. Both peptides and β2m are critical for the proper assembly of MHC class I complexes. Peptide-induced conformational changes stabilize MHC class I heavy chains during their assembly in the endoplasmic reticulum (ER), thereby preventing the rapid degradation of unassembled heavy chains. The requirement of HLA-B27 for higher concentrations of peptide to induce stabilization suggests that mishandling of peptides may be a factor in its tendency to misfold and form aberrant disulfide linked and β2m-bound heavy chain complexes in the ER. Recent results from whole genome association studies implicating ARTS-1 (also known as ERAAP) as a predisposing factor in AS, raise the possibility that additional events occurring in the ER, and influencing the immunobiology of HLA-B27, are involved in pathogenesis. However, the protein encoded by ARTS-1 is bifunctional, serving as a cytokine receptor ‘sheddase’ as well as an ER-associated aminopeptidase, and therefore the role of this gene product may be complex.

Considerable evidence generated in the 1990s using HLA-B27 transgenic mice deficient in β2m suggested that peptides generated in the cytosol and transported into the ER were not involved in the development of spontaneous arthritis. However, these results have not been reproduced in other laboratories, perhaps due in part to complex background strain differences, making it difficult to draw definitive conclusions about the role of peptides in mouse SpA. Nevertheless, in the rat model there is indirect evidence from CD8ββ T cell deletion studies to support the idea that classical T cell recognition of HLA-B27-restricted peptides is not required for disease. However, if peptides are important for stabilization of heavy chains in the ER and peptide ‘mishandling’ contributes to heavy chain misfolding, then they may be critical players in pathogenesis. This raises important possibilities for ARTS-1/ERAAP and peptide trimming in the ER as a factor in the pathogenesis of AS. Recent results from our laboratory suggest that HLA-B27 misfolding in the rat model of SpA may be linked to disease through the unfolded protein response (UPR), rather than peptide presentation to CD8+ T cells. Macrophages undergoing an HLA-B27-induced UPR produce more IL-23 than IL-12 in response to certain pattern recognition receptor (PRR) agonists. Interestingly, there is dramatic over-expression of IL-17 and expansion of IL-17 producing CD4+ T cells in the colon of HLA-B27 transgenic rats that correlates with development of colitis. These data implicate a novel mechanism to explain the role of HLA-B27 misfolding in Th17-driven inflammation in this animal model with implications for human disease.

Please note that as of September 2, 2008, my address will be:
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Background:
T-helper 17 (Th17) cells are a T-cell population that play a pivotal role in several inflammatory conditions and are dependent on interleukin-23 (IL-23) for their survival and expansion. More recently, a genetic association was discovered between polymorphisms in the gene coding for the IL-23 receptor and spondyloarthritides (SpA). Also, targeting IL-23 has been shown to be of clinical benefit in Crohn’s disease and psoriasis, two conditions that are closely related to SpA. Our aim was to evaluate the potential role of Th17 associated cytokines in SpA pathogenesis by measuring their levels in the joints and circulation of SpA patients as well as correlating them with disease activity parameters.

Methods: Paired synovial fluid (SF), serum and synovial biopsies were obtained from 53 SpA and 23 rheumatoid arthritis (RA) patients. Interleukin-17, IL-23 and CCL20 were measured by ELISA in the SF and serum of the patients and correlated with systemic and local parameters of disease activity.

Results: SF IL-17 levels were as high in SpA as in RA patients and correlated with disease activity parameters in RA. However, if peptides are important for stabilization of heavy chains in the ER and peptide ‘mishandling’ contributes to heavy chain misfolding, then they may be critical players in pathogenesis. This raises important possibilities for ARTS-1/ERAAP and peptide trimming in the ER as a factor in the pathogenesis of AS. Recent results from our laboratory suggest that HLA-B27 misfolding in the rat model of SpA may be linked to disease through the unfolded protein response (UPR), rather than peptide presentation to CD8+ T cells. Macrophages undergoing an HLA-B27-induced UPR produce more IL-23 than IL-12 in response to certain pattern recognition receptor (PRR) agonists. Interestingly, there is dramatic over-expression of IL-17 and expansion of IL-17 producing CD4+ T cells in the colon of HLA-B27 transgenic rats that correlates with development of colitis. These data implicate a novel mechanism to explain the role of HLA-B27 misfolding in Th17-driven inflammation in this animal model with implications for human disease.

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AS patients were divided into the presence (HIP+) or absence (HIP-) groups. Amongst 220 patients, 47 (21.4%) had radiographic evidence of hip dis-ease. Hip disease is a frequent finding in AS and is associated with clin-ical manifestations. Intra-articular and periarticular disease were noted. Furthermore, patients suffering from chronic arthritis (rheumatoid arthritis or anklyosing spondylitis) or Crohn’s dis-ease, TNF blockade has proven to be a valuable treatment. However, the role of iNKT cells in TNF-driven inflammation has not been appraised yet. iNKT cells are considered a suitable mouse model for Crohn’s disease associated arthritis because they develop peripheral arthritis, spondylitis, spondylitis and Crohn’s-like ileitis. Results: When these mice were backcrossed onto an iNKT cell deficient (J18−/−) background, we observed accelerated disease progression. Conversely, transferred purified iNKT cells from healthy controls into TNFα x J18−/− mice partially reversed the disease phenotype. It has been shown that further processing cells, especially dendritic cells, were enriched in inflamed regions, and expressed a semi-mature phenotype, with upregulation of CD1d. The endogenous presentation of glycolipids to iNKT cells was strongly promoted, and required lymosomal processing. Conclusions: These findings indicate that iNKT cells may regulate TNF-driven in-flammation by a mechanism of chronic TNFα induced maturation of antigen pre-senting cells, leading to marked enhancement of endogenous glycolipid presenta-tion by CD1d. This leads to activation of iNKT cells to exert their regulatory role.

Background: The heterodimeric receptor of IL23 is formed by the beta 1 subunit of IL12R and an IL23 specific subunit encoded by the IL23R gene. Both subunits are required for IL23 signaling. In a study by the Wellcome Trust Case Control Consor-tium (WTCCC) and the Anglo-Australo-American AS consortium (TASC), it has been shown that IL23R variants are associated with anklyosing spondylitis. Two further smaller studies have shown limited associations of IL23R variants with AS. To reduce the impact of lack of power in the assessment of the association between IL23R polymorphisms and AS, we undertook a meta-analysis of published studies and included unpublished data on additional 730 AS cases from the UK. The size of the effect and the causal variants in IL23R remain to be identified precisely.

Methods: In total, 3597 cases and 3150 controls from 4 different studies have been combined in the meta-analysis of association. Populations were from Canada, Spain, UK and USA. Data were analysed using STATSDIRECT software. DerSimonian-Laird test was used to calculate random effects pooled odds ratio with 95% confidence intervals and p-values.

Results: Statistically significant associations have been found between various IL23R polymorphisms and AS. IL23R SNP rs11209032 showed a strong association with AS (P<0.0001). SNPs rs10499629, rs1343151 and rs1495965 showed marginal associations with AS (P<0.0007, P<0.0002 and P<0.0004 respectively).

Conclusions: IL23R polymorphisms may be associated with either increased or decreased susceptibility to AS. In order to confirm these results, more polymorphisms covering the whole gene and its regulatory sequences should be tested. Functional consequences should also be investigated.

Background: In anklyosing spondylitis (AS) chronic inflammation in the sacro-iliac joint and spine is followed by anklyosis. In the hip, it is followed by cartilage erosion and joint destruction. The frequency and predictors of hip disease in AS have not been fully elucidated. We address these issues in the current study.

Methods: AS patients were divided into the presence (HIP+) or absence (HIP−) of hip disease by radiographic evidence of joint space narrowing or by total hip replacement (THR). Means (±SD) were calculated for various clinical variables and compared using the student’s t-test.

Results: Amongst 220 patients, 47 (21.4%) had radiographic evidence of hip dis-ease, and of these, 15 patients (12 males), 6.7% of the cohort, had had THR (8 bilateral, 7 unilateral). Mean age (±SD) was 42.8 (±14.7) in the HIP+ group and 38.9 (±12.9) in the HIP− group (p=0.08). There was a statistical difference in disease duration between the HIP+ (19.3 years ±11.6) and HIP− (15.6 years ±11.3) groups (p=0.05), but not in HIP-B27 positive patients, 75.7% (HIP+) and 82.3% (HIP−), or proportion with juvenile onset (17.5% HIP+) and 24.9% (HIP−). There was a trend towards more males in the HIP+ group (89.4% versus 78.6%) (p=0.10). There was no statistical difference in BASDAI ESR or CRP between the 2 groups. Mean mSASSS (±SD) was 32.4 (±27.7) in the HIP+ and 16.1 (±22.0) in the HIP− groups (p=0.001).

Conclusion: Hip disease is a frequent finding in AS and is associated with clini-cally and radiographically more severe spinal disease. The occurrence and severity seem to be linked and suggest common pathogenic mechanisms.
M. D’Agostino (PDUS) FOR THE DIAGNOSIS OF SPONDYLARTHROPATHY (SpA)

Further studies will prove the usefulness of inclusion of the thoracic spine in the cervical and lumbar spine and in 0.6 units after 2 years was 0.9 units. However, this part of the spine is not included in the mSASSS.

Recently, PDUS proved to be a highly sensitive tool to assess enthesis in SpA. In patients with a suspicion of SpA, diagnosis could be improved by detecting enthesis with PDUS.

**Objectives:** To constitute a French cohort suitable for assessing the diagnostic performance of PDUS for the diagnosis of SpA.

**Methods:** Prospective, multicenter French cohort study. Outpatients consulting for symptoms suggestive of SpA (inflammatory back pain (IBP), arthritis or inflammatory arthropathy (IA), enthesitis or dactylitis (ED), uveitis with HLA-B27 positivity (B27+U), familiarity for SpA (Fam)) were recruited. At entry, patients were submitted to clinical examination, pelvic x-ray, MRI and CT scan of sacroiliac joints, HLA-B typing. PDUS of 16 enthese was performed by an independent examiner blind to subject’s identity and symptoms. Diagnosis of SpA will finally be retained or excluded by an experts’ committee, blind to PDUS results, after 2 yrs of follow up. Sample size was set to 500 patients (estimated prevalence of SpA of 30% after 2 yrs).

**Results:** Between January 2005 and September 2007, 489 patients were included (96% of target). Mean age was 40 yrs, mean duration of symptoms was 42 yrs; 42% of patients were HLAB27+ and 62% were female. Primary inclusion criterion was IBP in 49%, IA in 28%, ED in 10%, B27+U in 9% and Fam in 4%. At inclusion, the opinion of the referral rheumatologist with regard to the suspicion of SpA was “probably yes” in 45%, “probably not” in 7%, and “doubtful” in 48%.

Regarding the 250 patients who have yet completed the study (2% of patients were lost to follow-up); a diagnosis of SpA was made by the referral rheumatologist in 32%, whereas SpA was excluded in 21% and a doubt persisted in 37% of them.

**Conclusion:** If the value of PDUS is confirmed, the consequences will be multiple, such as an improvement of diagnostic procedures and therapeutic management of SpA, and a reduction of diagnostic costs.

**O 8**

THE LOWER PART OF THE THORACIC SPINE ADDS IMPORTANT INFORMATION IN ASSESSMENT OF RADIOGRAPHIC PROGRESSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS)

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**Background:** The modified Stokes AS spinal score (mSASSS), the most reliable instrument to evaluate structural outcomes, assesses the cervical and the lumbar spine in patients with AS and is important for the outcome in studies with such patients. Magnetic resonance imaging studies have shown that the lower thoracic spine shows the most inflammatory lesions in AS.

However, this part of the spine is not included in the mSASSS.

**Objectives:** To assess the contribution of the lower thoracic spine to radiographic outcomes in AS.

**Methods:** Standard conventional radiographs of the cervical and lumbar spine of 80 AS patients were quantified for radiographic progression within 2 years by using the mSASSS.

All vertebral edges (VE) of the lower part of the thoracic spine segment (Th9 to Th12 that were assessable on lumbar spine radiographs were additionally scored (‘adjusted mSASSS’) and compared to the original mSASSS.

**Results:** In comparison to the original mSASSS, additional vertebral edges (VE) could be scored (86%), from segment Th12 to Th9. However, only data up to the lower segment of Th10 added significantly in depiction of radiographic progression, with 3.1±1.0 additional vertebral edges per patient. The mean change in mSASSS units after 2 years was 0.9±2.8 with the original mSASSS, and 1.7±3.1 with the adjusted mSASSS (p=0.001). Syndesmophytes/ankylosis were seen in 1.4±2.0 VEs per patient in the cervical and lumbar spine and in 0.6±1.2 VEs per patient in Th10-Th12.

**Conclusions:** The lower part of the thoracic spine is not included in the mSASSS but is usually visible in standard conventional radiographs in clinical practice. Its inclusion adds substantial information on additional syndesmophytes on an asymptomatic patient. Further studies will prove the usefulness of inclusion of the thoracic spine in the outcome of treatment in AS patients.

**O 9**

MAGNETIC RESONANCE IMAGING (MRI) OF THE ANTERIOR AND POSTERIOR SPINAL SEGMENTS DURING ADALIMUMAB (HUMIRA®) THERAPY FOR ACTIVE ANKYLOSING SPONDYLITIS (AS)

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**Objectives:** To evaluate the ability of facet joint scoring of the spine, in addition to an established MRI scoring method, to detect adalimumab effects on spinal inflammation.

**Methods:** MRI scans were performed for 58 patients from the open-label RAPHSODY trial. AS patients with BASDAS1 ≥4 received adalimumab 40 mg every other week for 12 weeks. Axial skeleton MRIs were performed at baseline and after 12 weeks. Active spinal inflammation was scored according to the Berlin MRI spine score (0-69). Facet joints of each spinous segment were scored for inflammation (0=inactive, 1=probable, 2=definite/active).

**Results:** Mean (SD) baseline spine score was 6.0 (7.8) and decreased to 3.2 (4.6) after 12 weeks of adalimumab (p<0.001) (47% reduction in spine inflammation). Mean MRI score of the facet joints decreased from 5.9 (7.8) at baseline to 2.0 (3.1) after adalimumab (p<0.001). Eight patients had no reduction in MRI score, but a reduction in facet joint score: two patients (3%, Reader 1) and six patients (10%, Reader 2). Inter-reader agreement was good-to-excellent for Berlin MRI spine score and facet score (Baseline ICC=0.94, Week 12: ICC=0.69). Facet and joint scores (baseline ICC=0.93, Week 12: ICC=0.71).

**Conclusions:** Adalimumab significantly reduced active inflammatory lesions of the spine. Facet joint scores detected change of inflammation in up to 10% of patients with no change in the anterior segment of the spine. Addition of facet joint scoring may increase the overall sensitivity to change in MRI assessments.

**O 10**

ANKYLOSING SPONDYLITIS AND THE RISK OF FRACTURE: RESULTS FROM A LARGE PRIMARY CARE-BASED NESTED CASE CONTROL STUDY

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**Background and Aims:** Ankylosing spondylitis (AS) is associated with bone loss in the vertebrae and an increased prevalence of vertebral fractures, but literature about the magnitude of the risk of fracturing is limited. One retrospective cohort study provided evidence of an increased risk of clinical vertebral fractures but not for non-vertebral fractures. This study further explores the risk of clinical vertebral and non-vertebral fractures in a large population database.

**Methods:** In a primary care-based nested case-control study, 231,778 fracture cases and 231,778 age- and sex-matched controls were recruited. A history of AS was assessed from the medical records. AS was diagnosed in a total of 758 people. Odds ratios (OR) and 95% confidence intervals (CI) were calculated after adjustment for medication, other illnesses, smoking and body mass index whenever known.

**Results:** The prevalence of AS was 0.18% in fracture cases and 0.15% in controls. Patients with AS had an increased risk of clinical vertebral fracture (OR: 3.26; CI: 1.51-7.02). The risk for forearm and hip fracture was not significantly increased (OR: 1.21 [CI: 0.87-1.69] and 0.77 [CI: 0.43-1.37], respectively). The risk of any clinical fracture was increased in AS patients with a history of inflammatory bowel disease (IBD) (OR: 2.79; CI: 1.10-7.08), whereas it was decreased in AS patients taking non-steroidal anti-inflammatory drugs (NSAIDs) (OR: 0.65, CI: 0.50-0.84). The risk was not associated with recent back pain, psoasitis, joint replacement therapy and use of sulfasalazine.

**Conclusions:** Patients with AS have an increased risk of clinical vertebral fracture, but not of non-vertebral fractures, while in patients with concomitant IBD the risk of any clinical fracture is increased. The mechanism by which intake of NSAIDs reduces the risk of any clinical fracture warrants further research.
ER STRESS MODIFIES THE IL-23 RESPONSE TO TOLL-LIKE RECEPTOR AGONISTS AND INTRACELLULAR BACTERIA INFECTION

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The secretion of IL-12 and IL-23 by dendritic cells plays a key role in co-ordinating protective and pathological immune responses. We have previously shown that LPS activation of monocyctic cell lines induces the unfolded protein response (UPR), we wished therefore to determine the contribution of the UPR to the induction of proinflammatory cytokine production following TLR activation or intracellular bacterial infection.

The ER stress inducing agent thapsigargin (TP) was added to monocyte derived dendritic cells isolated from the peripheral blood of healthy individuals, in the presence or absence of TLR agonists, to simulate microbiological infection. TP in combination with TLR2,3,4 and 8 stimulation synergistically enhanced TNF-α, IL-23 p19 but not IL-12 p35 mRNA.

Furthermore, UPR activation in combination with TLR agonists only enhanced TNF-α, IL-23 but not IL-12 p70 secretion. Using lentiviral delivery of short hairpin RNAs to reduce the expression of the ER stress signalling molecule, XBP-1, in U937 cells, we were able to demonstrate that UPR signalling was a critical component of this synergistic response.

Activation of the UPR by the addition of TP also induced phenotypic changes in immature dendritic cells and enhanced their ability to stimulate the differentiation of naive CD4+ T cells.

Infection of the monocyctic cell line U937 with the obligate intracellular bacterial pathogen Chlamydia trachomatis resulted in a significant increase in ER stress activation, again knockdown of XBP-1 in infected cells decreased the expression of IL-23 p19 mRNA. This suggests that UPR induction is an important component of the IL-23 response to intracellular infection. This work identifies a novel pathway of IL-23 activation that results in the super-induction of IL-23 mRNA in monocyte and dendritic cells. This study has demonstrated that the UPR can have significant affects on the function of immune cells that orchestrate proinflammatory immune responses.

MICROARRAYS IDENTIFY RGS1, A REGULATOR OF G-PROTEIN SIGNALING, AS A HIGHLY SENSITIVE AND SPECIFIC SpA BIOMARKER

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Aim: To discover blood-based biomarkers for SpA patients with inflammatory back pain, but lacking psoriasis, IBD, active uveitis, or reactive arthritis.

Method: Genome-scale microarray analysis was carried out on PBMC from 10 healthy and 49 SpA subjects. Genes with t-test p-values <0.000002 were evaluated by measuring their ROC area under the curve (AUC). An AUC >0.8 indicates high sensitivity and specificity.

Result: The gene expression pattern of SpA as a whole was heterogeneous. Correlation matrix of microarray data against 19 clinical variables unmasked existence of two uniform subsets: patients with radiological sacroiliitis score of < 2 (classified as USpA) showed 135 differentially expressed genes, whereas in patients with sacroilitis > 3 (classified as AS), only 6 of these same USpA genes were differentially expressed. 5 PCR-validated genes discriminated AS from normal subjects with an AUC of 0.8. The highest was again RGS1.

The others with AUC >0.9 were NR4A2, FoxO1, ATF3, IL-1alpha, IL-6, IL-8, MIP-1alpha, MIP-2alpha, PAI and HB-EGF. When all SpA patients were considered as a single group, RGS1 again showed high sensitivity of 84.3% and specificity of 95% (p<0.0001). These biomarkers were also evaluated by combining them into a single score. A combination of RGS1 plus NR4A2 provided for USpA almost perfect sensitivity of 93.3% and specificity of 100% (p<0.0001).

Conclusion: (1) RGS1 (a modifier of chemokine receptor signaling) and the transcription factor NR4A2 (a known modifier of arthritis inflammation) are highly sensitive and specific SpA biomarkers. (2) SpA patients with or without radiological sacroilitis displayed drastically different gene expression profiles. The surprising lack of correlation to the duration of disease questions whether USpA and AS are necessarily longitudinally overlapping entities.

HETEROGENEOUS MICRORNA PATTERN OF AS PATIENTS: ELEVATED MIR-27A AS A NEW BIOMARKER SIGNIFICANTLY DOWNREGULATED BY ENBREL TREATMENT

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Background: To investigate whether microRNA (miRNA) expression altered in AS and the effect of Enbrel treatment.

Methods: PBMCs from 10 healthy controls and 10 active AS patients before and after Enbrel treatment (50mg qw. Subcutaneously) were included in miRNA microarray with 428 miRNA probes. MiRNA expression profile differences between any two of the 3 groups were tested by calibrated value. Candidate miRNAs were performed with Beacon Probe miRNA real time PCR in a larger sample size (n=40 for each group). A fold change of >2 was considered significant. Spearman correlation analysis between miRNAs expression before Enbrel treatment and 16 clinical parameters of patients (BASDAI, BASFI, ESR, CRP, etc) was performed using SPSS13.0.

Results: The miRNA expression pattern of microRNA microarray in AS patients as a single group was heterogeneous. Results discovered 19 significantly differentially expressed miRNAs: 14 expressed higher in AS group than those in controls; 5 expressed lower in AS group than those in controls. 4 most significantly altered miRNAs (>5 folds) miR-17-5p, miR-29a, miR-126-3p and miR-27a were validated by miRNA real time PCR. Four miRNAs miR-17-5p, miR-29a, miR-126-3p and miR-27a were significantly higher in patients (Ct value: 7.83±3.67, 7.26±3.18, 3.52±3.67 and 10.97±1.38, respectively) than that in healthy controls (Ct value: 10.68±4.12, 11.06±0.94, 4.61±1.34 and 8.71±3.30, respectively).

Matched fold changes were 7.21, 13.93, 2.13 and 4.76, respectively. Three miRNAs miR-17-5p, miR-29a and miR-126-3p expression were again dramatically down-regulated after 12 weeks’ Enbrel treatment (Ct value: 9.83±3.62, 8.93±4.73 and 4.88±3.72). Matched fold changes were 3.97, 13.93 and 2.57, respectively. Moreover, elevated miR-27a expression was positively correlated with ESR (r=0.370, P=0.02) and CRP (r=0.358, P=0.02).

Conclusions: AS pathogenesis involved abnormal miRNA contribution. MiR-27a was a valuable biomarker to evaluate inflammation and disease activity in AS patients.

DISTINCT PROTEOMIC PROFILE IN ANKYLOSING SPONDYLITIS PATIENTS: TALIN1 IS A NEW VALUABLE BIOMARKER FOR DIAGNOSIS AND TREATMENT

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Background: To identify special proteins in peripheral blood mononuclear cells (PBMCs) and sera in AS patients.

Methods: Twenty patients were recruited: AS group (n=8), healthy individual group (n=6) and RA group (n=6) including their protein and mixed sera respectively. They were age and sex-matched. Proteins were separated from PBMCs by 2-Dimension- al Electrophoresis (2-DE) and analyzed by matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) and TOF-TOF mass spectrometry. Real-time RT-PCR was used to validate the proteins in enlarged age- and sex-matched samples of AS (n=30), RA (n=20) patients and healthy individuals (n=30).

Results: Among 1200 protein spots detected on the gels, 10 up-regulated and 3 down-regulated protein spots were found in AS group compared to other groups. Six proteins including Talin1, which were 5-fold up-regulated in AS patients, was identified by MALDITOF and TOF-TOF MS. Western blot showed Talin1 in AS, HC and RA group are 1.14±1.40, 0.49±0.64 and 0.38±0.50 respectively. Its expression is higher in AS group than that in HC and RA group (P<0.05).

Furthermore, the results of miRNA relative quantity showed that Talin1 expression was significantly increased in AS patients compared to that in healthy controls and RA patients (3.62±2.20 in AS,1.00±0.24 and 0.97±0.20 respectively, P<0.01).

In sera, 10 differentially expressed protein spots were detected. ELISA verified result of CP showed its expression in AS, HC and RA group are 0.29±0.05, 0.65±0.30 and 0.37±0.04 respectively. Transferrin expression in AS, HC and RA group is 0.99±0.19, 0.51±0.44 and 0.10±0.02 mg/ml respectively. CP and transferrin expression is significantly higher in AS and RA group than that in HC group (P<0.05).

Conclusions: Proteomic profile of AS is distinct and talin1 can be used as a useful biomarker for diagnosis and treatment.
P 5
ABNORMAL HIGH-EXPRESSION OF CD154 ON T CELLS OF AS PATIENTS IS DOWN-REGULATED BY THE ENBREL TREATMENT
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Background: To evaluate the expression of costimulatory molecule CD154 on T-cells in peripheral blood from patients with ankylosing spondylitis (AS) and their changes after treatment with Enbrel in a randomized, double-blind, placebo-controlled trial.

Methods: Sixty-six patients with AS (39 cases at active stages and 27 cases at inactive stages; according to the clinical features, they were divided into two groups: 35 cases with axial and peripheral joint involvement and 31 cases with axial involvement alone), 30 patients with rheumatoid arthritis (RA) and 30 healthy volunteers were recruited in this study. The expression of CD154 on CD3+ T cells as well as T-cells subsets were evaluated using flow cytometry.

Results: (1) The CD154 expression on CD3+ T cells in peripheral blood in AS patients was significantly higher than that in healthy volunteers and RA patients (p<0.05). Frequency of CD3+CD4+ T cell in AS and RA patients was respectively significantly higher than that in healthy volunteers, and frequency of CD3+CD8+ T cell in AS and RA patients were significantly lower than that in healthy volunteers (p<0.05). (2) The expression of CD154 on CD3+ T cells in peripheral blood in active AS cases or cases with peripheral joint involvement was respectively significantly higher than that in inactive cases or cases with axial involvement only (p<0.05), which was positively correlated with tender joint count and swollen joint count (p<0.05). (3) Compared with AS patients treated with placebo at 6-week, CD154 expression on CD3+ T cells decreased in patients treated with Enbrel (p<0.05).

Conclusions: There was no significant difference between patients with treatment of Enbrel and healthy volunteers at 6-week (p>0.05).

P 6
SOLUBLE LIGHT: A NOVEL CYTOKINE IN SPONDYLOARTHITIS
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Introduction: The lack of sensitive biomarkers remains a problem in AS. LIGHT (TNFSF14) is an anti-111; member of the TNF superfamily that recruits TRAF2 and TRAF5 leading to release of NF-κB. LIGHT (TNFSF14) is a newly identified member of the TNF superfamily that recruits TRAF2 and TRAF5 leading to release of NF-κB. LIGHT is elevated in patients with spondyloarthritis. The change in sLIGHT is strongly correlated to objective markers of inflammation following infliximab is strongly correlated to

Conclusion: LIGHT is elevated in patients with spondyloarthritis. The change in objective markers of inflammation following infliximab is strongly correlated to the change in sLIGHT.

P 7
LINKAGE ANALYSIS OF FAMILIAL ANKYLOSING SPONDYLITIS CONFIRMS A ROLE FOR ARTSI BUT THE CANDIDATE EXONIC VARIANT K528R IS NOT RELATED TO CYTOKINE RECEPTOR SHEDDING PROFILES
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Introduction: A recent genome-wide association scan reported that ARTSI is a major non-HC locus associated with ankylosing spondylitis (AS). ARTSI has two known functions: (i) promoting shedding of cytokine receptors such as TNFRI, IL-1RII and IL-6R; (ii) trimming peptides for MHC class I-mediated antigen presentation.

Objectives: I. To assess whether there is excess transmission of ARTSI alleles in multiplex families with AS. 2. To assess whether the 525R variant correlates with cytokine receptor shedding profiles.

Methods: We genotyped 231 multiplex AS families with two ARTSI exonic SNPs (rs30187 and rs27044), and performed family-based association analyses. Sera from 80 AS patients (not on biologic treatments) were assayed for sTNFRI, sIL-1RII and sIL-6R by ELISA.

Results: FBAT analysis on our AS families revealed that the exonic variant (rs30187[G]) is associated with AS (dominant model; p-value = 0.012). There was no significant association of the exonic variant rs27044 with AS. The AS cohort for the functional analysis (n=80) had a mean age of 42.3 ± 10.6 years. In this cohort, the ESR (mean 18 ± 15.6 mm/hr; CRP (mean 14.8 ± 18.8 g/dL; BASDAI (mean 5.3 ± 2.4) had no correlation with the major or minor alleles of rs30187 and rs27044. In terms of serum levels of sTNFRI, sIL-1RI, and sIL-6R, there was no relationship to the respective ARTSI alleles. There was a significant correlation of sIL-6R with sIL-1RI (R<0.49; p<0.0001) and with sTNFRI (R=0.31; p=0.007) but there was no correlation between sTNFRI and sIL-1RI.

Conclusion: This is the first report showing excess transmission of rs30187[G] in multiplex AS families, confirming population studies on the association of rs30187 with AS. However, we observed no relationship between the AS-associated ARTSI K528R variant and cytokine receptor shedding profiles. Our results suggest that the functional relevance of the ARTSI K528R variant might relate more to peptide trimming for antigen presentation.

P 8
THE INFLAMMATORY MILIEU AND HLA-B27 EXPRESSION IN ANKYLOSING SPONDYLITIS – IMPLICATION FOR DISEASE PATHOGENESIS
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Introduction: HLA-B27 is strongly linked with the pathogenesis of Ankylosing Spondylitis (AS) and increasing evidence suggests that a minimum threshold of gene expression is necessary to cause the disease. The aim of this study was to outline the influence of the inflammatory milieu in modulating B27 gene expression.

Methods: Twenty different cytokines were used as stimuli on CD14+ PBMCs from HLA-B27+ ASs and NCs, and on HLA-B27+ NCs in culture for 72 hours. IL-1, IL-2, IL-4, IL-5, IL-7, IL-8, IL-10, IL-12, IL-13, IL-15, IL-17, IL-18, M-CSF, GM-CSF, IP10, MCP-1, MIP-1, IFNα, TGF-β, TNFα were assayed at optimal concentration. HLA-B27 whole molecules were determined at the surface of CD14+ PBMCs by means of ME1 mAb and a cytofluorimetric quantitative technique in Antibody Binding Capacity (ABC) units. Data were expressed as mean ratio of stimulated versus unstimulated cultured cells (TCM only).

Results: A significant increase in B27 expression was observed for IFN-γ (2.9±1.2 p<0.002), IFN-α (1.9±0.3 p<0.041), IFN-β (2.6±0.8 p=0.015), IL-12p70 (2.1±0.2 p=0.041), IL-7 (2.1±0.8 p=0.026), and IL-15 (3±2.1 p=0.002). AS B*2705+ PBMCs showed a trend to major increase in B27 expression compared with B*2705+ and B*2709+ NC. Low variation of B27 expression was observed with the other stimuli (less than 1.5 fold of controls), including TNFα (p=0.69), even at high concentration (20ng/ml – 360ng/ml range).

Conclusions: The first steps of transcription are mainly controlled at the promoter region and cytokines are known to be able to activate transcription factors. An initial (infectious? mechanical?) stimulus may trigger the up-regulation of B27 determining more favourable condition for disease onset (antigen driven? unfolded protein response?, others?). The role of TNFα in the pathogenesis of disease, which is likely to be linked also to individual genetically-determined functional characteristics, may be not directly determinant in modulating B27 expression.
P 9
ANTIGEN SPONDYLITIS MONOCYTES SHOW UPRGULATION OF PROTEINS INVOLVED IN ANTIGEN PRESENTATION
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Introduction: Ankylosing Spondylitis (AS) is an autoimmune inflammatory disease of unknown aetiology. Transgenic rat studies have implicated Monocytes. We wished to quantify differences in protein expression in monocytes between patients with Ankylosing Spondylitis (AS), Rheumatoid Arthritis (RA) and healthy controls.

Methods: The protein expression of CD14 bead purified AS, RA and control monocytes was studied by 2D gel electrophoresis and by quantitative label-free expression profiling. Tryptic digestion of monocyte proteins was followed by nano ultra-performance liquid chromatography coupled to ESI MS/MS mass spectrometry. Data sets were analysed using Waters Expression Profiling System (WEPS) and Ingenuity Pathway Analysis (IPA). In vitro proteasomal digests of extended HLA-B27 epitopes were carried out in the presence or absence of the proteasome activator complex PA28.

Results: 2D gel electrophoresis identified the immunoprotasome protein PA28 as upregulated in some AS patient’s monocytes compared to healthy controls. AS and RA monocytes differed in protein expression the healthy controls using IPA. The most significant pathways for both the AS and RA pools, based on numbers of differentially expressed proteins were the Vascular Endothelial Growth Factor (AS:25, RA:24), leukocyte extravasation (AS:39, RA:35), NF-kB (AS:27,25), Integrin (AS:32, RA:36), Jak-Stat (AS:15, RA:16) and Toll-like Receptor signalling pathways (AS:11, RA:10). The only pathway in which a marked difference was observed was the number of differentially expressed proteins between the AS and RA controls; the Proteasome Ubiquitin Pathway. PA28 enhanced generation of HLA-B27 peptide epitopes in vitro.

Conclusions: We have combined quantitative label-free proteomics with Ingenuity Pathway Analysis to characterize differential protein expression in AS monocytes. AS monocytes shows significant changes in protein expression compared to matched RA and healthy controls. Our results support a role for proteasome-dependent proteolysis in AS monocytes. We further demonstrate the utility of novel proteomic techniques in investigating inflammatory rheumatic diseases.

P 10
IL-23 IS NOT ELEVATED IN THE SERUM OR UPRGULATED IN THE PERIPHERAL BLOOD MONOCYTES (PBMCs) OF ANKYLOSING SPONDYLITIS (AS) PATIENTS
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Background: IL-23 has been implicated in the pathophysiology of Psoiasis and Psoiatric Arthritis. However its role in AS has not been clearly determined. A IL-23 receptor polymorphism has been reported to associate with AS and the purpose of this study was to define the role of IL-23 in AS.

Methods: 22 AS patients classified by the modified New York criteria were assessed clinically and 10mls of heparinised blood and 5mls of serum was collected from each patient. RNA was extracted from PBMCs and IL-23 expression analysed by Taqman QRT-PCR. IL-23 levels in the serum were measured by ELISA. Standard acute phase response was assessed by measuring CRP. 25 Healthy subjects acted as controls. The study was approved by the local ethics committee.

Results: Detection of IL-23 in PBMCs was considerably lower in the AS patients compared with controls (p<0.001). Soluble IL-23 was detected in only 2 out of 22 AS patients and 3 out of 11 control subjects. There was no correlation between the IL-23 levels detected and clinical parameters of disease activity in the AS patients or with drug therapy.

Conclusions: In this small group of AS patients, IL-23 does not seem to be upregulated and there is a suggestion that IL-23 expression may be down-regulated when compared with controls. IL-23 may therefore not be a major component of the inflammatory response in AS.

P 11
FREQUENCY AND PHENOTYPE OF TH17 CELLS IN AS PATIENTS AND HEALTHY CONTROLS
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Introduction: T helper cells that produce IL-17 (Th17 cells) have been described as a new lineage of CD4+ T cells and are thought to have key roles in inflammatory arthritis.

Ankylosing spondylitis (AS) is a chronic inflammatory disease in which elevated serum levels of IL-17 have been reported. This study, we compared the frequencies of Th17 cells in AS and healthy controls, and studied the phenotype, chemokine receptor expression and other cytokines produced by Th17 cells.

Materials and Methods: 8-color flow cytometry was used to analyze surface phenotype, cytokine production, and chemokine receptor expression of PBMC-derived T cells from 20 AS and 16 healthy people. We also measured by ELISA secretion of IL-17 into culture supernatants by PBMC.

Results: (1) The percentages of IL-17+CD4+ T cells and IL-22+CD4+ T cells were increased in PBMC of AS as compared with healthy controls. The ratio of IL-17+CD4+ T cells to IFN-γ+ CD4+ T cells was much higher in AS than in healthy controls; conversely, the ratio of IL-10+CD4+ T cells to IL-17+CD4+ T cells in AS was much lower. (2) IL-17 concentrations in AS supernatants were significantly higher in compared to healthy controls by ELISA. There was a correlation between the percentages of IL-17+CD4+ T cells and the amounts of IL-17 in culture supernatants. (3) All Th17 cells were CD4+ and CD45R0+. Most of the Th17 cells expressed both CCR6 and CCR4. However, not all of the Th17 cells expressed the IL-23 receptor. (4) A significant proportion of cells that produced IL-17 also produced IL-22 and IFN-γ but not IL-10.

Conclusions: This study has shown that Th17 cells are significantly more prevalent in PBMC in AS. This supports the hypothesis that IL-17 producing cells contribute to the pathogenesis of AS.

P 12
INTERLEUKIN 17 ACTIVATION IN SMALL INTESTINE IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS
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Introduction: The purpose of the study was to investigate the involvement of interleukin 17 (IL-17) in rheumatoid arthritis (RA).

Methods: We studied IL-17 mRNA expression and the number of IL-17 positive cells in duodenal biopsy samples from 12 patients with RA with real-time reverse transcriptase polymerase chain reaction and immunohistochemistry, respectively. 3 duodenal and 3 ileal biopsy samples from patients with ankylosing spondylitis (AS) (AS) were analysed for IL-17 mRNA expression. We also measured IL-17 mRNA expression in synovial fluid and peripheral blood derived cells as well as soluble IL-17 concentration in synovial fluid and peripheral blood in patients with RA.

Results: The expression of IL-17 mRNA in duodenal biopsy samples from patients with RA was increased (p<0.05). In a subset of biopsy samples from AS patients IL-17 expression was elevated compared to samples obtained from control patients, and the medians in RA and AS patients were equal. We found elevated levels of IL-17 in serum samples taken from early RA patients, but no association with disease activity was seen. Soluble IL-17 was also detectable in 5 of 6 synovial fluid samples studied. The levels of IL-17 mRNA in peripheral blood or synovial fluid derived cells were low or undetectable in both the patients with early or chronic RA.

Conclusion: Our results here support the role of IL-17 in human RA and suggest intestinal activation of IL-17 pathway in both RA and AS. We demonstrate that increased production of IL-17 is seen locally in the synovial fluid from inflamed joints and also in serum from untreated patients with early RA. The source of IL-17 in RA is not the circulating leukocytes, but IL-17 is secreted most likely from the immune cells infiltrating synovium or other inflamed tissues, such as small intestine.
The association of HLA-B27 with spondyloarthopathies, including ankylosing spondylitis and reactive arthritis is one of the strongest between an MHC molecule and a disease. Chlamydia trachomatis, an obligate intracellular parasite, is a known pathogenic agent in reactive arthritis. Several bacterial sequences have been proposed as putative HLA-B27-restricted epitopes in the CTL responses of patients with reactive arthritis or have been shown to have high homology with constitutive self-antigens of HLA-B27. In this study we have set up an experimental system to address the issue of whether relevant sequences from individual bacterial proteins can be processed and presented by HLA-B27 in vivo. The method is based on the transfection of GFP-bacterial protein constructs into HLA-B27-positive cells, followed by mass spectrometry-based comparison of the HLA-B27-bound peptide repertoires from cells transfected or not with the bacterial protein. Using this approach we have identified Chlamydiai peptides which are endogenously processed in a proteasome-dependent way, are presented in vivo by HLA-B27 and show molecular mimicry with known self-antigens of this molecule. These findings validate this approach for the mapping of bacterial HLA-B27 ligands with putative relevance in the pathogenesis of reactive arthritis.

**P 14**

**HLA-B27 POLYMORPHISM IN CHINESE HAN POPULATION: A DISTINCTIVE DISEASE SUSCEPTIBILITY OF B*2715 FOR ANKYLOSING Spondylitis**

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**Background:** To investigate the distribution of B27 subtypes in AS patients of Chinese Han population and the association with disease phenotype by using the update B27 subtypes data.

**Methods:** One hundred AS subjects were recruited randomly from the spondyloarthritids patients’ data bank of our department. All the subjects should be independent pedigrees and the maximum combined LOD score was 6.44 at marker D2S2228 θ=0. All genotypes were checked for linkage disequilibrium with AS1 and the association is likely to be secondary to that of AS1. The results of this further genotyping will be presented.

**Conclusions:** The WTCCC genotyping of 14,500 nsSNPs identified many potential new SNPs outside the MHC for association with AS. We have genotyped a large number of these in an independent sample of AS cases and have replicated the association seen with AS1 and IL23R nsSNPs by iPLEX technology (MassArray, Sequenom). Genotype frequencies were compared to the 1958 birth cohort and non AS cases from the WTCCC. nsSNPs in four genes were significant at P<0.0001. For three of these genes we identified tagging SNPs in the gene region using HapMap data. Genotyping of these SNPs in a large number of cases and controls is performed by iPLEX technolo- gy to confirm and refine the original associations.

**Results:** SNPs in SNAPC4, CLSTN3, JAKR1A and LNPEP showed association with AS at P<0.0001. Fifty six SNPs, tagging a further 132 in SNAPC4 CLSTN3 and JAKR1A genes have been selected for genotyping in cases and controls. No further genotyping in LNPEP was done as this gene is in linkage disequilibrium with ARTS1 and the association is likely to be secondary to that of ARTS1. The results of this further genotyping will be presented.

**Conclusion:** The WTCCC genotyping of 14,500 nsSNPs identified many potential new SNPs outside the MHC for association with AS. We have genotyped a large number of these in an independent sample of AS cases and have replicated the association seen with AS1 and IL23R and with a further 4 SNPs. We have investi- gated the region around these SNPs to confirm and refine the associations.
ASSOCIATION OF IL-1 SINGLE NUCLEOTIDE POLYMORPHISMS WITH ANKYLOSING SPONDYLITIS IN THE CHINESE HAN POPULATION

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Background: To investigate polymorphisms of IL-1 complex with AS in the Chinese Han population and to determine whether they were associated with susceptibility/critical manifestation to AS.

Method: One hundred and three Chinese Han AS patients and 117 ethnically matched healthy controls were genotyped for five single nucleotide polymorphisms (SNPs) (IL1β-511, IL1β+3953, F103.1, RN.4, RN.6/1) and the IL1RN VNTR, markers previously associated with AS. Allele, genotype, and haplotype frequencies were compared between patients and healthy controls using SHEsis software. The distribution difference of IL-1 gene polymorphisms was also compared in AS patients with different clinical manifestations (coxitis, peripheral arthritis, tendonitis, acute anterior uveitis, BASDAI and age at onset).

Results: We observed significant association of alleles and genotypes of the SNP IL1F103 with AS (p=0.008 and p=0.028, respectively). Strong linkage disequilibrium was identified between IL1β-511, IL1β+3953 and RN.4 (D'=0.95). Haplotype construction analysis (6 markers) identified two haplotypes TCTTA1C and TCTTAIT which could increase disease risk significantly (p=3.32*10-5, OR=4.41, 95% CI: 2.1-9.3 and p=0.04, OR=2.16, 95% CI: 1.02-4.80, respectively). Two haplotypes TCTTA1C and TCTTAIT had a negative correlation to disease risk (p=0.010-0.04, OR=0.23, 95% CI: 0.10-0.51 and p=0.005, OR=0.32, 95% CI: 0.14-0.74, respectively).

Clinical data analysis found RN2. VNTR A2 as a risk factor of peripheral arthritis (p=0.025), and a deviation in the genotype distributions of F103.1 and RN.6/1 was observed in patients with different disease severity (p=0.04 and p=0.02, respectively). No significant association was observed between other polymorphisms and clinical manifestations of patients.

Conclusion: The present study demonstrates that IL-1 gene cluster appears to be a genetic susceptibility gene to AS in the Chinese Han population. It also implies IL-1 gene may be involved in the special clinical phenotypes such as disease severity and peripheral arthritis. It is valuable to verify these by extending samples size.

ASSOCIATION OF IL-23R AND ARTS1 GENES WITH SUSCEPTIBILITY TO ANKYLOSING SPONDYLITIS AMONG A MEDITERRANEAN/PORTUGUESE POPULATION

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Introduction: Association between ankylosing spondylitis (AS) and two genes, IL-23R and ARTS1, has recently been reported in North-American and British populations. The population attributable risk fraction for AS in this study was 25%, and for IL-23R, 9%. This indicates the reduction in the population prevalence of AS that would occur if the effect of the association concerned were removed from the population. Confirmation of these findings in other ethnic groups has not yet been demonstrated. We sought to test the association between single nucleotide polymorphisms (SNPs) in these genes and susceptibility to AS among a Mediterranean/Portuguese population.

Materials and Methods: The study was conducted on 360 AS patients and 284 ethnically matched Portuguese healthy controls. AS was defined according to the modified New York Criteria. Genotyping of IL-23R and ARTS1 allelic variants was carried out with TaqMan allelic discrimination assays. Association analysis was performed using the Cochrane-Armitage test as implemented in PLINK, with odds ratios calculated from allelic counts.

Results: A total of 14 nsSNPs markers (8 for IL-23R, 5 for ARTS1, 1 for LN-PEP) were analysed. Four markers (2 for IL-23R and 2 for ARTS1) showed significant single-locus disease associations, confirming that the association of these genes with AS in the Portuguese population. The strongest associated SNP in IL-23R was rs1004819 (OR=1.45, 95% CI=1.14-1.85, p=0.003). The other SNP (ARTS1) was rs27044 (OR=1.65, 95% CI=1.25-2.18, p=0.0042). Two haplotypes TCTTA1C and TCTTAIT were associated with the disease in this study. These variants were tested for strength of association with AS in 1500 patients and controls.

CONCLUSIONS: We have replicated the association of 5 nsSNPs in ARTS1. We have also identified 7 novel variants in the gene exhibiting a range of associations with AS which will help to identify the primary ARTS1 association(s) in this disease.
**Poster Presentations**

**Conclusion:** These results show that IL23R and ARTS1 genes are also associated with susceptibility to AS among this Mediterranean/Portuguese population, and that they contribute a significant proportion of the population risk for this disease. **(CORPOREA study group participation).**

**P 21 CHARACTERIZATION OF HLA GENETIC POLYMORPHISM IN A PORTUGUESE POPULATION WITH ANKYLOSING SPONDYLITIS**

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**Introduction:** The aim of this study was to characterize the distribution of gene B alleles and B*27 subtypes in Ankylosing Spondylitis (AS) patients from mainland Portugal. Variants from HLA class I and class II were also analysed.

**Material and Methods:** Patients with AS and healthy controls were matched according to ethnicity. Individuals from both AS and control groups that were positive for HLA-B*27 were defined at allelic resolution by sequence-based typing of exons 2 and 3 of the HLA-B gene. In a randomly chosen sub-group of 43 AS patients and 96 controls, HLA multi-locus A/B/Cw/DRB1/DQB1 haplotype frequencies were estimated using the iterative expectation-maximization (EM) algorithm PyPop.

**Results:** AS (n=335) patients: 211 males; mean age: 44.5±13 years; mean disease duration: 19.9±12.5 years; healthy controls (n=174). Positivity for B27 was 82% in AS patients; the equivalent figure for the healthy controls was 9.2%. The distribution of B27 alleles is shown in table 1. In the AS group, HLA-ABDRB1 haplotype frequencies were: A*02, B*27, DRB1*01 (5.68%); and A*24, B*27, DRB1*04 or A*02, B*27, DRB1*13 (4.55%). For the control group, we found a frequency of 3.1% for A*01, B*08, DRB1*03 as the most frequent haplotype. The first to be associated with B27 was A*02, B*02, DRB1*01 (0.31%).

**Conclusion:** The prevalence of HLA-B*27 in both the AS cohort and in the healthy controls was higher than previously described for a Southern European population. The distribution of B*27 allele subtypes is different in AS patients and healthy controls. This is the first study to perform high-resolution B*27 genotyping in a mainland Portuguese population and therefore can be useful in comparative population studies. **(CORPOREA study Group participation).**

<table>
<thead>
<tr>
<th>Table 1. Distribution of B27 alleles in Portugal.</th>
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<tr>
<td><strong>AS (n=130)</strong></td>
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<td>B*2705</td>
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<td>B*2702</td>
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<td>B*2704</td>
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<td>B*2707</td>
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**P 22 DISPARATE FOLDING AND STABILITY OF THE ANKYLOSING SPONDYLITIS-ASSOCIATED HLA-B*1403 AND B*2705 PROTEINS**

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**Introduction:** HLA-B*1403 is associated to ankylosing spondylitis (AS) as B*2705. The latter presents unusual folding properties. The purpose is to investigate the folding, assembly, maturation and stability of HLA-B*1403 (non AS associated) and B*2705, and the relationship of these features with (AS).

**Methods:** Stable transfectants expressing B*1402, B*1403 and B*2705 were used. Folding rates were estimated from the ratio of unfolded-to-folded heavy chain (HC), immunoprecipitated with specific antibodies, in pulse-chase experiments. HC misfolding was measured as the half-life of Endoglycosidase H (Endo H)-sensitive β2-microglobulin-free HC. Maturation/export rates were measured by acquisition of Endo H resistance. Association with calnexin or tapasin was analyzed by co-precipitation with chaperone-specific antibodies.

Surface expression of HLA heterodimers and free HC was estimated by flow cytometry. Thermotolerance of HLA/peptide complexes was assessed by immunoprecipitation with a heterodimer-specific antibody after incubation at various temperatures. HC expression was quantified by Western blot.

**Results:** B14 folding was faster and more efficient than for B*2705, and similar for B*1402 and B*1403, but some unfolded HC from both B14 subtypes remained in the endoplasmic reticulum with a long half-life. The export rate of B*1402 and B*1403 was slow, and the heterodimers partially dissociated after exiting the endoplasmic reticulum, as revealed by significant amounts of Endo H-resistant and surface-expressed free HC. Both interaction with tapasin and thermotolerance decreased in the order: B*2705>B*1402>B*1403, suggesting that the B*1402 and, specially, B*1403 bound peptide repertoire were less optimized than that of B*2705.

**Conclusion:** The folding, maturation and stability of B*1403 differ more from B*2705 than from B*1402. Thus, these features cannot account for the association of only the two former alleles with AS.

**P 23 HLA-B27 HEAVY CHAIN ACCUMULATES IN THE ENDOPLASMIC RETICULUM SELECTIVELY IN DISEASE ASSOCIATED SUBTYPES AND BIND SUBOPTIMAL PEPTIDE REPERTOIRES**

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The role of HLA-B27 in the pathogenesis of ankylosing spondylitis (AS) is unknown. HLA-B*2705 shows “aberrant” folding characteristics, being prone to misfold, and this property may be responsible for the association to disease. Since not all B27 subtypes associated with AS susceptibility, we analyzed the effect of subtype polymorphism on the maturation kinetics of HLA-B27 subtypes in an attempt to explain their differential association with AS. The formation of fully assembled B27 complexes was analyzed in C1R cells transfected with HLA-B27 subtypes and mutants mimicking B27 polymorphism by pulse-chase analysis and immunoprecipitation either with the monoclonal antibody H1C10, which recognizes MHC class I free heavy chains (HC), or with the conformation-sensitive monoclonal antibody ME1. N-linked glycosylation of heavy chains, was monitored by treatment with Endoglycosidase H (Endo H). The association of B27 heavy chain with tapasin was analyzed by pulse-chase analysis and co-immunoprecipitation with the monoclonal antibody P05a-1, which recognizes human tapasin. Optimization of peptide repertoires was analyzed by thermotolerance assay. Although 2m proceeds with β the rate of HC synthesis and the assembly of HC/ similar kinetics in B27 subtypes, they were heterogeneous in their maturation phenotype, some subtypes exiting rapidly the ER, while others remained in a transport-independent state. However the rate of maturation did not correlate with disease association. Only in disease-associated subtypes, except B*2707, most of the heavy chain 2m and sub-type polymorphism determined the assembly β failed to bind efficiency. This failure in folding or assembly leads to the retention of B27 HC in the ER and correlates with higher tapasin binding and the presence of suboptimal peptide repertoires.

**P 24 HLA-B27 TRANSCR GENOMIC RNA+24 DC EXHIBIT MULTIPLE CELLULAR DEFICIENCIES AND THE TOLERIGENIC CD4- SUBSET SUFFERS REDUCED VIABILITY**

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**Background:** Several lines of rats transgenic for HLA-B27 and human β2-microglobulin develop an inflammatory disease that strikingly resembles human SpA. It is hypothesized that disease in HLA-B27 transgenic rats arises as a consequence of interaction between antigen-presenting cells expressing high levels of HLA-B27 and peripheral T lymphocytes, and may result from a rupture of tolerance towards gut bacteria.

**Methods:** We used 2D PAGE and iTRAQ to compare the protein expression profile of HLA-B27 dendritic cells (DCs) to that of healthy HLA-B7 expressing and nontransgenic (NTG) rat DCs. MHC II surface expression and apoptotic sensitivity were quantified using flow cytometry.

**Results:** Three protein sets from the proteome analysis were indicative for aberrant cellular processes. First, all proteins involved in protein processing and MHC I assembly were upregulated in B27 DCs, illustrating the higher pressure on the ER due to misfolding of the HLA-B27 heavy chain. Second, all proteins directly influencing actin-dynamics were downregulated. We showed earlier that this not
only influences motility, but also plays an important role in deficient immunological
synapse formation. Third, the key third protease Cathepsin S involved in MHC
II synthesis was downregulated, which led us to quantify RTI-I and RTI-D surface
expression. Downregulation concerned both CD4+ and CD8+OX62+ HLA-B27
DC subpopulations and maturation enlarged differences in both population bias and
expression intensity. Deficient actin dynamics could also contribute to this lower
MHC II surface expression. Study of sensitivity to MHC class II-mediated apoptosis
by antibody stimulation showed that compared to NTG, both B7 and B27 CD4+ DC
were more prone to apoptosis but did not mutually differ. In contrast, overnight
culturing resulted in a higher cell death in B27 than in control CD4+ DC, even
without antibody stimulation. Interestingly, decreased actin dynamics could also be
involved in DC apoptosis.

Conclusion: DCs suffer greatly from HLA-B27 expression, with probable major
physiologic implications.

P 25
LEUKOCYTE SIGNALLING PROFILES IN HEALTHY SUBJECTS
WITH A HISTORY OF YERINSIA-TRIGGERED REACTIVE
ARHIIITIS
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Objective: Reactive arthritis (ReA) is a disease that manifests as a sterile joint infection.
It is triggered by an extra-articular bacterial infection such as salmonella and yersinia infections in the gastrointestinal tract or chlamydia infections originating from the urogenital or respiratory tract. ReA is in general self-limiting,
and most patients will recover within a year. The majority of ReA patients are HLA-B27-positive. However, the precise mechanisms that account for this genetic
disease susceptibility are not known. We therefore examined whether there are
differences in intracellular signalling in selected signalling pathways in ten HLA-B27-positive healthy subjects who had completely recovered from yersinia-
triggered ReA compared with ten HLA-B27-positive and ten HLA-B27-negative healthy individuals.

Methods: Phosphorylation levels of NF-κB p65 and p38 in fresh leucocytes stimu-
lated with TNF (0-100ng/ml) for 1 to 10 min, LPS (0-100 ng/ml) for 5 to 20 min
or MDP (0-1000ng/ml) for 10 to 40 min at 37°C, were determined using phos-
phospecific monoclonal antibodies in whole blood flow cytometric assay. Similarly,
phosphorylation levels of STAT1, STAT3, STAT5, STAT6 and ERK1/2 in fresh
leucocytes stimulated with IFN-γ (0-5 ng/ml), IL-6 (0-100 ng/ml), GM-CSF (0-5
ng/ml), IL-2 (0-100 ng/ml), IL-4 (0-100 ng/ml) or 5 μM PMA and Ca-ionophore for 5 min at 37 °C were determined. Areas under curve (AUC) values for dose
response and time course of NF-κB and p38 phosphorylation and RFU values of
STAT1, STAT3, STAT5, STAT6 and ERK1/2 were used in comparison of patients
and controls (Mann-Whitney U test).

Results: Phosphorylation levels of the different intracellular signalling molecules in monocytes, lymphocytes and neutrophils did not differ significantly between the subjects with previous ReA and the healthy controls.

Conclusions: The findings demonstrate that the intracellular immune cell signal-
ling profiles of HLA-B27-positive healthy subjects with the history of ReA and those of HLA-B27-positive and -negative healthy subjects are comparable.

P 26
ASSOCIATION OF MARKERS OF BONE- AND CARTILAGE
DEGRADATION WITH RADIOLOGICAL CHANGES AT BASE-
LINE AND AFTER 2 YEARS FOLLOW-UP IN PATIENTS WITH
ANKYLOSING SPONDYLITIS
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Background: There is a lack on knowledge of factors that reliably can predict radiological changes in patients with ankylosing spondylitis (AS).

Objective: to investigate whether urinary C-terminal cross linking telopeptide of type I (CTX-I) and type II (CTX-II) collagen, as specific biochemical markers of bone and cartilage degradation respectively, are associated with radiological dam-
age and progression, and with bone mineral density (BMD) in patients with AS.

Methods: Eighty three patients with AS (mean (SD) age: 50.4 (12) years, 65% male, mean (SD) disease duration after diagnosis: 16.7 (10) years) who participate in an ongoing cohort study of patients with AS (OASIS: Outcome in Ankylosing Spondylitis International Study cohort) were assessed for urinary CTX-I and –II.

Results: of both biochemical markers were compared with baseline scores for radio-
logical damage (modified SASSS, primarily reflecting syndesmophyte formation and bone bridge formation), and with scores for radiological progression after 2 years follow-up. Markers were also associated with disease activity parameters and bone mineral density (BMD).

Results: Mean duration of complaints was 28.6 years. At that time 54% of patients
had signs of radiological damage, and 35% of them showed radiological progres-
sion after 2 years. Baseline radiological damage (eta=0.24; p=0.05) correlated with
CTX-I, but not with CTX-II. CTX-II correlated with serological markers of infl am-
mmation (ESR=0.29 and CRP=0.30; p<0.01), but not with baseline BASDAI or BMD.

There was a negative correlation between CTX-I and BMD of the trochanter (eta=0.31; ps=0.01) in multivariate analyses CTX-II significantly and independently contributed to explaining variation in radiological damage (standardized β = 0.27; p<0.03) and progression (β = 0.27; p=0.05).

Conclusion: In AS, cartilage degradation plays a role in explaining radiological damage and –progression in the spine.

P 27
DKK-1 LEVELS ARE COMPARABLY INCREASED IN PATIENTS
WITH AS AND RA, SHOW SIMILAR DECREASES WITH ANTI-
TNF THERAPY, AND ARE NOT ASSOCIATED WITH MARKERS
OF BONE REMODELING
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Introduction: Preliminary data in patients with AS show that levels of DKK-1 are
low compared to RA and healthy controls suggesting that this might account for the
propensity to new bone formation in AS. We aimed to 1. Compare DKK-1 levels in
a large population of patients with AS compared to controls and active RA. 2. Evaluate correlations between DKK-1 and markers of bone remodeling in AS. 3. Examine the effects of anti-TNF alpha therapy on DKK-1 in AS.

Methods: We studied 126 patients with AS (mean BASDAI 4.1), 41 patients with
RA (mean DAS 5.1), and 74 controls. We also assessed DKK-1 in 38 AS patients
and 21 RA patients at baseline and 3 months after initiating anti-TNF alpha therapy
(etanercept = 17, infliximab = 42). DKK-1 was assayed by ELISA. We evaluated biomarkers of bone formation (C-terminal Pro-propeptide of Collagen Type-I (CICP),
bone-specific alkaline phosphatase) and resorption (C-terminal telopeptide of type I
collagen (Cross-Laps), N-terminal telopeptide of type I collagen (NTx)) by ELI-
SA. Groups were compared using the unpaired t-test. Pearson correlation was used
to analyze associations between DKK-1, bone biomarkers, and clinical indices of
disease activity.

Results: Mean serum DKK-1 levels (ng/ml) were similar in AS (24.5) compared to
RA (22.0) and significantly greater than in controls (13.0) (p<0.001 for both).

Levels were non-significantly higher in female (14.5) than in male (11.2) controls,
and in female (23.2) versus male (20.2) RA patients. This was not observed in AS
patients (female (24.3) vs male (24.7)). Non-significant reductions in DKK-1 levels
were noted after treatment with anti-TNF alpha that were comparable for RA (mean
change: -1.06) and AS (mean change: -1.8) with no significant difference between
anti-TNF alpha therapies. No significant correlations were observed between DKK-
1 and bone biomarkers, BASDAI, nocturnal pain, morning stiffness, and CRP.

Conclusions: In contrast to a previous report we show increased DKK-1 in AS that
is comparable to RA. Our data does not support a role for DKK-1 in the pathogen-
esis of new bone formation in AS.

P 28
UTILITY OF THE MODIFIED STOKE ANKYLOSING SPONDYL-
TIS SPINE SCORE (MSSASS) P. Wordsworth¹, C. Farrar¹, C. Swales¹, H. Stevens², J. Fisher², J. Pointon³, K. Chapman³, P. Bowns³
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Introduction: Objective evaluation of disease severity in ankylosing spondylitis (AS) is of critical importance in defining the phenotype for genetic studies and in
evaluating the outcome of treatments. Validated scores of spinal disease progress-
ion potentially offer a useful objective measure of disease severity which may be
more robust than other indices. The modified Stoke AS spine score (mSASSS) has been
developed as an objective radiographic index of the severity of AS in the
cervical and lumbar spine. We wished to assess the reproducibility and utility of
mSASSS and its relationship to other markers of disease severity.
Methods: We ascertained 73 patients with AS (disease duration 5-36 years) attending a specialist clinic to compare clinical assessments of disease severity. These included the Bath AS indices of disease activity (BASDAI), function (BASFI), methodology (BASMI); lumbar flexion by the modified Schober test and mSASSS. Clinical measurements were made by 2 experienced physiotherapists and each mSASSS was duplicated by 2 blinded readers. Correlation co-efficients and regression analyses were performed in the software programmes STATIST DIRECT and SPSS.

Results: In 37 patients for whom full data were available for each of the assessments mSASSS was moderately correlated with BASMI (r=0.50, p<0.001). In contrast no significant correlation was seen in the subsets of patients with data on mSASSS and lumbar flexion (r=0.2, p=0.2), BASDAI (r=0.19, p=0.2), BASFI (r=0.08, p=0.5).

Conclusions: Even objective measurements of severity of AS are quite poorly correlated. Radiographic scoring systems fail to take account of the posterior spinal elements and may therefore be misleading. The development of more robust radiographic scores is desirable.

P 29
AGREEMENT BETWEEN EVIDENCE AND BELGIAN RHEUMATOLOGISTS' EXPERIENCE ON HLA B27 DETERMINATION IN PATIENTS WITH SPECIFIC IMAGING FEATURES INankylosing Spondylitis
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Objective: To develop an evidence-based and experience-based recommendation to the question: “Is the determination of HLA B27 useful for the diagnosis of AS in the presence or absence of specific imaging features?”

Methods: A systematic literature search was conducted during August-October 2001.

Different imaging features used in the different stages of sacroiliitis visible on X-ray, MRI, CT, and ultrasound were evaluated. Whenever possible, sensitivities, specificities, and likelihood ratios of HLA B27 for the diagnosis of AS were calculated. The results were presented to 59 Belgian rheumatologists. Based on the evidence in the literature, which was categorized according to the EULAR evidence hierarchy (1,2), a recommendation was made.

The strength of the recommendation (1,2) was assessed by voting on level of agreement.

Results: Through a combination of MeSH terms and keywords, very few relevant publications were found. Moreover, no single study has yet been performed in which the correlation between HLA B27 status and different imaging features had been studied.

Therefore, a recommendation was made based on experts’ opinions. The Belgian rheumatologists made the following recommendation: “Conventional imaging should be performed before HLA B27 determination. HLA B27 determination should be considered in case of doubtful diagnosis of AS (e.g., in the case of negative SI imaging). In case of doubtful (stage 1) SI imaging, a CT scan or MRI should be performed prior to HLA B27 determination.” 74% of the attendees agreed with this recommendation. The category of evidence was deemed “IV,” and the strength of the recommendation was deemed “D.”

Conclusion: A recommendation on the role of HLA B27 determination for the diagnosis of AS in the presence or absence of certain imaging features in AS was developed using a combination of research-based evidence and expert consensus. Because of lack of evidence, the recommendation is based on experts’ opinions.

References:

P 30
WRIST AND HAND INVOLVEMENT IN PSORIARTIC ARTHRITIS AND RHEUMATOID ARTHRITIS: AN ULTRASOUND COMPARISON
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Introduction: Very little is known about the possible differences in the involvement of joints and periarticular structures in rheumatoid or psoriartic arthritis (PsA).

The main pathological features detected by US in rheumatoid arthritis (RA) are synovitis and bone erosion while, in spondyloarthropathies, entheseal inflammation is the common feature. Tendon involvement is particularly frequent and dactylitis is a typical PsA manifestation.

Aim of the Study: To investigate the features of wrist and hand involvement in PsA and RA.

Materials and Methods: Bilateral ultrasound (US) examination of the wrist and hand was performed, by the same physician, in a group of subjects affected by RA (n=15) and PsA (n=15), using a Logiq 9 (General Electrics Medical Systems, Milwaukee, WI) with a linear probe operating at 14 MHz. We examined radiocarpal, intercarpal, metacarpophilangal, proximal interphilangal and distal interphilangal (DIP) joints and flexor and extensor tendons (both in wrist and hand).

The patients were recruited on a time-criteria (the last 15 patients for each diagnosis) from the whole number of subjects referring to the US unit of our Clinic.

Results: US examination showed joint wrist synovitis in 7/15 (46.6%) patients (both in RA and PsA), hand synovitis in 9/15 (60%) and in 11/15 (73.3%) RA and PsA patients respectively. We found DIP joint involvement in only 1 PsA patient, as it was for dactylitis (in a different PsA patient). Bone erosions were present in 7/15 (46.6%) and 5/15 (33.3%) RA and PsA patients respectively. Tendon involvement was present in the 4/15 (26.6%) and 3/15 (20%) in the wrist and 5/15 (33.3%) and 6/15 (40%) in the hand respectively.

Conclusion: We did not observe significant differences in wrist or hand involvement (both in joint and tendon structures) between RA and PsA patients, except for a more frequent involvement of PIP joints in PsA group.

P 31
INTERRELATIONS BETWEEN INFLAMMATORY SPINAL MRI LESIONS AND LOCALIZATION OF AXIAL PAIN, BASDAI IN PATIENTS WITH ANKYLOSING SPONDYLITIS
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Objective: To compare inflammatory spinal MRI lesions (IL) in patients (pts) with ankylosing spondylitis (AS) with localization of the axial pain and level of BASDAI.

Methods: We studied 36 pts with idiopathic AS fulfilled the modified NY criteria (22 males and 14 females, median age 26 yrs (range 19-55), median disease duration 8 yrs (range 1.8-24); 34 pts were HLA-B27 positive). The majority (58%) of pts had active AS (median BASDAI 4, range 3,0-5.6) and severe pain in the spine [median (100-mm VAS) 45 mm, range 30-50]; night spinal pain had 22 (61%) pts. T2-weighted sequences with fat suppression were used to detect IL. Calculations of IL were undertaken only in 29 patients in whom tomography of spine in sagittal and axial plane was performed.

Results: Overall 50 MRI were performed in 36 AS pts (30 – thoracic, 12- lumbar and 8 – cervical spine). MRI signs of IL were detected in 35 pts (97%). Calculation of IL were undertaken only in 29 patients in whom tomography of spine in sagittal and axial plane was performed.

Conclusion: In 29 patients in whom tomography of spine in sagittal and axial plane was performed, the localization of IL was analyzed with BASDAI in 29 pts (97%). Calculation of IL changes in separate anatomical structures of spine was made on 41 images performed in 29 pts in 2 planes. The IL exactly corresponded to pain localization (26 of 29 pts; 90%). In 3 patients the localization of MRI changes and pain did not correspond. IL were most commonly detected on tomograms of thoracic spine (average number of changes on one image was 7.1). In lumbar and cervical spine IL were revealed more rarely; (3,7 and 2,1 respectively. Median number of IL (25-75% range and extremes) in 12 patients with low AS activity (BASDAI <40) was 6 (4-16; 2-28), which did not constitute any significant difference between these patients groups (p = 0.35; Mann-Whitney test).

Conclusions: Inflammatory MRI lesions are observed in 90% pts in the localisation of axial pain. More frequently these findings are observed in thoracic spine. We did not observe any relationship between the number of inflammatory MRI changes and AS clinical activity.
Objective: To assess and quantify the natural course of radiographic progression in active ankylosing spondylitis (AS) patients, we retrospectively analyzed for detection of differences in progression over time.

Methods: A total of 146 AS patients (age 54.2±12 y, symptom duration 23.6±11 y, 81% male) were included. Radiographs were taken at baseline and after 2 years. At each visit, the Bath Ankylosing Spondylitis Radiology Index (BASRI) and Bath Ankylosing Spondylitis Metrology Index (BASMI) were determined. The rate of new syndesmophytes at vertebral edges (VE) was assessed using a 45° cut-off of growth.

Results: Both BASRI and BASMI were significantly increased in males vs females (mean difference 2.0±1.5 and 1.6±1.2, respectively). The rate of new syndesmophytes at VE was significantly higher in males vs females (mean difference 1.2±0.6 vs 0.8±0.4, respectively). The number of bilateral syndesmophytes observed at baseline was significantly higher in males compared to females (mean difference 4.0±2.0 vs 1.0±1.5, respectively).

Conclusions: Although enthesis is the most affected part of the Achilles tendon, significant Achilles tendon thickness differences between genders necessitate referral to a gynecologist. Achilles tendon thickness was more prevalent in females compared to males, which was not observed in the Achilles tendon thickness.

Background: Spinal inflammation is best detected by MRI and contributes to decreased spinal mobility and function. In addition, MRI can aid in planning and monitoring treatment at individual AS sites.

Methods: Spinal MRI and conventional radiographs were performed in all patients with AS at baseline and after 2 years. The Bath Ankylosing Spondylitis Radiology Index (BASRI) and Bath Ankylosing Spondylitis Metrology Index (BASMI) were determined. The rate of new syndesmophytes at vertebral edges (VE) was assessed using a 45° cut-off of growth.

Results: There were no differences in the proportion of VE with radiographic damage and infl ammation at baseline in AS patients treated with anti-TNFα. In the post-treatment group, the proportion of VE with radiographic damage and infl ammation decreased significantly (p<0.001) after 2 years. The proportion of VE with radiographic damage and infl ammation also decreased significantly (p<0.001) after 2 years. The proportion of VE with radiographic damage and infl ammation also decreased significantly (p<0.001) after 2 years.

Conclusions: MRI and conventional radiographs are valuable tools for assessing the natural history of AS and monitoring treatment response.
P 36
RELIABILITY OF HIGH-RESOLUTION ULTRASONOGRAPHY IN THE ASSESSMENT OF ACHILLES TENDON ENTHESOPATHY IN SERONEGATIVE SPONDYLOARTHRITIDES

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Introduction: The present study was mainly aimed at investigating the interobserver and intraobserver reproducibility of US in the assessment of Achilles tendon enthesisopathy in patients with seronegative spondyloarthropathies (SpA).

Material and Methods: Twenty-eight patients presenting at the Rheumatology Department of the Università Politecnica delle Marche with a SpA diagnosis according to the EULAR/ECCO classification criteria were included. Patients with skin diseases were excluded. Achilles tendon US examinations were carried out independently by three rheumatologists using a linear 6-18 MHz transducer. Each patient was seen twice within 3 months. The following was scored: hypoechogenicity, thickness, calcifications, calcifications, erosions and power Doppler signal. Each enthesis was scored separately, assessing the presence or absence of US findings indicative of enthesisopathy according to the American College of Rheumatology (ACR) preliminary definition. The same findings were also scored on a 3-grade semiquantitative scoring system on which investigators reached a consensus prior to the study. Total additive scores per Achilles tendon were calculated.

Results: Moderate to excellent interobserver and intraobserver agreements were found for most of the US findings indicative of enthesisopathy according to the ACR preliminary definition (interobserver agreement: weighted kappa values estimating soft tissue inflammation were 0.656-0.671; kappa values for tissue damage were 0.548-0.613). Similar results were obtained using semiquantitative assessments (interobserver agreement: weighted kappa values estimating soft tissue inflammation were 0.656-0.671; kappa values for tissue damage were 0.597-0.711) (intraobserver agreement: weighted kappa values were 0.816 for soft tissue inflammation and 0.901 for tissue damage).

Conclusion: US assessment of Achilles tendon enthesisopathy in patients with SpA, using the ACR preliminary definition, was found reliable. Bone irregularity and entheseal hypoechogenicity resulted the most difficult abnormalities to find agreement.

P 37
ULTRASONOGRAPHIC ASSESSMENT OF ACHILLES ENTHESITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A PROSPECTIVE FOLLOW-UP UNDER ANTI-TNF THERAPY

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Introduction: Enthesitis is considered as the primary anatomical lesion in ankylosing spondylitis (AS). Evidence of imaging changes induced with anti-TNF drugs in enthesitis treatment is still limited to case reports or small trials. We aimed to investigate the effects of anti-TNF therapy on Achilles tendons in AS patients by ultrasonography (US).

Materials and Methods: AS was performed in 44 active AS patients by a blinded rheumatologist to physical examination, using a MyLab 70 US system (Esaote Biomedica, Genoa – Italy) with a linear probe 6-18 MHz. Scoring system to evaluate ultrasound (US) features used was previously developed by our group. Achilles tendon, enthesitis, retrocalcaneal bursa and calcaneus were investigated for hypoechogenicity, thickness, calcifications, calcifications, erosions and power Doppler signal. Each enthesis was assessed using a grey-scale score (GSS) and power Doppler score (PDS). Each enthesis was scored separately, assessing the presence or absence of US findings indicative of enthesisopathy according to the European Spondyloarthropathy Study Group criteria were included. Achilles tendon US examinations were carried out independently by three rheumatologists for patients with or without PsA (PsA vs. without PsA: GSS: 7.1-19 vs. 5.2-14; PDS:0-0.5 vs. 0.0-5; DS: 60-20 vs. 5-0; TS: 8-19 vs. 6-34). In multiple regression analysis, GSS was significantly correlated to duration of spondylitis and body mass index (BMI), while PDS was significantly higher in patients with PsA (GSS: 1.05-5.51; p=0.039) and elevated CRP (OR 2.59, 95% CI 1.23-5.45; p=0.012) as well as in non-radiographic axial SpA (31.6 vs. 7.77; p=0.001). Multivariate regression analysis revealed that OR 2.38, 95% CI 1.19-4.73; p=0.014 but not HLA-B27, disease activity or symptom duration to be associated with definite radiographic sacroiliitis, and found a trend for elevated CRP (OR 1.85, 95% CI 1.06-3.56; p=0.066). Similarly, male sex (OR 2.40, 95% CI 1.05-5.51; p=0.039) and elevated CRP (OR 2.59, 95% CI 1.23-5.45; p=0.012) were associated with the presence of at least 1 syndesmophyte in the spine. Male AS patients (n=118) had higher mSASSS scores at baseline as compared to female patients (n=61); mean mSASSS 5.8 vs. 3.1; p=0.025. There was neither an influence of HLA-B27 nor of BASDAI on radiographic damage of the SI joints and the spine.

Conclusion: HLA-B27 determines age at onset in early AS and in non-radiographic axial SpA. Male sex and elevated CRP but not HLA-B27 are associated with structural damage in both SI joints and spine.
**P 40**

REAPPRAISAL OF THE MSASSS: HOW CAN RELIABILITY BE IMPROVED?


The Alberta Heritage Foundation for Medical Research, Medicine, Edmonton; University of Alberta, Medicine and Radiology, Edmonton, Canada

**Introduction:** We aimed to examine the frequency and reliability of detection of the different features of the mSASSS to determine if reliability can be improved by (i) excluding infrequent and/or less reliable features, and (ii) incorporation of a damage score for facet joints.

**Methods:** In stage 1, 4 readers scored the mSASSS of 40 AS patients at baseline and 2 years. Vertebral corners with CIL on baseline MRI developed new syndesmophytes as compared to those without CIL (91.2%).

**Results:** In the analysis of the prospective cohort where 5 of 43 (11.6%) of new syndesmophytes developing where there is no prior inflammatory lesion.

**Conclusions:** A simplified mSASSS that scores syndesmophytes and bridging together with damage in the facet joints is more reliable.

**Reference:**


**Poster Presentations**

**P 42**

INFLAMMATORY LESIONS IN THE SACROILIAC JOINTS AND SPINE IN ACTIVE AXIAL SPONDYLOARTHRITIS WITHOUT RADIOGRAPHIC SACROILIITIS: BASELINE PATIENT CHARACTERISTICS FROM A CLINICAL TRIAL WITH ADALUMABUM

H. Haibel, A. Amentbrink, M. Rudwaleit, R. Wong, H. Kupper, J. Braun, J. Sieper

Charité Campus Benjamin Franklin, Rheumatology, Berlin, Germany; Abbott Laboratories, Immunology, Parsippany, USA; Abbott GmbH & Co KG, Immunology, Ludwigshafen; Centre of Rheumatology Roehigen, Rheumatology, Heidelberg, Germany

**Introduction:** To investigate sacroiliac (SJ) joint and spinal inflammation in patients with active, axial Spondyloarthritis (SpA) without radiographic sacroiliitis.

**Methods:** MJRs of SJ joints and spine were conducted at baseline in a 12-week, placebo-controlled trial of adalumabum, with a 40-week open-label extension. Patients with BASDAI≤4 and insufficient response to ≥1 NSAIDs were included.

**Results:** At baseline, 40% of patients had SJ joint inflammation.

**Conclusion:** Adalumabum SJ joint inflammation was scored according to Hermann et al. (1), with each SJ joint divided into quadrants and with modifications for additional points of intensity for each SJ joint (0-34).

Active spinal inflammation was scored by Berlin MRI spine score (0-69). Posterior segments were scored (0 = no inflammation, 1 = inflammation).

**Reference:**

P 44
EVALUATION AND INTER-AND INTRA-OBSERVER RELIABILITY OF POWER DOPPLER ULTRASOUND-GRAPHY (PDUS) FOR DETECTING, SCORING AND SCANNING ENTHESITIS IN SPONDYLOARTHITIS (SPA) PATIENTS: DEVELOPMENT OF A MULTI-STEP METHODOLOGICAL APPROACH


Ambroise Parei Hospital UWSQ University, Rheumatology and ‘Epidemiology, Bouloigne-Billancourt; ‘CHU Cavale Blanche, Rheumatology, Brest; ‘CHU Nancy, Rheumatology, Nancy; ‘CHU Caen, Rheumatology, Caen; ‘CHU Grenoble, Rheumatology, Grenoble; ‘CHU Marseille, Radiology, Marseille, France

Enthesitis is a distinctive feature of SpA, which can be detected by using PDUS (1). However PDUS is considered as an imaging technique highly dependent of operator experience.

Objectives: To develop a multi-steps methodological approach, for improving the reliability of detecting, scoring and scanning enthesitis in SpA patients among a group of sonographers with different level of experience from PDUS experience.

Methods: The study was divided in 3 steps. In step 1, we evaluated the standard reliability of 6 sonographers by scanning bilaterally and twice 5 entheses of 5 patients. Morphological abnormalities in B mode (thickness/echogenicity, calcification/enthesophytes, and erosions) as well as Doppler signal at cortical bone areas were recorded. In step 2, based on disagreements observed during the first part, we worked on consensus by evaluating 90 PDUS images of enthesitis, by using a dedicated website, and by scanning again 5 patients after a period of 1 month of own training session. Finally step 3 aimed at evaluating if one year of daily practice would improve the reliability of sonographers by scanning 5 more patients.

Kappa values were used to analyze data.

Results: Reliability of images reading was excellent: intra-observer kappa ranged from 0.7 to 1 and mean inter-observer kappa was 0.87. Table shows the improvement of the inter-observer reliability on scanning patients along steps.

<table>
<thead>
<tr>
<th>Step</th>
<th>Mean Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.55</td>
</tr>
<tr>
<td>2</td>
<td>0.59</td>
</tr>
<tr>
<td>3</td>
<td>0.66</td>
</tr>
</tbody>
</table>

Conclusion: This study shows that the standardization of PDUS technique among sonographers with different levels of experience followed by their personal PDUS practice was associated with a strong improvement in inter-observer reliability for detecting enthesitis in SpA patients. This approach can be proposed to standardize PDUS assessment of musculoskeletal disorders.

P 45
WEBSITE – WWW.SPA-IMAGING.ORG – ILLUSTRATING MR FINDINGS IN SPONDYLOARTHOPATHIES

A.G. Jurik, B. Schlietz-Christensen

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Background: Magnetic resonance imaging (MRI) is increasingly used to confirm the early diagnosis of ankylosing spondylitis (AS) and other forms of spondyloarthopathy (SpA). MRI is also suitable to monitor these diseases. The value of MRI may improve by a uniform image interpretation in departments performing MR-scanning. To achieve this, there is a need for easy accessible image examples showing typical disease manifestations, normal findings and differentials at MRI. A valid method for grading chronic changes of the sacroiliac joint (SIJ) at magnetic resonance imaging (MRI) is generally lacking. The purposes of this study were: 1) to elaborate and test a grading method based on semi-cortical slice orientation and 2) evaluate the validity of the method compared to conventional radiology (CR).

Materials and Methods: A total of 15 males and 22 females (mean age 37 years (range 16-51 years)) were examined by MRI and CR. The MRI sequences encompassed a semi-cortical T1-weighted (T1) and a T1 fat saturated sequence. The chronic changes assessed were: 1) Erosion and 2) Fatous marrow degeneration (FMD). Each joint was analyzed separately (a total of 74 joints) and was divided in an upper and lower iliac and sacral part. On every slice each quadrant was scored dichotomously for the presence of abnormality; one point was added to the erosion score if there was partial ankylosis and two points for complete ankylosis. Similarly, one point was added if the depth of FMD extended more than one cm beneath the joint surfaces covering more than 1 cm2 of the subchondral area. The sum of scores for all slices indicated the degree of severity. The MRI images were assessed by two viewers and the radiographs by one senior radiologist according to the New York criteria.

Results: The inter-observer agreement regarding erosion, FMD, and the total scores was good. For all parameters 36 of 37 patients were within the 95% limits of agreement with ranges of (-3.6 to 3.9), (-5.1 to 4.5) and (-6.5 to 6), respectively. The corresponding kappa values were 0.89, 0.86 and 0.81. The total MRI scores were significantly related to the radiographic scores (p<0.01).

Conclusion: The method seems usable for estimating chronic SIJ changes having a high inter-observer agreement.

P 46
A METHOD FOR ESTIMATING CHRONIC CHANGES OF THE SACROILIAC JOINT BY MRI

A. Jurik, K.B. Madsen, B. Schlietz-Christensen

‘Aarhus University Hospital Århus Sygehus NBG, Radiology, Århus C; ‘Eira Århus, Rheumatology Clinic, Århus N, Denmark

Introduction: A valid method for grading chronic changes of the sacroiliac joint (SIJ) at magnetic resonance imaging (MRI) is generally lacking. The purposes of this study were: 1) to elaborate and test a grading method based on semi-cortical slice orientation and 2) evaluate the validity of the method compared to conventional radiology (CR).

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Conclusion: The method seems usable for estimating chronic SIJ changes having a high inter-observer agreement.

P 47
COMPARISON OF RADIOGRAPHIC PROGRESSION IN EARLY AND LATE ANKYLOSING SPONDYLITIS

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Introduction: Radiographic progression in Ankylosing spondylitis (AS) has been studied in patients with longstanding disease, only. Whether the rate of radiographic progression is different at certain stages of disease is unknown.

Materials and Methods: Sixty-three AS patients full-filling the modified New York criteria were enrolled to the study for prospective follow-up. Patients with two visits of at least one year interval were included. Radiographs of cervical and lumbar spine were scored according to mSASSS by an independent reader who was blinded for clinical data and time point of the radiographs. Definite radiographic progression (formation of new syndesmophytes, determined by score 2 and 3) and any radiographic progression (worsening of mSASSS=1 point) was recorded and progression in patients with early (<10 years) AS and longstanding disease were compared.

Results: Radiographs from 63 AS patients (77% HLA-B27 positive) were analysed. Mean (SD) duration of symptoms was 13.6 (±2.6) years and did not differ between groups. Definite radiographic progression was detected in 23 (36%) patients. Mean radiographic follow-up (2.0±3.0 vs. 1.7±1.2 years, respectively) and BASDAI, BASFI, ESR, CRP levels and HLA-B27 status were similar in both groups. Mean mSASSS scores were higher in the longstanding AS group but mean change in mSASSS did not differ significantly (Table I). Progression was more frequent in patients with longstanding disease (Early AS=31/35, 23.8% vs. Longstanding AS=15/32, 46.8%; p=0.042).

Table I: mSASSS scores (mean (SD)) at baseline and after 2 years

<table>
<thead>
<tr>
<th></th>
<th>Early AS (n=65)</th>
<th>Late AS (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.52</td>
<td>7.23</td>
</tr>
<tr>
<td>Follow-up</td>
<td>8.33 (11.49)</td>
<td>20.23 (23.28)</td>
</tr>
<tr>
<td>Change in mSASSS</td>
<td>3.81</td>
<td>4.07</td>
</tr>
</tbody>
</table>

Conclusion: Mean rate of radiographic progression did not differ between AS patients with early and late disease. High mSASSS scores and tendency towards a more frequent radiographic progression in the late stages may implicate the progressive nature and continuous formation of new syndesmophytes.
P 48
ENTHESIS ULTRASOUND RESPONSIVENESS IN EARLY SPONDYLOARTHRITIDES
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Introduction: Enthesitis ultrasound (US) has shown to be valid and reliable, but the ability of US to change over a time frame have to be demonstrated and this was the objective of this study.

Materials and Methods: Prospective, blind, longitudinal 6 month study in early SpA. Patients fulfilled the diagnostic classification ESSG criteria. Clinical data was collected. The US MASEI index was used. Smallest detectable change (SDC) and standard response mean (SRM) was calculated. An inter-reader and an inter-explorer was done for reliability.

Results: We analyzed 45 consecutive patients, 34 received only non steroidal anti-inflammatory drugs (NSAIDs). The table shows the six months US score and sub-scores patient’s evolution. The SDC was 4.19 for global score, 3.85 for activity sub-index and 1.72 for structural damage sub-index. Using the SDC, 17 (38%) improve the score and 9 (20%) worsened. The SRM was 0.27 for global score, 0.43 for activity sub-index and 0.30 for structural damage sub-index. Using the SDC the improvement of higher MASEI was 0.01 (p<0.01), erosion (p<0.05), Doppler signal and ESR (p<0.05) basal values.

The US inter-explorer intraclass correlation coefficients (ICC) was 0.86 and the inter-reader ICC was 0.83.

Table. Longitudinal evolution of ultrasound score.

<table>
<thead>
<tr>
<th>Basal</th>
<th>6 Months</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASEI score Total</td>
<td>25.96</td>
<td>22.89</td>
</tr>
<tr>
<td>MASEI score NSAIDs group</td>
<td>25.56</td>
<td>21.91</td>
</tr>
<tr>
<td>MASEI activity sub-index</td>
<td>13.13</td>
<td>8.62</td>
</tr>
<tr>
<td>MASEI activity sub-index NSAIDs group</td>
<td>12.38</td>
<td>7.42</td>
</tr>
<tr>
<td>MASEI structural damage sub-index</td>
<td>12.84</td>
<td>14.24</td>
</tr>
<tr>
<td>MASEI structural damage sub-index NSAIDs group</td>
<td>13.18</td>
<td>14.50</td>
</tr>
</tbody>
</table>

Conclusions: In early SpA ultrasound can be a useful and valid tool to monitoring enthesis responsiveness in a six months period.

Reference:
1 Validity of Enthesis Ultrasound Assessment in Spondyloarthropathy. Ann Rheum Dis published online 7 April 2008; doi:10.1136/ard.2007.084251

Supported by an unrestricted grant in spondyloarthropathies from Wyeth.

P 49
HYPOPHOSPHATAEMIA: AN UNDER-RECOGNIZED CAUSE OF SPONDYLOARTHROPATHY
P. Wordworth, C. Swales
Oxford University Institute of Musculoskeletal Science, Nuffield Dept of Orthopaedic Surgery, Oxford, UK

Introduction: A 52 year old patient with probable Dent disease had pronounced hypophosphataemia and floral hip joint capsule ossification. For twenty years he was thought to have ankylosing spondilitis (AS) on clinical grounds with the additional finding of minor magnetic resonance imaging (MRI) changes in the sacroiliac joint (SIJ). We therefore studied individuals with other causes of persistent hypophosphataemia for clinical features mimicking AS. X-linked hypophosphataemia (XLH) caused by mutations in the PHEX gene causes vitamin D resistant rickets. Less commonly appreciated is the widespread enthesisopathy which occurs in this disorder which can mimic AS.

Methods: We have identified 4 individuals with XLH attending the Oxford skeletal dysplasia clinic in whom axial skeletal symptoms were prominent. Clinical and radiographic assessments of axial skeletal abnormalities were performed. MRI of the thoraco-lumbar spine and SIJ was undertaken.

Results: One HLA-B27 positive male patient with recurrent iritis aged 52 had severe vertebral osteopenia with ossification of the capsule of both hips grossly restricting movement. The B27 and iritis were felt to be coincidental findings. The second male patient (aged 26) had severe spinal disease and restricted hip movements due to enthesisopathy. The other two patients were female; one aged 28 had radial head subluxation due to spinal stenosis from ossification of the ligamentum flavum; the other also aged 28 had severe limitation of spinal movement due to enthesisopathy. Restricted stature and pronounced bony deformities were apparent in only two of these individuals but all had a positive family history of XLH.

Conclusions: Enthesopathy complicating XLH is common and may affect individuals of either sex. Minor MRI changes in the SIJ may be seen. The clinical features may closely resemble spondyloarthropathy due to other causes but short stature, bony deformities and a positive family history help to discriminate these conditions.

Reference:

P 50
UNILATERAL SACROILIITIS DETECTED BY QUANTITATIVE BONE SCINTIGRAPHY – DIAGNOSTIC VALUE COMPARED TO BILATERAL SACROILIITIS
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Background: In daily practical routine unilateral sacroiliitis in quantitative bone scintigraphy is often given a higher diagnostic value for making a diagnosis of axial spondyloarthritis (SpA) compared to bilateral sacroiliitis in scintigraphy. However, very limited data is available about the diagnostic value of scintigraphy showing unilateral sacroiliitis.

Methods: We performed a retrospective analysis of patients who have been seen in our rheumatological back pain clinic between August 2004 and May 2007. We screened all patients’ charts and identified those patients who had undergone quantitative bone scintigraphy examination for the evaluation of sacroiliitis. A diagnosis of axial SpA or non SpA back pain was made according to the expert’s opinion. Sensitivity, specificity and likelihood ratio for scintigraphic sacroiliitis as a diagnostic tool for axial SpA were calculated.

Results: Out of 980 patients who have been referred to our clinic for the evaluation of back pain, in 157 cases (16.0%) a scintigraphic examination of the sacroiliac joints had been performed. Among 73 patients with axial SpA (66 with ankylosing spondilitis and 27 with non-radiographic axial SpA) scintigraphy showed evidence of bilateral sacroilitis in 35.6% (26/73) while isolated unilateral sacroilitis was found in 17.8% (13/73). Among 76 patients who had been diagnosed with non-rheumatic back pain (controls) basal values.

Validity of Enthesis Ultrasound Assessment in Spondyloarthropathy.

P 51
CHARACTERISTICS OF ANKYLOSING Spondylitis PATIENTS IN THE UNITED KINGDOM
C. Farrar1, L. Bradbury2, J. Pointon1, M. Brown1, P. Wordworth1
1Oxford University Institute of Musculoskeletal Science, Nuffield Dept of Orthopaedic Surgery, Oxford, UK; 2Diamantina Institute of Cancer Immunology and Metabolic Medicine, University of Queensland, Brisbane, Australia

Introduction: In total 1,983 patients with ankylosing spondylitis (AS) from the UK were recruited for genetic studies. We have recorded the clinical associations in this large patient sample which will be used for future phenotype-genotype correlations.

Methods: AS patients of western European origin, fulfilling the New York criteria for AS, were recruited. Clinical details were abstracted from a structured validated questionnaire which included age of symptom onset, presence or absence of uveitis, psoriasis (Ps), inflammatory bowel disease (IBD) - Crohn’s disease (CD) or ulcerative colitis (UC), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index (BASFI) were calculated. Associations between continuous variables were assessed with the Student’s t-test, and between dichotomous variables using the chi-square test. BASDAI and BASFI were uncorrected for disease duration.

Results: 88% of patients have HLA-B27 positive. 41% of patients have uveitis and a younger age of disease onset (mean±standard deviation) 23 (42.1±4.9 vs. 25.1±4.0, p=0.06±0.005). Average BASDAI is higher in patients with Ps (4.4±2.3 vs. 4.0±2.1, p=0.01±0.005) and IBD (4.6±2.3 vs. 4.0±2.1, p=0.01±0.005) but lower in males (3.9±2.2 vs. 4.3±2.2, p=0.01±0.005) and in IBD (4.7±2.7 vs. 3.8±2.7, p(1)±0.01±0.005). Patients with Ps are more likely to have IBD than those without (24% vs. 16%, p=0.01±0.005). Patients with Ps have more UC (15% vs 10%, p=0.01±0.005) and more likely to have UC (15% vs 10%, p=0.01±0.005). Male patients have more UC (12% vs. 8%, p=0.04±0.005).

Reference:
P 52
THE NATURAL COURSE OF RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS – EVIDENCE FOR NON-LINEAR PROGRESSION IN A LARGE PROPORTION OF PATIENTS
X. Baraliakos, J. Listing, A. von der Recke, J. Braun,
Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Herne; ʼGerman Rheuma-
tis Research Center, Epidemiology, Berlin, Germany

Background: New bone formation of the spine is pathognomonic in AS. This is best assessed by conventional x-rays.

Objective: To describe the natural course of radiographic progression and to differen-
tiate rates of progression in AS patients.

Methods: 146 AS patients who had never received biologics were retrospectively evaluated. Inclusion criterium was the availability of at least 2 complete sets of cervical and lumbar radiographs within 6 years. Using the mSASSS, two readers quantified the structural changes in concealed time order and assessed different rates of radiographic progression velocity. The association between baseline characteristics and the degree of progression was also examined.

Results: The mean age of the 146 patients was 54.2±12.3 years and the mean time since onset of AS-related symptoms was 23.6±11.2 years. 81% of the patients were male and 78% were HLA-B27 positive. The mean BasDAI was 4.4±1.9 (range 0.5-7.3) and 58.3% of patients had BasDAI values ≥4. The mean follow-up time (FU) was 3.8±1.7 years (1-6y). The mean mSASSS change per year was 1.3±2.5 units. However, radiographic progression was not linear since >43% of patients showed a 4-fold higher progression than the mean, and 22.5% had no progres-
sion. ‘Fast progression’ was calculated as a change >5 mSASSS units or ≥2 new syndesmophytes, ‘moderate progression’ as change of 2.0-5.0 mSASSS units or <2 new syndesmophytes, and ‘slow progression’ as change of ≥2 mSASSS units or no more than 1 new syndesmophyte within 2 years. Only the amount of baseline syndesmophytes was significantly predictive of a later classification.

Conclusions: Radiographic progression in AS is not linear over time in a large group of patients. Different rates and velocities of radiographic progression can be retrospectively identified on an individual level by assessment of new syndes-
ophytes or change in mSASSS scores every 2 years. Prediction of progression is possible by detection of syndesmophytes at presentation.

P 53
EPIDEMIOLOGY OF HIP INVOLVEMENT IN ANKYLOSING SPONDYLITIS
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Background: Although clinicians recognise hip involvement as an important fea-
ture of ankylosing spondylitis, data on the epidemiology, nature of the disease and therapeutic strategies are scarce.

Aims: To describe the epidemiology of hip involvement in ankylosing spondylitis in 2 European countries: Belgium and Spain.

Methods: Two large databases, containing data from 847 Belgian (ASPECT data-
base) and 1421 Spanish (REGISPONDER database) cross-sectionally evaluated AS patients, fulfilling the modified New York criteria for definite AS were merged. In the ASPECT database, hip involvement was defined as current or past hip arthritis. In the REGISPONDER database, hip involvement was defined as pain or limitation of the hips during clinical examination.

Results: One out of four AS patients presented previous or current hip involvement (27% in ASPECT, 24% in REGISPONDER). Patients with hip involvement had signif-
icantly worse BASDAI (ASPECT: 5.6 vs 5.2, p<0.001, REGISPONDER: 4.6 vs 3.9, p<0.001) and worse BSA (ASPECT: 5.8 vs 4.8, p=0.001, REGISPONDER: 3.4 vs 5.2). Patients with hip involvement had also a significant earlier disease onset compared to patients without hip involvement. Other differences are listed in table 1. Also reflecting the hip, 36%, 45% and 19% of patients in ASPECT had normal/mildly, moderately or severely impaired intermalleolar distance and 78%, 12% and 10% had normal/suspicious, mild, moderate/severe damage on conventional radiography of the hip in REGISPONDER.

Conclusion: Hip involvement is a common feature of ankylosing spondylitis in-
volving about one fourth of AS patients. Patients with ankylosing spondylitis have higher disease activity, measured by BASDAI, and an impaired functioning re-
flected by higher BASFI.

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IS THERE A RELATIONSHIP BETWEEN FUNCTIONALITY AND PRODUCTIVITY IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS? RESULTS FROM THE GO-RAISE STUDY
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Introduction: Patients with ankylosing spondylitis (AS) report significant func-
tional impairment, which could affect their productivity. We wanted to establish the relationship between functionality and productivity in patients with active AS.

Methods: Patients with AS (modified NY criteria: BASDAI and back pain scores ≥4) were enrolled into a multicenter, randomized, placebo (PBO)-controlled study (GO-RAISE). 356 patients were randomized (1:1:1:1 ratio) to receive sub-
cutaneous golimumab (GLM) 50mg or 100mg or PBO q4wks. Endpoints included the change from baseline in a 24-Hour BASHIP and self-reported productivity measured on a 0-10 cmVAS. At wk16, PBO or GLM 50mg patients with <20% improve-
ment from baseline in total back pain and morning stiffness entered early escape in a double-blind fashion. All other patients remained on their previous medication until wk24. GLM 50mg or PBO patients who entered early escape had their last observa-
tion prior to change in treatment carried forward for the wk24 analyses. Observed values at wk24 were used for GLM 100mg patients. An ANOVA on van der Waerden normal scores was performed for between-group differences. Spear-
man’s Rank correlation was used to measure the associations between changes in BASFI and productivity at wk24. Regression analysis was used to determine the predicted value of productivity for improvements in BASFI.

Results: GLM 50mg and 100mg groups showed significant (p<0.001) improve-
ments in both BASFI and self-reported productivity at wk24 vs PBO. There was a positive correlation between change from baseline in BASFI and self-reported productivity at wk24 for all patients (r=0.67, p<0.0001), the GLM 50mg (r=0.68, p<0.0001) and GLM 100mg group (r=0.60, p<0.0001). A significant positive cor-
relation between change from baseline in BASFI and productivity was also evident for PBO (r=0.57, p<0.0001). The regression model showed that a change of one BASFI amounts to a change in the productivity scale of 0.86 (r=0.47, p<0.0001) adjusted for treatment.

Conclusions: The GO-RAISE results show a definite relationship between im-
proved functionality and self-reported productivity in GLM-treated AS patients.

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GOLIMUMAB SIGNIFICANTLY IMPROVES PRODUCTIVITY IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM THE PHASE 3 GO-RAISE STUDY
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Introduction: We evaluated the impact of golimumab (GLM) on productivity in ankylosing spondylitis (AS) patients.

Methods: GLM was studied in a multicenter, randomized, placebo (PBO)-control-
led study (GO-RAISE). 356 patients were randomized (1:1:1:1:1 ratio) to receive subcutaneous GLM 50 mg or 100 mg or PBO q4wks. Patients with AS according to the modified NY criteria (BASDAI and back pain score each ≥4) were eligible. Productivity was measured on a VAS scale (0-10 cm). Change in productivity from baseline to wk16 and wk24 was compared between groups. At wk16, patients in the PBO or GLM 50 mg group who had <20% improvement in total back pain and morning stiffness measures entered early escape in a double-blind fashion. All other patients remained on their previous medication until wk24. For GLM 50 mg or PBO patients who entered early escape, their last observation prior to change in treatment was carried forward for the wk24 analyses. Observed values at wk24 were used for GLM 100 mg patients. An ANOVA on van der Waer-
den normal scores was performed for between-group differences.

Conclusion: Hip involvement is a common feature of ankylosing spondylitis in-
volving about one fourth of AS patients. Patients with ankylosing spondylitis have higher disease activity, measured by BASDAI, and an impaired functioning re-
flected by higher BASFI.
Results: Patients in the GLM 50 mg, 100 mg, and PBO groups had similar mean ± SD baseline scores of 6.6±2.5, 6.8±2.3 and 6.3±2.5, respectively. Mean improvement in self-reported productivity was significantly greater in the GLM 50 mg group vs. PBO at wk16 (-2.8±3.0 vs. -0.4±2.7; p<0.001) and wk24 (-2.7±3.1 vs. -0.3±2.5; p<0.001). The change from baseline in productivity was similar in the GLM 50 mg and 100 mg groups at wk16 and wk24.

Conclusions: AS patients treated with GLM 50 mg and 100 mg had significant improvement in self-reported productivity, with improvement at wk16 maintained through wk24.

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WORK STATUS, PHYSICAL FUNCTION AND QUALITY OF LIFE IN WORKING-AGE PATIENTS WITH ANKYLOSING SPONDYLITIS

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Introduction: Physical disability and impairment of Quality of Life (QoL) can be major problems in ankylosing spondylitis (AS) patients and result in work disability. Our aim was to determine the relationship between work and QoL in AS patients aged 18-65 years.

Material and Methods: The study was conducted on AS patients defined according to the modified New York criteria. Demographic data were recorded and patients classified by: 1) disease activity – Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), 2) functional repercussion – Bath Ankylosing Spondylitis Functional Index (BASFI), and Bath Ankylosing Spondylitis Metrology Index (BASMI), 3) QoL – HAQ and SF-36, and 4) radiological severity – mSASSS. Comparisons between working and retired groups of patients were performed.

Results: Among the 224 patients studied, 136 were working (60.7%) and 54 (24.1%) retired. Working patients were younger and had shorter disease duration. The activity, functional/radiological impact of the disease, and QoL parameters were clearly better in the working group (as presented in Table I). Work, after adjusting for sociodemographic, therapeutic and disease characteristics, continued to be positively associated with parameters of wellbeing. Retirement is associated with: increasing age/disease duration; greater physical functional disability as assessed by BASFI (r=0.19; p=0.027), and BASMI (r=0.51; p=0.003); more severe radiological impact as assessed by mSASSS (Pearson=0.86; p=0.018); and greater deterioration of QoL as assessed by HAQ-AS (Pearson=0.51; p=0.037).

Table I.

<table>
<thead>
<tr>
<th>Working (n=136)</th>
<th>Retired (n=54)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40.4 (SD=10.6)</td>
<td>53.7 (SD=7.9)</td>
<td>0.002</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70% male</td>
<td>70% male</td>
<td>ns</td>
</tr>
<tr>
<td>Disease Duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.6 (SD=10.1)</td>
<td>26.1 (SD=11.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>BASDAI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.9 (SD=2.3)</td>
<td>4.5 (SD=2.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>BASFI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.3 (SD=2.5)</td>
<td>5.2 (SD=2.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>BASMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (SD=2.2)</td>
<td>5.6 (SD=2.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>HAQ-AS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.7 (SD=0.5)</td>
<td>1.2 (SD=0.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>56.9 (SD=18)</td>
<td>48.3 (SD=17.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>mSASSS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.8 (SD=17.2)</td>
<td>32.9 (SD=25.9)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: There are remarkable differences in functional and QoL parameters between the two groups. Disability, disease ‘severity’, and disease duration, impact on capacity to remain employed in AS.

P 57

PATIENTS WITH ANKYLOSING SPONDYLITIS ELIGIBILITY FOR ANTI-TNF ALPHA TREATMENT IN THE UNITED KINGDOM

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Objective: To determine the prevalence of ankylosing spondylitis across Europe.

Methods: We carried out a literature review of studies published in the last decade, irrespective language that was listed on PubMed, Cochrane Database, EMBASE and MEDLINE. The key terms included: first: ankylosing spondylitis, spondyloarthropathies, morbus bechterew, spondylitis ankylopoetica), AND (second: prevalence, epidemiology, incidence). Studies with data the prevalence of ankylosing spondylitis in European subjects were included. Review articles and studies from a non European background have been used for further substantiating the literature search, but were excluded from the analysis. Two independent reviewers reviewed the titles and abstracts and any differences were agreed by consensus.

Results: Of 13 studies, seven fulfilled the inclusion criteria. Two studies from Norway, one from the Netherlands, and one from the United Kingdom reported prevalence rates for ankylosing spondylitis. These studies reported prevalence rates of 0.05%, 0.08%, 0.11%, 0.15%, 0.19%, 0.23%, 0.45%, and of 0.86%. The overall prevalence for European patients with ankylosing spondylitis were 0.24%.

Conclusion: AS is an inflammatory disease of the spine, with a typical onset in late teenage years. The prevalence of AS in unknown, with current estimates ranging from 0.05% to 0.23% based on data from Hungary and the UK from 1949 and 1977. The findings of this analysis provide a more robust and up to date estimate of the true prevalence of AS. However, overall epidemiological data on AS is scarce. These results may have an impact on the resource planning in different national health services.

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THE PREVALENCE OF ANKYLOSING Spondylitis in EUROPE

M. Lehmeier1, M. Bains1, V. Koscielny1, 2Wyeth, Strategic Planning, Taplow; 3Wyeth, Medical, Taplow, UK

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Conclusion: AS is an inflammatory disease of the spine, with a typical onset in late teenage years. The prevalence of AS in unknown, with current estimates ranging from 0.05% to 0.23% based on data from Hungary and the UK from 1949 and 1977. The findings of this analysis provide a more robust and up to date estimate of the true prevalence of AS. However, overall epidemiological data on AS is scarce. These results may have an impact on the resource planning in different national health services.
patients were receiving Infliximab, 23 (31.9%) Etanercept and 21 (29.16%) Adalimumab. Pre-treatment, 22 were unable to work and 10 were working part-time because of AS. After a mean 21.01 months 5 of the 22 had returned to full- or part-time work and 3 of the 10 part-time workers had progressed to full-time work. Thus, 8 had increased their work commitment whilst 24 had not. Data are shown in Table I. In those who remained in full-time work, the mean days of sick leave improved from 15.6 to 1.76 days (p=0.0001).

Table I.

<table>
<thead>
<tr>
<th></th>
<th>Total pre-treatment (72)</th>
<th>Back to work increased (8)</th>
<th>No increase in work (24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASQoL</td>
<td>11.11</td>
<td>3.71*</td>
<td>10.84*</td>
</tr>
<tr>
<td>BASDAI</td>
<td>6.45</td>
<td>0.97*</td>
<td>2.25*</td>
</tr>
<tr>
<td>BASFI</td>
<td>5.89</td>
<td>2.7*</td>
<td>5.01*</td>
</tr>
<tr>
<td>Mean age at onset</td>
<td>24.21 (7-60) yrs</td>
<td>18.42 (14-22) yrs</td>
<td>30.82 (8-60) yrs</td>
</tr>
<tr>
<td>Mean age at treatment</td>
<td>44.41 (18-64) yrs</td>
<td>40 (27-55) yrs</td>
<td>49.53 (33-63) yrs</td>
</tr>
<tr>
<td>Duration of disease</td>
<td>22.85 (4-54) yrs</td>
<td>22.85 (4-54) yrs</td>
<td>21.94 (4-54) yrs</td>
</tr>
<tr>
<td>Male/Female</td>
<td>53 /19</td>
<td>7 /1</td>
<td>12 /5</td>
</tr>
<tr>
<td>p=0.05</td>
<td></td>
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</tbody>
</table>

Conclusions: Increased work capacity is associated with improvement in ASQoL, BASDAI and BASFI. There was a non-significant trend towards improvement with age at onset and age at treatment but not disease duration.

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A TREATMENT OPTION FOR PATIENTS WITH SEVERE ACTIVE ANKYLOSING SPONDYLITIS: THE COSTS AND BENEFITS ASSOCIATED WITH ETANERCEPT

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Background: Etanercept (ETN) has recently been recommended as a treatment option for adults with severe active ankylosing spondylitis in the UK. The objective was to examine the costs and benefits associated with long-term treatment of ETN in patients with severe ankylosing spondylitis (AS) in the UK.

Methods: A mathematical model was used to project the long term costs and benefits associated with ETN plus non-steroidal anti-inflammatory drugs (NSAIDs) compared with NSAIDs alone. Individual patient level data from Phase III ETN trials was used to inform the magnitude of initial response. The proportion of responders was estimated using British Society for Rheumatism guidelines. Disease costs were based on a retrospective costing exercise involving patients attending an AS clinic in the UK. A relationship between disease progression (BASDAI and BASFI) and EQ-SD measurements were used to estimate quality adjusted life years (QALYs). Long term disease progression was projected over 25 years using published evidence. Quality adjusted life years were calculated using probabilistic sensitivity analyses.

Results: With the majority of results falling below £25k per QALY, this study demonstrates ETN treatment in AS patients in the UK could be considered cost effective. Over the 25 year horizon, patients treated with ETN plus NSAIDs gained 1.58 additional QALYs compared with those receiving NSAID treatment with an additional cost of £36k the cost per QALY was estimated to be £23k per QALY.

Conclusion: Patients with AS that have substantial disease related sick leave, experience inefficiency at work and perform additional work hours to catch up unfinished work. Moreover, patients have hindrances in unpaid tasks and often these have to be taken over by others. The costs associated with paid or unpaid productivity loss are substantial.

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RELATIONSHIP BETWEEN FUNCTIONAL DISABILITY AND BONE LOSS IN SPONDYLOARTHRITIS PATIENTS

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Introduction: Relationship between functional disability and bone mineral density (BMD) in spondyloarthropathy (SpA) patients was studied.

Materials and Methods: 116 SpA patients (54 ankylosing spondylitis (AS), 31 psoriatic arthritis (PsA), 5 enteropathic arthritis (EA) and 26 reactive arthritis (ReA); 91 rheumatoid arthritis (RA) and 96 healthy controls (HC) were investigated. Groups did not differ in body mass index, comorbidities, and mean age of initial position for osteoporosis. SpA group (81M, 35F, mean age 42.81 yrs., SD =12.72) differed from RA (28 M, 63F, mean age 50.14, SD = 11.38) and HC group (32 M, 64F, mean age 48.91 yrs. SD =12.89) by gender and age.

Excluded were persons having metabolic bone diseases or receiving medication effecting bone metabolism (except corticosteroids). BMD was determined at the lumbar spine (L5), and upper part of right and left femur by DEXA. Functional disability of SpA patients were assessed using BASFI, HAQ and spinal mobility index.

Results: BMD scores of SpA patients did not differ and were significantly lower than HC (p<0.0000). No differences were found comparing BMD of AS, PsA, EA, and ReA patients (p>0.05). HAQ correlated with BMD scores of LS (r = -0.185, p=0.08), whereas BMD scores of left and right femur correlated with BASFI (left)=0.256, p=0.006; right= 0.290, p=0.002), HAQ (right)=0.323, p=0.000; right= 0.290, p=0.000; modified Schober’s distance (left)=0.195, p=0.036; right= 0.193, p=0.038, lateral flexion (right)=0.207, p=0.026; (right)= 0.222, p=0.17), intermalleolar distance (left)=0.292, p<0.001; right)= 0.336, p=0.000), tragus-to-wall distance (right)=0.241, p=0.009; tragus-to-wall distance (right)= 0.242, p=0.009).

Conclusion: Bone loss similar to that of RA patients was found not only in AS but also in PsA, EA, and ReA. Our findings reveal a direct correlation between functional status and BMD of SpA patients, most clearly found at femur sites.
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LOW BONE MINERAL DENSITY IS RELATED TO MALE GEN- DER AND FUNCTION IN EARLY SPONDYLARTHROPATHIES

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¹VU University Medical Center, ²Rheumatology and Clinical Epidemiology and Biostatistics, Amsterdam; ³Jan van Breemen Institute, Rheumatology, Amsterdam, The Netherlands

Introduction: Osteoporosis is a well known complication of longstanding Ankylosing Spondylitis (AS). However, data about bone mineral density (BMD) both early in AS and other spondylarthropathies are very scarce. The objective was to determine the value of BMD in early SpA patients and which factors are of influence at a low BMD.

Methods: 131 spondylarthropathy patients with a DEXA of the lumbar spine and hips within 3 years after diagnosis were studied. The outcome measure BMD obtained with DEXA measurement was defined as three ordinal levels: 1) normal, 2) osteopenia (T-score <-1.0) and 3) osteoporosis (T-score <-2.5). Ordinal logistic regression was used to study univariate and multivariable (backward regression, p-value<0.10) relationships of the variables: gender, age, disease-duration, HLA-B27, CRP, ESR, BASDAI, BASFI, BASMI.

Results: In our cohort 29%/28% of the patients had osteopenia/osteoporosis present in the femur and 30%/38% in the spine. Overall 53% of the early SpA patients had a normal BMD, compared to 97%/89% of osteoporosis in the femur and spine. Univariate; male gender (OR: 4.9; 95%CI 1.9 - 10), CRP (OR: 1.0; 95% CI 0.7 - 1.4), BASFI (OR: 1.2; 95%CI 1.0 - 1.4) and BASMI (OR: 1.6; 95%CI 1.3 - 2.0) were significantly associated with a low BMD. Factors retained in the multivariable model; male gender (OR: 3.9; 95% CI 1.7 - 9.3), CRP (OR: 1.0; 95% CI 0.8 - 1.3), BASFI (OR: 1.3; 95%CI 0.9 - 1.3) and BASMI (OR: 1.0; 95% CI 1.0 - 1.6).

Conclusions: Within 3 years after diagnosis 47% of the early SpA patients showed osteopaenia or osteoporosis which was significantly associated with male gender, and decreased functional capacity (BASFI and BASMI).

P 64
PANCA, ASCA AND ANTI-OMPc ANTIBODIES ARE PRESENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Introduction: About 5-10% of the AS patients suffer from Inflammatory Bowel Disease (IBD) either Cohn’s disease (CD) or ulcerative colitis (UC). In asympotomatic AS patients gut inflammation is observed in 25-49%. The presence of antig- lycan antibodies to the cell wall mannan of Saccharomyces cerevisiae (ASCA) or antibodies to porin protein C of Escherichia coli (anti-OmpC) are specifically found in CD. These markers rarely occur in healthy controls. Perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) are expressed by the majority of UC patients. ASCA and anti-OmpC have been found to be associated with male gender, and decreased functional capacity (BASFI and BASMI).

Methods: 52 AS patients without gastrointestinal complaints were compared with 26 patients with IBD and AS, as well as with 50 UC and 51 CD patients matched for age- and sex. IBD was ascertained by clinical, endoscopic and microscopic findings. The UC serological profile was defined as pANCA+ in 1:80, ASCA (IgG or IgG)≥25U/ml, anti-OmpC≥25U/ml. The AS serological profile was defined as pANCA- or + in 1:20, ASCA (IgA or IgG)≥25U/ml or anti-OmpC≥25U/ml. Results: In 48% of the AS patients without gastrointestinal disease, these serologi- cal markers were observed more often than reported in healthy controls (pANCA+ n=11(21%); ASCA IgG+ n=9 (19%); ASCA IgA+ n=4 (8%); Anti-OmpC+ n=10 (19%)). Remarkably, also anti-OmpC, a marker of perforating CD, was positive in 19% of the AS patients. pANCA was more frequently present in AS+UC than in AS alone (OR 8.8, 95%CI (2.0-38.6)), thus being an indicator for IBD-associated spondylarthropathy.

Conclusions: In 48% of the AS patients, without gastrointestinal complaints, sero- logical markers characteristic for IBD are observed. pANCA is more often present in AS+UC than in AS (p<0.004). These results suggest a pathogenic link between AS and IBD, whereas pANCA is an indicator for IBD-associated spondylarthropathy in UC patients.

P 65
ADALIMUMAB (HUMIRA®) EFFECTIVELY PREVENTS UVEITIS FLARES IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS)
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¹Charité Campus Benjamin Franklin, Berlin, Germany; ²St. Olavs Hospital, Trondheim, Norway; ³Regionalhospital Silkeborg, Silkeborg, Denmark; ⁴Universi- ty Hasselt, Hasselt, Belgium; ⁵Abbott GmbH & Co KG, Ludwigshafen, Germany

Objective: To investigate effects of adalimumab on uveitis episodes in AS. Methods: AS patients with BASDAI≤4 despite ≥1 NSAID received open-label adalimumab 40 mg every other week for 12 weeks (RHAPSODY). History of uveitis (≥1 prior uveitis flare) was documented and characterized as acute (AU) or chronic (persistent uveitis with symptom-free interval <3 months to next relapse). Uveitis episodes within past year prior to baseline were reported as “0 flares,” “≥1-2 flares,” or “≥3 flares.” Rates of previous flares per 100-patient-years (100-PYs) during the past year were calculated using mean of 1-2 flares (1.5) and minimum of ≥3 (3.0) flares. Rate of uveitis flares reported as AES was calculated as events per 100-PYs. Uveitis flares/100-PYs before vs. during adalimumab therapy were compared. Results: Of 1,250 patients, 25 (2%) reported 27 AU flares. Of 274 who had a history of uveitis, 23 (8%) reported 25 AU flares. Of 106 patients with symmetric AU in the past year, 19 (18%) reported 21 AU flares. Of 28 with active AU at base- line, 9 (32%) reported 10 AU flares. New-onset uveitis occurred in 2 males. Of 274 with prior uveitis, 43 had chronic uveitis; 10 flares occurred during adalimumab therapy in this group.

Uveitis flare rates per 100-PYs before and during adalimumab therapy

<table>
<thead>
<tr>
<th>Uveitis flare type</th>
<th>Rate per 100-PYs before adalimumab</th>
<th>Rate per 100-PYs during adalimumab</th>
<th>Reduction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n=1,250)</td>
<td>15.0 (7.4)</td>
<td>7.4 (3.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Symptomatic uveitis (n=43)</td>
<td>19.2 (9.6)</td>
<td>50% (25%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: Adalimumab effectively reduced the rate of anterior uveitis flares in AS, including patients with a recent history of AU flares and patients with chronic anterior uveitis.

P 66
CLINICAL FEATURES OF ANKYLOSING SPONDYLITIS IN KOREANS
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Introduction: There have been studies on clinical features of Ankylosing Spondy- litis (AS) depending on the race and areas. However, the precise study toward this study was to determine the clinical profile of AS. Methods and Materials: A total of 732 men and 98 women with AS were recruit- ed. Clinical data included age, sex, duration of disease, age at onset of AS symp- toms, family history of AS, history of uveitis/iritis, peripheral arthritis, enthesitis and HLA-B27 carriage status. Results: Demographic features The mean onset age (SD) was 20.9 (8.1) years. The male to female ratio was about 8:1. Two hundred thirty-six patients (28.7%) were found to be the juvenile onset AS (JoAS). Seven hundred twenty-seven (94.8%) have HLA-B27. Other extra-articular organ involvements such as lung, heart, kid- ney, and colon are uncommonly seen. Comparison of clinical features between male and female patients Women had a later age at disease onset. The frequency of uveitis was statistically different (28.2% of men vs. 40.8% of women).
Comparison between JoAS and AoAS JoAS group had more enthesitis than AoAS group. The peripheral arthritis and hip joint involvement were more frequent in JoAS group.

Comparison between HLA-B27 positive and negative patients HLA-B27 positive cases had a significantly younger age of symptom onset (by 5.3 years, p=0.002), more uveitis (p=0.001), and greater hip involvement (p<0.001) than HLA-B27 negative patients.

Conclusion: The clinical features of our patients appeared largely similar to those in other studies, except a few noticeable differences: 1) AS is eight times more common in men than in women, 2) AS patients in Korea had a higher prevalence of peripheral arthritis, 3) female patients had more uveitis than male, 4) JoAS was common in our group.

P 67

ACUTE ANTERIOR UVEITIS IN REITER’S DISEASE (REACTIVE ARTHRITIS)

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Aim of Study: To investigate ocular manifestations - acute anterior uveitis (AAU) in Reiter’s disease according to disease form.

Methods: A total of 918 (819 males, 99 females) consecutive pts with Reiter’s disease - Rd were treated during the period from 1966 until 2005. The clinical and laboratory data as well as ocular manifestations were analyzed. The diagnosis of AAU was made by an ophthalmologist.

Results: The classic forms of the disease were present in 479 (52%) pts, and two signs in 439 (48%). The age at onset was between 20-39 yrs in 659 (72%) pts. Acute anterior uveitis (AAU) was found in 113 (12.3%) out of 918 pts with Rd. In more than 50% of pts it was of a relapsing form, four of them had between 15 and 20 recurrences. The occurrence of AAU depended on the duration of the follow-up: it was present in 31 (5%) pts out of 623 acute/subacute form of Rd, in 46 (22%) pts of recurrent form and in 41 (42%) out of 86 pts with chronic form of the disease. The appearance of AAU was independent of the severity and the course was present in 31 (5%) pts out of 623 with acute/subacute form of Rd, in 46 (22%) pts of recurrent form and in 41 (42%) out of 86 pts with chronic form of the disease. The appearance of AAU was independent of the severity and the course was present in 31 (5%) pts out of 623 with acute/subacute form of Rd, in 46 (22%) pts of recurrent form and in 41 (42%) out of 86 pts with chronic form of the disease.

Conclusion: The occurrence of acute anterior uveitis (AAU) was independent of the severity and the course was present in 31 (5%) pts out of 623 with acute/subacute form of Rd, in 46 (22%) pts of recurrent form and in 41 (42%) out of 86 pts with chronic form of the disease.

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THE PATTERN OFankyLOSINg SPONDYLITIS (AS) IN IBERO-AMERICA (IBA): THE RESPONSE GROUP REPORT II

Rheumatology, San Jose, Costa Rica; Rheumatology, Lima, Peru; Rheumatology, Santiago, Chile; Rheumatology, Montevideo, Uruguay; Rheumatology, Lisbon, Portugal; Rheumatology, Caracas, Venezuela; Rheumatology, San Jose, Costa Rica; Rheumatology, Cordoba, Spain

Background: RESPONSIA is an IBA group of rheumatologists interested in SpA whose work started in 2006.

Objective: To describe the demographic and clinical characteristics of patients with AS collected by 85 rheumatologists across Argentina, Brazil, Chile, Costa Rica, Mexico, Peru, Portugal, Uruguay, and Venezuela.

Patients and Methods: This is a cross sectional study including 1099 consecutive AS patients collected between Jan 2006 and Dec 2007. Assessments included demographic and clinical features. Data was stored in the Spanish SpA Registry website.

Results: 75% were males; mean (SD) age at onset was 31 (14) years; 72% had HLA-B27 and 18% family history of SpA. Symptoms at onset: inflammatory back pain (IBP) 840 (76%), peripheral arthritis 483 (44%), neck pain 438 (40%), enthesitis 319 (29%), coxitis 293 (27%), tarsoitis 55 (14%) and dactylitis 80 (7%). Mean (SD) time to diagnosis was 8.8 (8.3) years. Baseline data are shown in the Table.

Conclusion: While IBP is the commonest manifestation around 50% of the patients present with or developed peripheral arthritis and/or enthesitis. BASRI score and metrology suggest AS has induced significant structural damage; BASDAI and lab tests indicate the disease is still active, but >10% receive TNF blockers. The role of educational level and diagnosis delay appear important.

Baseline data (n, % or mean SD)

IBP 1057 (96) NSAID daily 494 (46)
Peripheral arthritis 622 (57) NSAID on demand 408 (38)
Enthesitis 587 (54) Sulfasalazine 335 (31)
Buttok pain 614 (56) Methotrexate 332 (31)
BASDAI 4.5 (3.4) Glucocorticoids 200 (19)
BASFI 4.8 (2.9) Infliximab, n (%) 55 (5)
BASRI 8.4 (4.0) Etanercept 31 (3)
ESR, mm/h 24.7 (20.1) Adalimumab 8 (1)
CRP, mg/dL 10.2 (21.9) Married 191 (18)
Modified Schober, cm 2.7 (2.0) University degree 641 (59)
Chest expansion, cm 2.8 (1.6) Deficient house living, n (%) 57 (11)
Occiput-to-wall, mean (SD) cm 6.3 (7.7)

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AGREEMENT BETWEEN EVIDENCE AND BELGIAN RHEUMATOLOGISTS’ EXPERIENCE ON THE USE OF DMARDS IN ARTHRITIS AND/OR ENTHESITIS IN ANKYLOSING SPONDYLITIS

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Objective: To develop an evidence-based and experience-based recommendation to the question: “Is there a place for DMARDs in the treatment of AS patients with peripheral arthritis or enthesitis not responding to NSAIDS?”

Methods: A systematic literature search was conducted during August–October 2007. The following pharmaceuticals were selected for the analysis: sulfasalazine, methotrexate, leflunomide, thalidomide, azathioprine, chloroquine or antimarialarials, anakinra, pamidronate, and biphosphonates. Whenever possible, the effect size was calculated. The results of the search were presented to 59 Belgian rheumatologists, analyzed, and discussed. Based on the evidence in the literature, which was categorized according to the EULAR evidence hierarchy (1,2), these rheumatologists developed a recommendation. The strength of the recommendation (1, 2) was assessed by voting on level of agreement.

Results: Through a combination of MeSH terms and keywords, the total number of relevant articles found in PubMed was 360. Eight other articles were identified from reference lists. The search yielded a relatively small number of publications on RCT results (n=11) for the above pharmaceuticals in the treatment of AS. After presentation of the evidence and discussion, the Belgian rheumatologists made the following recommendation: “In case of AS with peripheral enthesitis/arthritis (except hip arthritis) refractory to NSAIDs, corticosteroid injections should first be tried. If they are ineffective, sulfasalazine should be considered for at least 3 months.” 73% of the attendees agreed with this recommendation. The category of evidence for advice on corticosteroid use was deemed “IV,” and the category for sulfasalazine was “II.” The strength of the recommendation was deemed “D.”

Conclusion: A recommendation on the use of DMARDs in the treatment of arthritis and enthesitis of AS not responsive to NSAIDs was developed using a combination of research-based evidence and expert consensus. There was only a limited amount of evidence available.

References:

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CLINICAL REMISSION IN PATIENTS WITH PSORIATIC ARTHRITIS (PsA) TREATED WITH ADALIMUMAB (HUMIRA®).

RESULTS OF THE STEREO TRIAL
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Objectives: To determine percentages of PaA patients who achieve absence of arthritis, psoriasis, or both during 12 weeks of adalimumab therapy.

Methods: In an open-label study (STEREO), patients with PaA (≥3 TJC, ≥3 SJC) despite ≥1 DMARDs received adalimumab 40 mg every other week for 12 weeks, and optionally for another 20 weeks. Evaluations at Weeks 2, 6, and 12 (optional at Week 20) included SJC76 and PGA of psoriasis. Only patients with both arthritis (SJC>0) and symptomatic psoriasis (PGA not “clear”) at baseline were included. Remission was both SJC=0 or PGA=“clear” together, or either. Remission of psoriatic nail disorder (NAPSI=0) was analyzed for patients who also exhibited nail disorder at baseline.

Results: Of 442 patients, 414 (94%) completed Week 12, and 161 (36%) completed Weeks 26–44. At Week 26, 58% had SJC=0 and PGA=“clear” at baseline; for the 366, baseline PGA was “almost clear” in 76 (21%); “mild” in 84 (23%); “mild to moderate” in 59 (16%); “moderate” in 82 (22%); “severe to moderate” in 46 (13%); and “severe” in 19 (5%). 64% (231/366) exhibited PA-related nail changes.

Remission during Adalimumab Therapy: Patients with active arthritis and active Ps

<table>
<thead>
<tr>
<th>Remission: arthritis</th>
<th>SJC=0, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Wk 2 Wk 6 Wk 12 Wk 20</td>
<td>N=366 N=360 N=355 N=341 N=134</td>
</tr>
<tr>
<td>0</td>
<td>43 (12)</td>
</tr>
</tbody>
</table>

Remission: Ps of the skin

<table>
<thead>
<tr>
<th>Remission: Ps of the skin</th>
<th>PGA=“clear”, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Wk 2 Wk 6 Wk 12 Wk 20</td>
<td>N=366 N=360 N=355 N=341 N=134</td>
</tr>
<tr>
<td>0</td>
<td>16 (4)</td>
</tr>
</tbody>
</table>

Remission: Arthritis + Ps of the skin

<table>
<thead>
<tr>
<th>Remission: Ps of the skin</th>
<th>SJC=0 and PGA=“clear”, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Wk 2 Wk 6 Wk 12 Wk 20</td>
<td>N=366 N=360 N=355 N=341 N=134</td>
</tr>
<tr>
<td>0</td>
<td>1 (0.3)</td>
</tr>
</tbody>
</table>

Remission: psoriatic nail disorder

<table>
<thead>
<tr>
<th>Remission: psoriatic nail disorder</th>
<th>NAPSI=0, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Wk 2 Wk 6 Wk 12 Wk 20</td>
<td>N=366 N=360 N=355 N=341 N=134</td>
</tr>
<tr>
<td>0</td>
<td>ND</td>
</tr>
</tbody>
</table>

Observed values. *only for patients with baseline NAPSI>0 (n=231); ND=not done.

Conclusions: Adalimumab provided clinical remission of arthritis, psoriasis, and psoriatic nail disorder in a clinically relevant percentage of PaA patients.

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ANTI-TUMOUR NECROSIS FACTOR INankylosing Spondyloarthropathies: TREATMENT LESS EFFECTIVE THAN IN PUBLISHED TRIALS

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University of Glasgow, Centre for Rheumatic Diseases, Glasgow, UK

Background: Inflimixim, etanercept and adalimumab have all been shown in randomised, controlled trials to be effective and safe in the treatment of AS. The prediction of likelihood of response to treatment is an area in which the evidence is weaker. There is clearly a need for further investigation here, along with clinical audit to evaluate efficacy of anti-TNF agents in a non-trial, patient population.

Methods: A retrospective audit was performed to evaluate the outcomes for all patients treated with Anti-TNFs at one specialist rheumatology centre in Scotland. Data was extrapolated from clinical notes in which outcome scores were routinely recorded at follow-up appointments. BASDAI improvement at 3 and 6 months was considered the primary outcome. BASFI, Pain Score, Patient Global Assessment, Physician Global Assessment, ESR and CRP and the proportion of subjects achieving ASAS 20, 40, 50 and 70 responses was also examined.

Results: Of 61 patients, 58 were included. There were 22 males and 10 females. The mean age of females was 47.3 years and the mean age of males was 45.0. The mean duration of disease was 17.4 years. The mean BASDAI change at 3 and 6 months were 2.21cm (32.8%) and 2.34cm (37.2%), respectively; and the proportion of subjects with a ≥20% reduction in BASDAI at baseline, was 50.4% at 3 months and 41.7% at 6 months. All outcomes indicated improvement over the first six months of treatment, in some cases by up to 50%, and 41.7% of treatments resulted in an ASAS 20 response. Scatter-graphs for each predictor versus outcome showed no obvious relationships and the 2-sample t-tests for difference in BASDAI change between CRP positive and CRP negative, and short disease duration and long disease duration were not significant.

Conclusions: The results of this audit show that anti-TNF therapies are moderately effective in a hospital outpatient setting. More than a third of patients responded well. However, compared with published trial results, the responses to anti-TNF therapy were less impressive.

No convincing evidence of a predictor-response relationship was found.

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EFFICACY OF ADALIMUMAB IN THE TREATMENT OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS (SpA) AND NO RADIOGRAPHIC SACROIILITIS: CONTINUOUS ADALIMUMAB (HUMIRA®) THERAPY IS NECESSARY TO PREVENT RELAPSES AFTER TREATMENT WITHDRAWAL

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Objectives: To assess duration of ASAS40 and ASAS partial remission in early axial SpA patients after therapy withdrawal at Week 52; to assess response rates of patients who were treated again with adalimumab after relapse.

Methods: Of 46 patients enrolled, 23 (52%) male; mean age, 32 years [range 24–45]; mean disease duration before treatment, 4 years [range 1–10]; 74% HLA-B27+ sustained a major response after 1 year of adalimumab 40-mg eow therapy (mean BASDAI, 1.2±0.9). Adalimumab was discontinued in these 23 patients and followed up for 1 year without adalimumab treatment. In case of flare (ie, no longer reaching an ASAS40), adalimumab 40-mg eow therapy was started again. 12-week results of this second treatment period for this group of good responders are reported here.

Results: Over the 1-year period without treatment, 19 of 23 (83%) of initial ASAS40 responders had a renewed increase in disease activity (BASDAI 4.8±1.8); 4 of 23 (17%) had maintained their responses. Mean duration of ASAS40 until flare was 14.8 weeks (range 3–27). Nine of the initial 46 (19.6%) reached ASAS partial remission after 52 weeks of adalimumab; 7 of these 9 patients (78%) relapsed during the 1-year observation period without treatment. After restart of adalimumab, 9 of 18 (50%) reached ASAS40 and 4 of 18 (22.2%) attained ASAS partial remission after 12 weeks. In one patient, adalimumab was not re-started because of planned pregnancy.

Conclusions: In 23 patients with early axial SpA who had achieved a good response after 52 weeks of adalimumab, the majority (83%) had a relapse when adalimumab was discontinued. 17% remained in a low state of disease activity over 1 year after withdrawal. When adalimumab was reinstalled, not all relapsed patients responded to re-treatment after 12 weeks. Continuous therapy with adalimumab appears to be necessary to prevent relapses.

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ADALIMUMAB (HUMIRA®) IS EFFECTIVE IN TREATING PATIENTS WITH ADVANCED STAGE OF ANKYLOSING SPONDYLYTIS (AS)

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1Charité Campus Benjamin Franklin, Berlin, Germany; 2Hospital Monte Naranco, Oviedo, Spain; 3Rheumatologische Schwerpunktklinik, Zvezb, Germany; 4Abbott Laboratoris, Parsippany, NJ, USA; 5Abbott GmbH & Co KG, Ludwigshafen, Germany

Objective: To evaluate the effectiveness of adalimumab in patients with advanced AS.

Methods: AS patients with BASDAI≥4 despite ≥1 NSAID received adalimumab 40 mg every other week plus standard antiinflammatory therapy in a 12-week, open-label study. Investigators documented baseline presence of advanced ankylosis, defined as at least Stage IV (>2 spinal segments>13 to 19 vertebral). For patients with advanced ankylosis, the investigator provided information about presence of syndesmophytes or fusion for each of 23 intervertebral units (C2-L5/S1). Only patients with radiographs available for all 3 spinal segments were included. Effective parameters were BASDAI50, BASFI, BASDAI, BASMI, duration of morning stiffness (BASDAI variable), PaGA of disease activity, and patient’s assessments of total back pain (BPI) and nocturnal pain (NociP).

Results: Of 1,250 patients, advanced AS was present in 330 (27%) and absent in 897. In 72 of 116 with information about all three spinal segments, advanced AS
was documented: Presence of syndesmophytes or fusion of 13–19 (Stage IV) and 20–23 vertebrae (Stage V) was reported for 31 and 41 patients. Median percentage of complete fusion across all 23 intervertebral units was 36% (Stage-IV patients) and 78% (Stage-V patients).

Adalimumab in Patients with/without Advanced Stage AS

<table>
<thead>
<tr>
<th>Predictors of Good Clinical Response (BASDAI 50 or ASAS Partial Remission) in 1,250 Patients Treated with Adalimumab (Humira®) for Active Ankylosing Spondylitis (AS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds Ratios (OR) for BASDAI 50 and Partial Remission (PR) and 1 additional predictor for each parameter (Table).</td>
</tr>
<tr>
<td>Predictors</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Age [decades]</td>
</tr>
<tr>
<td>HLA-B27*</td>
</tr>
<tr>
<td>CRP [mg/dl]</td>
</tr>
<tr>
<td>Prior anti-TNF therapy</td>
</tr>
<tr>
<td>BASFI</td>
</tr>
<tr>
<td>BASMI</td>
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</tbody>
</table>

**Conclusions:** RAPHOSDY identified several predictors of good clinical response in patients with active AS after 12 weeks of adalimumab therapy; younger age, greater CRP concentration, lower BASFI, HLA-B27+, and no history of anti-TNF therapy.

**P 75 EXERCISE IN ANKYLOSING SPONDYLITIS: DISCREPANCY BETWEEN RECOMMENDATIONS AND REALITY**

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**Introduction:** The AS/EULAR recommendations for management of ankylosing spondylitis (AS) identifies exercise as the cornerstone of comprehensive management of AS. The purpose of this study was to examine patients’ perceptions of exercise and to determine the type and extent of exercise/physical activity used by the AS population.

**Methods:** The Exercise Benefits and Barriers Scale (EBBS) and an exercise inventory questionnaire were administered to AS patients attending the spondylitis clinic of a large teaching hospital. Benefits and barriers subscales of the EBBS were analyzed to identify the degree of perceived benefits of, and barriers to, exercise. Higher benefits scores (range 29-116) indicate a more positive perception of exercise. Higher barriers scores (range 14-56) indicate a greater perception of barriers to exercise.

**Results:** Sixty-one patients (46 males) with AS completed the questionnaires. Mean age was 38.0 years, and mean disease duration was 14.7 years. The mean benefits EBBS score was 87.1±12.5. Most frequently reported benefits of exercise were “exercising increases my level of physical fitness” (96.4%) and “exercise improves functioning of my cardiovascular system” (96.4%). The mean barriers EBBS score was 29.2±5.3, and the most frequently reported barrier to exercise was “exercise tires me” (71.4%). Walking (twice/week or greater), and home stretching (twice/week or greater) were the most commonly reported types of exercise; however, these were reported in only 46.7% and 41.0% respectively. Overall, 14.8% of patients reported exercising once per month or less.

**Conclusions:** Scores on the EBBS benefits subscale revealed that patients perceive the benefits of exercise, with average EBBS benefits scores comparable to historical controls with OA and RA. Despite positive perceptions of the benefits of exercise, the majority of AS patients did not report participating in forms of exercise on a frequent basis. Strategies to improve adherence to recommendations for exercise in AS will have to address disincentives through comprehensive and sustainable education programs.

**P 76 NEUROLOGICAL ADVERSE EVENTS ON ANTI-TNF THERAPY**

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Toronto Western Hospital, Rheumatology, Toronto, ON, Canada

**Background:** We present a series of seven patients who developed neurological manifestations while on anti-TNF treatment.

**Methods:** All patients attended a rheumatology clinic in a teaching hospital, with 150 patients currently on anti-TNF therapy. In the past three years seven patients developed various neurological adverse effects. Data was collected by chart review.

**Results:** Five patients had AS while 2 had RA. The median (range) age was 49 (31-67) yrs. The median (range) disease duration was 14 (4-41) years. Two patients had family history of autoimmunity. Five patients were on infliximab (3-5 mg/Kg QSwk) and 1 each was on adalimumab (40 mg weekly) and etanercept (50 mg weekly). Three patients were on methotrexate + HCQ before the event. The median (range) duration of anti-TNF therapy at the time of onset of neurological events was 24 (4-60) months. All patients had good control of their rheumatic disease at the time of the neurological event. The adverse events were (i) peripheral numbness and paresthesias (3 patients) (ii) diplopia with trochlear nerve palsy (iii) memory loss (iv) intention tremor (v) recurrent falls (one patient each). NCV revealed axonal ulnar neuropathy in one patient and was normal in one patient. Brain MRI was performed in 3 patients and was normal in all. ANA developed in 3/5 AS patients and one RA patient. Anti-TNF was stopped in 6 patients and all patients recovered neurologically over a median (range) duration of 6 (4-8) months. The serial anti-antibody (ANA ± dsDNA) titre decreased after stopping anti-TNF medication in all patients. One patient was restarted on infliximab with resultant worsening of symptoms. The respective biological agent was changed to an alternative anti-TNF agent in 2 patients with no recurrence of the neurological symptoms.

**Conclusions:** Anti-TNF therapy can be associated with significant, but reversible neurological adverse events. In our experience a switch to an alternative anti-TNF agent was safe in such patients.
Infliximab is an effective therapy for very early inflammatory back pain, providing a rapid reduction in disease activity clinically and on MRI. This is the first therapy to show suppression of the inflammatory lesions on MRI in very early ankylosing spondylitis.

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**DRUG-FREE CLINICAL REMISSION AFTER INFlixIMAB THERAPY IN A PATIENT NEWLY DIAGNOSED WITH ANKYLOSING SPONDYLITIS**

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**Introduction:** Infliximab significantly improves clinical signs and symptoms of patients with active AS. Attempts to discontinue anti-TNF therapy for long time in AS have been mostly unsuccessful.

**Objective:** We present a case of a recently diagnosed AS patient who, after therapy with infliximab for 3 years, has remained in drug-free remission.

**Methods:** Clinical and imaging data were collected at the initiation of therapy (BL), thereafter continuously for 3 years (FU1), and then 4 years after discontinuation (FU2).

**Results:** This 30-year-old HLA-B27 positive patient started infliximab within one year after the onset of clinical symptoms and 5 months after the diagnosis made based on of the 1984 New York criteria. The CRP was 5.3 mg/l at BL and 1.4 mg/l and 1.2 mg/l at FU1 and FU2, respectively. The corresponding BASDAI values were 7.0, 0.2 and 0.4. Already during the 2nd week of the patient was a BASDAI 50% and an ASAS 5/6 responder, showing later persistent partial clinical remission. Antibodies to infliximab were not detected after treatment discontinuation. Conventional radiographs at BL showed only one syndesmophyte at the level of C2 and no change occurred after 7 years. MR images at FU2 showed minor inflammatory activity in 4 thoracic vertebral edges. No NSAIDs nor extra analgesic medication was required after infliximab discontinuation.

**Conclusions:** This is the first example of an AS patient in drug-free clinical remission after anti-TNF therapy with infliximab. Discontinuation of anti-therapy is currently the only way to identify such patients. Patients with early and strong clinical responses are likely to be the best candidates for such an intervention. It is unclear how long the anti-TNF therapy should have at least lasted before trying that. Although this seems to be an overall rare event this case may encourage rheumatologists to proceed accordingly. Further studies are needed to clarify whether patients with early disease and short disease duration are the best candidates for this attempt.

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**LONG TERM EFFICACY AND SAFETY OF PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH ETANERCEPT FOR 5 YEARS – ANALYSIS OF DIFFERENT TYPES OF RESPONSE**

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**Background:** Etanercept has shown significant clinical efficacy in patients with active AS with no concomitant treatment.

**Objectives:** To assess the long term clinical efficacy and differences to response to etanercept treatment in AS for 5 years.

**Methods:** After an initial treatment of 12 weeks and readministration following a short discontinuation, 26 patients started continuous open-label etanercept treatment (BL) up to 5 years until now. Primary clinical outcome was the proportion of patients in clinical remission according to the ASAS criteria after 5 years. Furthermore, possible differences in response to therapy over time were analyzed and reported.

**Results:** Of the 26 patients at BL, 18 (69%) completed week 260 of the study. In the complete analysis, 6/18 patients (33%) were in partial remission. A BASDAI 50% response was achieved by 58%, an ASAS 40% response by 62% and a ‘5-out-of-6’ response by 65% of the patients. All clinical parameters showed significant improvement over the entire study period. Detailed analysis confirmed differentiation to response type A (remission at most time points), response type B (state of disease activity (BASDAI<4) at most time points), and response type C (remainer), as recently proposed: 5% patients (83%) in clinical remission already at week 12 showed clinical remission in more than 90% of all visits. Similarly, 8/11 patients (72.7%) with a BASDAI3 showed this result also in more than 90% of all following visits. In comparison, in 4/18 patients (22%), did not reach ASAS 20%
response during the entire study period. There were no serious adverse events leading to treatment discontinuation.

**Conclusion:** The majority of AS patients remained on anti-TNF-α treatment with etanercept, being in a state of clinical remission or showing low levels of disease activity over time. The degree of response to anti-TNF therapy varied among patients, confirming the differentiation between different types of response to anti-TNF therapy, as recently proposed.

**Poster Presentations**

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**PERSISTENT CLINICAL EFFICACY AND SAFETY OF INFLIXIMAB IN PATIENTS WITH ANKYLOSING SPONDYLITIS OVER 7 YEARS – EVIDENCE FOR DIFFERENT RESPONSE TO ANTI-INFETA THERAPY**


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**Background:** There is limited knowledge on the long-term efficacy and safety of anti-TNFα treatment in AS.

**Objective:** To study the long-term clinical response and differentiative types of response to anti-TNF treatment in patients with AS after 7 years.

**Methods:** Sixty-nine patients with active AS at baseline (BL) were continuously treated with infliximab (5mg/kg i.v./6w) with the exception of a short discontinuation period after 3 years (FU1). Primary outcome of this extension was remission according to the ASAS criteria after 7 years (FU2). Secondary outcome was the identification of differences in the response to therapy.

**Results:** Of the 42 patients who continued after discontinuation, 77% (88%) finished year 7. Partial remission was achieved in 12/37 patients (32.4%) at FU1 and FU2, showing no signs of loss of response. All other parameters (BASDAI, BASFI, BASMI) similarly showed persistence of efficacy of infliximab over 7 years. BASDAI values <4 were seen in 78% of patients at FU1 and FU2. ASAS 20% and 40% responses were seen in 31 (82%) and 23 (62%) patients at FU2, respectively. Three groups of patients were identified according to the level and degree of response: A) patients who were in remission at most time points, B) patients in a state of low disease activity (BASDAI <3) at most time points, and C) the remainder. Some differences between these groups in age, disease duration and function at baseline could be identified. No major side effects occurred during years 4 to 7 of infliximab therapy.

**Conclusions:** The majority of the patients with AS remained on infliximab therapy which proved to be safe and efficacious over 7 years. Most patients remained in remission or had low levels of disease activity over time. Continuous therapy is necessary to achieve a lasting effect in almost all patients. Different types of response to anti-TNF treatment could be confirmed.

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**DISEASE ACTIVITY AND QUALITY OF LIFE IN CROHN’S-ASSOCIATED SPONDYLOARTHROPATHY AFTER SWITCHING FROM INFIXIMAB TO ADAFILUMAB**

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**Introduction:** No published studies have addressed the effect of switch from infliximab to adalimumab in patients with Crohn’s-associated spondyloarthropathies. Purpose of the present study was to evaluate the clinical response to adalimumab in patients with Crohn’s-associated spondyloarthritides discontinued from infliximab treatment due to intolerance or loss of efficacy.

**Materials and Methods:** 17 patients were studied (9 Males and 10 Females, mean age 47.0±12.5 years). All patients had been discontinued from infliximab due to side effects (n=6) or articular recrudescence (n=11), and started on adalimumab 40 mg i.v. after 6 to 8 weeks. Follow-up visits were performed at 1, 3, 6, 9, and 12 months of treatment. Articular disease was assessed by the BASFI and the BASDAI scores, Crohn’s activity by the CDAI score, and quality of life by the SF-36 questionnaire. Mean differences were evaluated by Wilcoxon test.

**Results:** In two patients adalimumab was discontinued due to Crohn’s or articular flare-ups. The table shows the changes in disease scores during adalimumab treatment. At no time point differences vs. basal values were significant (p>0.05).

**Table:** Disease Scores during treatment with Adalimumab

<table>
<thead>
<tr>
<th>Disease Score</th>
<th>5</th>
<th>4</th>
<th>24</th>
<th>36</th>
<th>52</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI</td>
<td>4.7±2.5</td>
<td>3.3±1.9</td>
<td>3.3±1.6</td>
<td>4.2±1.8</td>
<td>4.1±1.6</td>
</tr>
<tr>
<td>BASFI</td>
<td>3.2±2.3</td>
<td>2.3±2.2</td>
<td>2.3±1.9</td>
<td>3.0±1.7</td>
<td>2.7±1.6</td>
</tr>
<tr>
<td>CDI</td>
<td>76.8±35.2</td>
<td>72.6±27.7</td>
<td>58.8±15.3</td>
<td>46.0±28.4</td>
<td>54.2±27.5</td>
</tr>
<tr>
<td>SF-36 Physical</td>
<td>34.3±10.2</td>
<td>36.8±9.2</td>
<td>37.5±7.9</td>
<td>39.5±8.0</td>
<td>34.8±9.4</td>
</tr>
<tr>
<td>SF-36 Mental</td>
<td>46.1±12.7</td>
<td>46.6±13.4</td>
<td>45.0±11.9</td>
<td>47.0±10.7</td>
<td>42.0±11.6</td>
</tr>
</tbody>
</table>

**Conclusions:** The results of our study suggest that switching to adalimumab in patients with intolerance or poor response to infliximab may successfully control both articular and intestinal disease activity in patients with Crohn’s-associated spondyloarthropathy.

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**DECREASED CLINICAL RESPONSE TO ADAFILUMAB IN ANKYLOSING SPONDYLITIS IS ASSOCIATED WITH ANTIBODY FORMATION**


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**Introduction:** Despite the good response to adalimumab in the majority of the Ankylosing Spondylitis (AS) patients this treatment does not seem to be effective in approximately 40% of the cases. An explanation could be that disease activity in these patients is caused by a different mechanism than TNF-alpha or because of insufficiently high adalimumab levels. The latter might be caused by antibody formation against adalimumab (anti-adalimumab). Previously we found that formation of anti-infliximab was associated with a poor response to infliximab. In AS patients treated with etanercept however, antibodies against etanercept could not be detected within 6 months of therapy.

**Objective:** To examine whether the production of anti-adalimumab is associated with a poor response of AS to treatment with adalimumab.

**Methods:** Consecutive AS patients treated with 40 mg of adalimumab every other week according to the international ASAS consensus statement were enrolled. Sera were collected at baseline, after 3 and 6 months of treatment. Clinical response was defined as an improvement of 50% or an absolute improvement of 2 points of the BASDAI (0–10). As previously described, anti-adalimumab was measured at Sanquin, the Netherlands, with an antigen binding test, with a cut-off value for positive of 12 AE / ml.

**Results:** A total of 42 patients was enrolled. After three months of treatment 21 patients (50%) were ASAS responders. Within 6 months 11 patients (26%) showed positive of 12 AE / ml. Ankylosing Spondylitis (AS) patients this treatment does not seem to be effective in approximately 40% of the cases. An explanation could be that disease activity in these patients is caused by a different mechanism than TNF-alpha or because of insufficiently high adalimumab levels. The latter might be caused by antibody formation against adalimumab (anti-adalimumab). Previously we found that formation of anti-infliximab was associated with a poor response to infliximab. In AS patients treated with etanercept however, antibodies against etanercept could not be detected within 6 months of therapy.

**Conclusions:** The results of our study suggest that switching to adalimumab in patients with intolerance or poor response to infliximab may successfully control both articular and intestinal disease activity in patients with Crohn’s-associated spondyloarthropathy.

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**IMPROVING FUNCTIONALITY IMPROVES SLEEP IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM THE GO-RAISE STUDY**

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**Introduction:** Patients with ankylosing spondylitis (AS) report significant functional impairment, which could affect their sleep. We wanted to establish the relationship between functionality and sleep in patients with active AS.

**Objectives:** To determine the relationship between functionality and sleep in patients with active AS.

**Methods:** Data from a multicenter, randomized, placebo (PBO)-controlled study (GO-RAISE) were used to establish the relationship between functionality and sleep as measured by the Bath Ankylosing Spondylitis Functional Index (BASFI)
GOLIMUMAB, A NEW, HUMAN, TNF-ALPHA ANTIBODY ADMINISTERED SUBCUTANEOUSILY EVERY 4 WEEKS, IN ANKYLosing Spondylitis: 24-Week Efficacy and Safety Results of the Randomized, Placebo-Controlled GO-RAISE Study

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Introduction: This multicenter, randomized, placebo (PBO)-controlled study was conducted to evaluate the efficacy of golimumab (GLM) on signs and symptoms of active ankylosing spondylitis (AS).

Patients: (n = 356) were randomized to subcutaneous GLM 50 mg or 100 mg or PBO q4wks. Patients with AS according to the modified New York criteria (Bath AS Disease Activity Index score of ≥4 and a back pain score of ≥4) were eligible. The primary efficacy endpoint was the proportion of patients with an ASAS20 response at wk 14. At wk 16, patients in PBO or 50 mg group who had <20% improvement from baseline in total back pain and morning stiffness measures entered early escape in a double-blind fashion. All other patients remained on their previous medication until wk 24.

Results: The primary endpoint at wk 14 was met. ASAS 20 responses for both GLM groups were significantly higher than that for PBO (GLM 50 mg, 59% and GLM 100 mg, 60% vs. PBO, 22%; p<0.001 for each comparison). Clinical benefit was maintained through wk 24, with ASAS 20 responses for both GLM groups significantly higher vs. PBO (56% and 66%, respectively, vs. 23% for PBO; p<0.001 for each comparison). All secondary endpoints were achieved except for the change from baseline in BASMI score at wk 14. Antibodies to GLM were detected in 11 patients (4.1%) through wk 24. Adverse events through 24 wks were reported in 79.9% of GLM-treated patients and 76.6% of PBO-treated patients, with an increased incidence of infections, primarily upper respiratory, in GLM-treated patients. Through wk 24, 5 patients (6.5%) receiving PBO, 5 patients (3.6%) receiving 50 mg GLM, and 9 patients (6.4%) receiving 100 mg GLM reported a serious adverse event.

Conclusions: GLM improved signs and symptoms and physical function in AS patients through 24 wks. GLM was generally well-tolerated.

GOLIMUMAB, A NEW, HUMAN, TNF-ALPHA ANTIBODY ADMINISTERED SUBCUTANEOUSILY EVERY 4 WEEKS, IN PSORIATIC ARTHRITIS: 24-Week Results of the Randomized, Placebo-Controlled GO-REVEAL Study

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Introduction: We assessed the efficacy and safety of golimumab (GLM) for treatment of active psoriatic arthritis (PsA).

Patients: Adult PsA patients with ≥3 swollen/tender joints were randomized to SC placebo (PBO) or GLM (50mg or 100mg) at wks 0,4,8,12,16, and 20. Patients with inadequate arthritis response after receiving PBO or GLM 50mg at wk 16 were switched in a blinded manner to GLM 50mg (PBO group) or GLM 100mg (GLM 50mg). PBO and GLM 50mg patients had their last observation prior to change in treatment carried forward for the wk 24 efficacy analyses. Observed values at wk 24 were used for GLM 100mg patients. Concomitant methotrexate (MTX) was allowed but not required. The primary endpoint (ACR20 at wk 14) was analyzed by the Cochran-Mantel-Haenszel test with stratification by MTX use.

Results: 405 PsA patients were randomized (median age: 47.0 years). Baseline characteristics (range) were: mean swollen/tender joint counts (12-14/22-24), mean PsA disease activity score (PASI) 10.3±4.4, 11.1±4.8 and 9.9 ±4.7, respectively, indicating similar levels of disturbed sleep.

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GOLIMUMAB SIGNIFICANTLY IMPROVES SLEEP IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM THE PHASE 3 GO-RAISE STUDY

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Introduction: We evaluated the impact of golimumab (GLM) on reducing sleep disturbance in patients with ankylosing spondylitis (AS).

Methods: GLM was studied in a multi-center, randomized, placebo (PBO)-controlled study (GO-RAISE). 356 patients were randomized (1:8:1.8:1 ratio) to SC GLM 50mg or 100mg or PBO q4wks.

Results: The GLM 50mg, 100mg, and PBO groups had mean ± SD JSEQ baseline scores of 10.3±4.4, 11.1±4.8 and 9.9 ±4.7, respectively, indicating similar levels of disturbed sleep. GLM 50mg and 100mg patients showed significantly greater improvement (decline of disturbed sleep).

Conclusions: GLM improves sleep in patients with active AS. GLM 50 mg and 100 mg treatment significantly improved functionality leading to improved sleep in AS patients.
identified from reference lists in those publications. Overall, the search yielded a relatively small number of useful studies for analysis of the role of CRP in outcome of disease. No studies were found on long-term outcome parameters, and none of 15 key, selected, PROPS contained data on persistent CRP elevation. The Belgian rheumatologists made the following recommendation: “CRP must be evaluated in all AS patients, including those with stable clinical status or those without overt articular disease activity (persistent increased CRP must be further investigated).” 88% of the attendees agreed with this recommendation. The category of evidence was deemed "IV," and the strength of the recommendation was deemed "D."

**Conclusion:** A recommendation on the role of CRP in relationship to outcome of AS was developed using a combination of research-based evidence and expert consensus. Because of lack of evidence concerning the topic, the recommendation was based on expert opinion (Level IV).

**References:**
state (PASS), and considerable improvement in health by the patient. Sensitivity to change (SRM) and discrimination between groups of different status and/or change scores were analysed.

Results: 650 treatment starts at baseline were available; Between 90 and 450 patients for 3 and 6 month scores depending on the anchor variable. Correlations between the ASDAS scores and physician global assessment of disease activity were moderate and with patient global assessment of disease activity good. The SMD in patients judging themselves being in PASS vs not being in PASS and the discrimination between high and low disease activity according to the physician was high for all ASDAS scores. Also presence or absence of considerable improvement by the patient showed good discrimination; SRMs were good for all ASDAS scores. Discrimination between response to TNF-blockers versus DMARDs was good. In all comparisons the ASDAS scores performed very similar and at least as good as the BASDAI. This was confirmed for patients with normal and elevated CRP.

Conclusion: The performance of 4 ASDAS scores with respect to truth and discrimination was similar and at least as good as the BASDAI. The ASDAS is the first index in AS that correlates well with both patient and physician global assessment of disease activity and promises to be a highly discriminatory tool in clinical trials.

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AN EVALUATION OF THE GLASGOW ENTHESIS INDEX (GEI) IN ANKYLOYSING SPONDYLITIS (AS) AND A COMPARISON WITH THE MODIFIED MASES INDEX (MMI)
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Background: Enthesitis is a common feature of the Seronegative Spondarthritides but is difficult to evaluate clinically. We have previously published a Musculo-skeletal ultrasound (MSUS) assessment of the lower limb component of the GEI and shown a good correlation between clinical and MSUS findings although the MSUS proved to be more sensitive. There are a number of enthesis indices and in this study we have validated the GEI and compared it with the MMI.

Methods: 21 unselected patients with AS (modified New York criteria) were assessed by 2 independent observers and the GEI and MMI were recorded. Standard indices of disease activity such as BASDAI, ESR and CRP were measured and the time taken to perform the GEI and MMI on each patient was noted. Inter-observer variation between the observers for the GEI was recorded and the intra-class correlation calculated. Non-parametric statistics were used to calculate correlation of continuous variables.

Results: 21 AS patients were examined by 2 observers for the GEI and 15 were assessed by one observer for the time taken to measure the GEI and MMI. A good level of agreement for the GEI was achieved by the 2 observers (intra-class correlation 0.85, 95% CI. 0.68-0.94). There was no correlation between AS disease activity measures and the GEI. The mean time to undertake the GEI was 2.4 mins (SD 0.83) and for the MMI was 2.5 mins. (SD 0.92). The Pearson correlation between the GEI and MMI scores was 0.840 indicating an acceptable level of agreement.

Conclusions: The GEI is a quick and easy clinical measure of enthesitis with a good inter-observer agreement. It compares well with the MMI but does assess slightly different sites of enthesal insertion. Longitudinal studies to compare several Enthesitis indices are required to determine the best method of measuring this clinical feature and to quantify the influence of Enthesis on functional outcome in AS.

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THE DEVELOPMENT OF A SIMPLE ACCUMULATION INDEX AND ITS USE IN Spondyloarthritides
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Acculturation is the process by which members of one culture acquire the norms and values of another culture.

Methods: An acculturation index developed based on perceived ethnicity, country of birth, ancestry origin, and language spoken in household. Grade 0 represents not needing acculturation, while grade 3t o those not acculturated. Grades 1 suggests fully acculturated foreign inhabitants who can be considered close to no need accluation and grade 2 suggests partly acculturated foreign inhabitants by birth but speaking both native language and the host country’s language. SpA clinical, epidemiological, social and dietary data were analyzed with regards to acculturation.

Results: Acculturation index was produced from 363 patients. The total BASDAI and BASFI scores of the group (mean + SD) were 6.1 + 2.0 and 5.1 + 2.7 respectively

The wellbeing (past week) was 5.8 + 2.7, well-being (past 6 mo) was 6.3 + 2.4. No statistical significance difference between the acculturation index groups and BAS- DAI, BASFI [Pearson’s (0.033, p=0.5, and -0.090, p=0.098 respectively), while significance found with smoking (0.427**, p=0.000); alcohol (0.551**, p=0.000), disease duration -0.150**, p=0.008); BASDAI (0.125; p=0.021); BASDAI (-0.018; p=0.029); BASFIH (-0.112*, p=0.03); steroid use (-0.116** p=0.04); being partly vegetarian (0.220** p=0.000), fish intake (-0.198** p=0.001), egg intake (-0.262**, p=0.000) fish oil intake (-0.143**, 0.009) and reason of unemployment (-0.163*, p=0.010). Acculturation and clinicians opinion, showed negative association with the Undifferentiated cohort (-0.183*, p=0.012); positive association with symmetrical disease (0.405**, p=0.000); asymmetrical disease (0.300**, p=0.004) symmetrical hand disease (0.295**, p=0.004); wrists disease (right 0.412**, p=0.000; left 0.397**, p=0.006); symmetrical feet disease (0.437** p= 0.000); ankle disease (p=0.000), shoulders disease (p=0.002); knees (p=0.000) and right but not left hip (0.337**, p = 0.003).

Conclusions: Disease differences between ethnic groups can be studied through separation of the groups into acculturation categories.

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DEVELOPMENT AND TESTING OF A OMERACT PSORIATIC ARTHRITIS MRI SCORING SYSTEM (PSAMRIS)
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Background: The MRI features of peripheral joint pathology in psoriatic arthritis (PsA) have been described, but no well-accepted semi-quantitative scoring system for outcome assessment exists. The aim of this study was, within the OMERACT MRI in Inflammatory Arthritis Special Interest Group, to develop a consensus-based semi-quantitative tool for MRI-scoring of peripheral PsA.

Methods: At a 2-day consensus meeting in Spain in June 2007, MRI definitions of key PsA pathologies were developed, and decisions were made concerning features to include in the score sheet, based on data from a previous preliminary exercise. All features were scored separately at each of MCP 2-5, PIP 2-5, DIP 2-5 (range of possible scores in parentheses): Synovitis (0-3), flexor tenosynovitis (0-3), periarticular inflammation (0-1, volar and dorsal aspects separately), bone oedema (0-3, proximal and distal bone separately), bone erosion (0-10, proximal and distal bone separately); bone proliferation (0-1). Subsequently, MRI sets of 2nd-5th fingers of 10 PsA patients (3D T1-weighted gradient-echo (voxel size 0.5x0.5x1.0 mm) before and after i.v. contrast, with subsequent axial, coronal and sagittal reconstructions, and sagittal and axial STIR sequences) were read blindly by 8 readers, without formal prior reader calibration.

Results: The intraclass correlation coefficients (ICCs, average measure) of sun scores were: Synovitis: 0.88, periarticular inflammation 0.25, bone oedema 0.86, bone erosion 0.91 and bone proliferation 0.91. The MRI definitions and the score sheet will be presented at the conference.

Conclusions: MRI definitions of relevant PsA pathologies and a preliminary score sheet were developed by consensus. Without prior reader calibration, the inter-reader reliability was good to very good for synovitis, tenosynovitis, bone oedema, bone erosions, and bone proliferation, but poor for periarticular inflammation. Further development, testing and reader calibration is needed before the OMERACT PsAMRIS can be recommended for use in clinical trials.

P 95
EARLY AND SIGNIFICANT INCREASES IN HEALTH RELATED QUALITY OF LIFE IN SPONDYLOARTHRITIS PATIENTS TREATED WITH TNF-α INHIBITORS
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Introduction: Health-related quality of life (HRQoL) is an important outcome in clinical trials. We evaluated changes in the generic quality of life questionnaire Short-Form Health Survey (SF-36) in SpA patients during anti-TNF-α treatment.

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Materials and Methods: 54 patients fulfilling the ESSG criteria for SpA, with sacroiliitis on MRI or x-rays, and BASDAI >50 mm despite NSAIDs were included. At week 22 treatment response/non-response was evaluated according to the BAS-DAI50%-criteria. Results: 37 patients were responders. At baseline, responders scored lower in social functioning (p=0.03). All 10 SF-36 scores rapidly (at week 2) and markedly improved (p<0.001) in responders and stayed increased at week 22 (p<0.001). In non-responders, bodily pain, vitality and mental health (p=0.01–p=0.03) improved at week 2, but at week 22 all scores were unchanged. Conclusion: In SpA patients receiving anti-TNF-α therapy, HRQoL rapidly and markedly improved in clinical responders but not in clinical non-responders. (Me-}
DISEASE SEVERITY IN ANKYLosing SYPHLOITIS: THE INFLUENCE OF ASSOCIATED INFLAMMATORY BOWEL DISEASE AND PSORIASIS

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Introduction: Ankylosing Spondylitis (AS) is a common form of inflammatory arthritis, affecting ~5-10000000. Although predominantly affecting the axial skeleton, the clinical link between AS, psoriasis (Ps) and inflammatory bowel disease (IBD) is well known. The aim of this study was to determine whether these patients have similar disease activity and severity.

Methods: 40 pre-TNF patients were identified from the AS Specialist Clinic, Brisbane. Disease severity was assessed by questionnaire (BASDAI, BASFI), metrol-

Disease duration of 6.2 vs. 5.7 than those without IBD but similar ESR (44 vs.39), CRP (57 vs. 53), BASDAI (6.6 vs. 6.0) and BASMI (6.2 vs. 5.7) than those without IBD but similar ESR (40 vs 20) and BASMI (6.5 vs. 20) groups. In the Oxford cohort, BASDAI and BASMI were also increased in both Ps (BASDAI 4.5 vs. 4.2, Ps=0.01; BASFI 4.5 vs. 4.0, Ps=0.002) and BASMI (BASDAI vs. 4.1, Ps=0.015; BASFI vs. 4.0, Ps=0.017) and confirming the Birmingham findings. Patients with both Ps and IBD had even higher BASDAI and BASMI than those with either Ps or IBD alone (mean BASDAI 5.0, BASFI 5.3).

Conclusion: These findings suggest that AS patients with coexistent Ps, and poten-
tially IBD, are a worse prognostic group than those with primary AS.

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REPRODUCIBILITY OF MEASUREMENTS OF PHYSICAL FUNCTION IN ANKYLosing SYPHLOITIS

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Poster Presentations

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DOES INITIAL JOINT INVOLVEMENT PATTERN INFLUENCE RADIOGRAPHIC DAMAGE IN PATIENTS WITH USPA/AS?

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Introduction: Axial manifestations of spondyloarthritides (SpA) can be minimal or are evident at disease onset. We investigated whether there are differ-

ences in clinical and radiographic features among undifferentiated SpA or ankylos-
ing spondylitis (AS) patients in terms of initial joint involvement pattern.

Methods: We studied the consecutive 102 patients with undifferentiated SpA (USpA) or AS who visited the Rheumatology clinic from Jan 2008 to March 2008.

Results: Joint involvement patterns at disease onset were axial (51%), peripheral (19%), enthesopathic (5%) or mixed (26%). Men were predominant, especially in patients with axial disease (65%). Mid-finger and wrist joints were more frequent in Ps cases (49%). Radiographic changes were more frequent in Ps patients (65%) than in AS patients (53%). Baseline disease activity at the time of diagnosis was similar between the two groups (BASDAI 4.5 vs. 4.0, Ps=0.01).

Conclusion: These findings suggest that AS patients with Ps have similar disease activity and severity.

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RELATIONSHIPS BETWEEN THE BASFI QUESTIONNAIRE AND PERFORMANCE MEASURES IN PATIENTS WITH ANKYLosing SYPHLOITIS

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cal Centre, Rehabilitation Medicine and EMGO Institute, Amsterdam, The Netherlands

Introduction: The objective of this study was to assess the relationships between the BASFI questionnaire and eight performance measures of daily activities extracted from the BASFI in patients with AS.

Materials and Methods: Data were obtained from 75 patients with AS. They all completed a BASFI questionnaire and eight performance measures within a one-

month period. Eight performance measures reflecting daily physical function were extracted from the BASFI. (1. Putting on socks. 2. Bending forward. 3. Reaching up. 4. Reclining and declining from a chair. 5. Getting up from the. 6. Climbing stairs. 7. Looking over the shoulder. 8. Doing physically demanding activities). For tests 1-6 and 8 the time to actually perform the test was measured. For test 7 the ability to look over one shoulder was measured by the compound movement of the rotation of the neck and the field of vision. Relationships between the BASFI items and cor-

responding performance tests were established by calculating Spearman Correlation

Coefficients.

Results: Correlations between tests 1-6 and the corresponding BASFI items ranged from 0.36 to 0.49 (P<0.01). Test 7 showed a significant correlation of 0.55 (P<0.01). For test 8 no significant correlation was found with the corresponding BASFI item.

Conclusions: The BASFI seems to poorly reflect actual physical performance. This could indicate that performance tests provide unique information on physical function, in addition to the BASFI questionnaire. Further validation of the perform-

ance measurements has to be done in future.

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CORRELATIONS BETWEEN METROLOGY AND RADIOGRAPHIC SCORES IN AS

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Introduction: Patients with AS are routinely assessed in the clinical setting using the BASMI. The mSASSS is widely used to quantify radiographic change. The aim of this study was to determine the correlation between the two known methods of assessment whilst considering the extra components of radiographic cervical facet joint and hip disease.

Methods: 100 patients were randomly identified from the AS Specialist Clinic, Brisbane, all of whom met the modified New York diagnostic criteria. Each patient’s mSASSS, and scores assessing the extent of cervical facet joint and hip damage, were determined by 2 scorers. BASMI measurements were performed by trained metrologists.

Results: The mSASSS and BASMI were closely correlated with each other ($R=0.827$). Both mSASSS and BASMI were correlated with disease duration ($R=0.488$, mSASSS; $R=0.383$, BASMI). The relationship of both scores with disease duration was linear, and there was no tendency for either score to plateau over time. By 18 years disease duration all patients had spinal radiographic change, suggesting that this outcome is inevitable in AS. mSASSS does not assess hip disease; removing the intermalleolar distance from the BASMI score did not improve the correlation of BASMI and mSASSS ($R=0.816$). The cervical component of the mSASSS was more closely correlated to cervical rotation than the tragus to wall measurement ($R=0.811$ vs. $R=0.726$). The cervical facet score was less strongly correlated with either cervical rotation or tragus to wall measurement ($R=0.787$ and 0.639 respectively) than cervical mSASSS. Cervical spine disease was more severe than lumbar spine disease in this cohort (mean cervical mSASSS 12.8, LS 6.2; $p<10^{-4}$). Intermalleolar distance correlated with radiographic hip disease and disease duration. No patient with an intermalleolar distance of $>116$cm had radiographic hip disease.

Conclusion: Both mSASSS and BASMI document accurately the relentless progressive spinal fusion associated with AS. Metrology closely reflects radiographic change.
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Manuscripts must be typed double-spaced with wide margins (at least 2 cm on all sides). Single-spaced material is not acceptable. Begin each of the following sections on a separate page: title page; abstract and key words; text; acknowledgements; references; individual tables; and legends. Number the pages consecutively, beginning with the title page.

The title page should include: a) a concise but informative title (do not use acronyms); b) the first name, middle initial and last name of each author, with their highest academic degree(s) and institutional affiliation; c) the name of the department(s) and institution(s) to which the work should be attributed; d) the name, address, telephone and fax numbers, and E-mail address of the author responsible for correspondence; e) the name and address of the author to whom reprint requests should be addressed, or the statement that reprints will not be available from the author; and f) a short running title (45 characters or less).

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