This clinical form of OA may be associated with a so called "erosive" radiographic aspect marked by subchondral erosions of the finger joints and ankylosis. Many mediators of inflammation have been involved in the pathogenesis of osteoarthritis such as prostaglandin E2, free radicals and main cytokines (IL1B, IL6, and TNFa). Using Doppler power ultrasonography and magnetic resonance imaging, it has been shown that synovitis is frequently associated with HOA and correlates with pain and with disease progression.

Taking all those considerations together, it appears logical to target synovitis in HOA, especially with an erosive form.

Because erosive hand OA is a polyarticular disease, the treatment is more systemic than local.

Local or oral NSAIDs are out of scope because this presentation focuses on patients with HOA non responders to analgesics and NSAIDs. So far, none of the disease modifying drugs such as methotrexate has proved its efficacy.

Regarding biologics, several strategies have been approached. The first biotherapy used in HOA was IL2 receptor plus hydroxychloroquine in a very limited number of patients. Then and more recently, anti-TNFa strategy has been tested in well done RCT, in painful hand OA: one with adalimumab over a year, one with adalimumab 40 mg with 2 sub-cutaneous injections, one using Etanercept (50 mg/week 24 weeks and then 25 mg/week the next 24 weeks). None of those anti-TNFa blockers demonstrated a structural or an analgesic effect. However in the long term trial published by Verbruggen G, the incidence of new erosive lesions was decreased in Adalimumab group compared to placebo, only in a subgroup of patient with clinically inflamed IP joints.

Using anti-IL1B strategy, a decrease in pain has been observed in 3 patients using daily subcutaneous injection of Anakinra (100mg) over 3 months ().

In this Eular meeting a double inhibition of IL-1 Beta and IL-1 Alpha (using a monoclonal antibody directed against both cytokine) failed to demonstrate any benefit compared to placebo injection over 26 weeks.

Finally anti-IL6 strategy has been presented in this 2017 Eular meeting in a limited number of patients (n=18) with erosive HOA. Using monthly IV perfusion, the authors showed an improvement in pain level and functional status.

Conclusion: though anti-inflammatory strategy in painful HOA is logical, no treatment so far has been able to demonstrate a beneficial effect. Further studies should contemplate either new targets, or new modalities of repeated injections and should be adapted according to the phenotype of pain.

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SATURDAY, 17 JUNE 2017

Why we do develop autoimmunity

SP0181 FAILURE OF NATURAL REGULATORY AUTOANTIBODY NETWORK AS CAUSE OF AUTOIMMUNITY

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The role of autoantibodies in normal physiology is under debate. In investigating autoantibody (aab) concentrations against G protein-coupled receptors (GPCR) in different autoimmune diseases, we found both increased and decreased aab concentrations, which suggests physiological anti-GPCR aab levels may be dysregulated in autoimmune diseases. During our analysis of healthy donor antibodies to 16 GPCR and 15 growth factors and related signaling molecules, we discovered several clusters of correlations in these antibody concentrations. Possible functional interactions of these 31 autoantibody target molecules were studied by STRING, DAVID, and enriched Gene Ontology analyses. Through these analyses, a network of GPCR, growth factors, and signaling molecules with endothelin receptor type A (ETAR) in the center was revealed. Migration and locomotion were suggested to be the most significant functions regulated by the antibody network. Accordingly, IgG from healthy donors induced both IL-8 expression by peripheral blood mononuclear cells (PBMCs) as well as migration of neutrophils and tumor cells, which was specifically diminished by the ETAR inhibition. These data supports a change of paradigm from the notion that autoantibodies are an exclusive autoimmune phenomenon to the concept that they are part of the normal human physiology, which become dysregulated under the influence of different factors and subsequently cause autoimmune diseases.

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SP0182 ALTERATIONS IN THE ANTIBODY REPERTOIRE AND SUGAR MODULATION AS CAUSE FOR AUTOIMMUNITY

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Many auto-immune diseases are hallmarked by the presence of auto-reactive B cells that can develop into autoantibody-secreting plasma cells. In most cases, the secreted autoantibodies have extensively been studied in their role as disease-associated biomarkers, and for some, specific pathogenic effector functions have been demonstrated supporting the use of interventions that target the plasma cell compartment. In other cases such as rheumatoid arthritis (RA), however, the

pathogenicity of specific autoantibodies is less clear, and the therapeutic efficacy of B cell depleting therapy that spares the plasma cell compartment indicates that auto-reactive B cells themselves can have pathogenic effector functions that contribute to disease. In this context, it is of great interest to understand the mechanisms that allow auto-reactive B cells to emerge from the naïve repertoire, a process that marks the onset of systemic autoimmunity and frequently precedes the clinical onset of disease.

RA is characterized by a remarkable appearance of autoantibodies that target post-translational modifications of proteins, of which anti-citrullinated protein antibodies (ACPA) display the highest specificity for disease. In addition, ACPA associate with active destructive RA and pose individuals with arthralgia at-risk for progression towards arthritis. We recently found that ACPA display significant alterations with regard to the glycosylation of both the Fc-tail as well as the F(ab)-domain. While the ACPA-IgG Fc-tail loses galactose and sialic acid residues prior to the onset of arthritis, a process associated with enhanced inflammatory antibody activity that occurs potentially under the influence of IL-17 producing T cells, ACPA also carry abundant glycans in the antigen-binding region of the F(ab) domain. These latter glycans are reminiscent of F(ab)-glycans found in follicular lymphoma B cells, and were here identified as N-linked, biantennary glycans composed of a remarkably high frequency of sialic acid residues. Notably, N-glycosylation requires the presence of glycosylation consensus sequences in the protein. As such sequences are normally scarce in the germline encoded variable regions of B cell receptors (BCR), the acquisition of F(ab)-glycans requires mutations of the amino-acid sequence to generate N-glycosylation sites. This process is mediated by somatic hypermutation, which is mainly induced by T cells that provide help to B cells. As >90% of all ACPA-IgG molecules carry such F(ab)-linked N-glycans, and as protective antibodies in the same individuals and many autoantibodies in other diseases do not show this feature, it is conceivable that the acquisition of F(ab)-glycans by ACPA-IgG is a T cell-mediated process that provides a selective advantage to ACPA-expressing B cells. This notion is supported by the observation that additional F(ab)-glycans are not found on ACPA-IgM. How F(ab)-glycans facilitate the emergence and/or expansion of auto-reactive B cells in this context, however, remains unclear. Using recently developed technology to identify and isolate citrullinated antigen-specific B cells from patients, we can now address this question by studying the frequency and localisation of N-glycosylation sites in the antibody repertoire and by studying the phenotype and functional characteristics of ACPA-expressing B cells. Together with our investigations on the modulation of ACPA Fc-glycans, these studies provide a deeper understanding of mechanisms that allow the development of autoimmunity as such, and of the mechanisms that underlie the progression from systemic autoimmunity towards overt autoimmune disease.

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SP0183 FAILURE OF TREG CONTROL TO UNDERSTAND AUTOIMMUNITY

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Regulatory T cells (Treg) expressing the transcription factor FoxP3 are crucial for the maintenance of immunological tolerance to self and thus for the control of autoimmunity. There is strong evidence that numeric or functional defects in Treg cell biology are involved in the pathogenesis of particular autoimmune diseases. Here we will focus on the fundamental role of Treg cells in diverse autoimmune and rheumatic diseases and will explain how a failure of the Treg cell system can evolve and contribute to the development of such diseases. Furthermore, therapeutic approaches aiming to overcome these Treg cell defects and to restore Treg cell activity in the patients will be discussed.

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SP0184 ROLE OF MICROENVIRONMENT AND ENDOGENOUS PATHWAYS TO BREAK TOLERANCE

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Break of tolerance driving autoimmune disease is initiated by a combination of predisposing genetic and environmental factors resulting in self-perpetuating chronic inflammation and tissue damage. Effector molecules and cells targeting tissues housing the inciting autoantigen(s) maintain tissue damage and the autoimmune response. Granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis) is a prototypical autoimmune disease characterized by extravascular necrotizing granulomatous inflammation and a systemic autoimmune vasculitis associated with anti-neutrophil cytoplasmic autoantibodies specific for the neutrophil- and monocyte-derived serine-protease proteinase 3 (PR3-ANCA). GPA is strongly associated with HLA-DPB1*0401 polymorphisms. Its association with the R620W variant of the PTPN22 gene has been linked to reduced immune-regulatory interleukin (IL)-10 transcription. Epidemiological studies and molecular analysis of immune cells suggests a multifactorial pathogenesis of GPA, in which a potentially metachronous and individually varying sequence of infectious agents contributes to the break of tolerance and chronic inflammation sustaining autoimmunity in GPA.

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Closing the gap between objective measures and self-report in fibromyalgia

SP0185 DIVERGENCES BETWEEN OBJECTIVE AND SELF-REPORTED PHYSICAL FUNCTION IN FIBROMYALGIA

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In fibromyalgia (FM), intolerance to physical activity, with increased pain and experience of early muscle fatigue, is a predominant feature. Furthermore, shorter endurance times and higher perceived effort during physical activity compared with healthy controls are characteristic. However, there are discrepancies between physical functioning as perceived by the patients and as measured objectively or during performance tests. For example, in 840 FM patients and 122 healthy controls, we found reduced muscle strength in approximately 50% of the FM patients. However, the patients with subnormal muscle strength did not self-report worse symptoms or more physical disablement than those with normal muscle strength. Much like central sensitization of pain, it has been suggested that impaired sensory-motor interaction is present in FM, which may be a cause for observed discrepancies between perceived and objective signs of muscle fatigue. That is, the sensory inputs to the central nervous system during a physical activity are over-interpreted, leading to amplified sensations of fatigue and discomfort normally associated with exhausting muscle work.

To illuminate this we conducted a controlled experiment, in which FM patients and health controls completed a muscle exhaustion test, while objective measures of muscle fatigue were collected by electromyography in parallel with reporting of perceived muscle fatigue. The results suggest that among FM patients, central nervous system processes normally associated with muscular fatigue were present, yet without any evidence of peripheral muscle fatigue. The study supports a hypothesis about abnormal sensory-motor interaction among FM patients that can explain the discrepancies between perceived and observed physical disability in FM.

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SP0186 COGNITIVE FOG: SUBJECTIVE AND OBJECTIVE UNDERSTANDINGS OF THE SYMPTOM OF DYSCOGNITION

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Dyscognition refers to the complaint that a person's ability to perform thinking tasks is impaired. This complaint is colloquially known as "brain fog". It is a major symptom of a variety of disorders and associated with considerable work and social disability for those experiencing it. However, attempts to demonstrate objective cognitive impairment in persons reporting "brain fog" have not been straightforward. In this lecture, the symptom of cognitive dysfunction will be described from the patient's point of view, using fibromyalgia as a disease model. The cognitive tests used to determine objective alterations in cognitive ability will be reviewed, the amount of objective impairment demonstrated in fibromyalgia will be placed into clinical context, and the "disconnect" between what the experience of dyscognition is and the cognitive content measured by modern testing will be discussed. The poor relationship between the magnitude of subjective dyscognition and objective cognitive performance will be examined, including evidence gleaned from neurological imaging studies. In conclusion, the experience of cognitive fog is not well captured by current testing paradigms. Subjective complaint is a poor predictor of objective cognitive performance. The neuronal mechanisms responsible for the experience of cognitive fog may be separate from those required to perform cognitive tasks.

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SP0187 ASSOCIATIONS OF PAIN-RELATED COGNITIONS WITH THE DISCORDANCE BETWEEN SUBJECTIVE AND OBJECTIVE PHYSICAL FUNCTION IN FIBROMYALGIA: THE AL-ÁNDALUS PROJECT

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Background: In fibromyalgia, there is a disagreement between patients' self-reports and performances; i.e., subjective and objective status, respectively.

Objectives: First, to test the discordance between subjective and objective measures of physical function. Second, to determine whether catastrophizing and self-efficacy are independently associated with this discordance.

Methods: Four hundred and five fibromyalgia females and 193 age-matched female controls. Participants filled out the Pain Catastrophizing Scale, Chronic Pain Self-efficacy Scale, and physical functioning subscales of the Revised Fibromyalgia Impact Questionnaire (FIQR) and Short Form-36 (SF-36) health survey. Objective physical function was measured with a battery of performance-based tests (e.g., 6-min walk test). Subjective and objective physical function were expressed as deviation from the general population in standard deviation (SD) units using means and SD of the control group.

Results: Fibromyalgia participants reported a worse physical function than performed ($p < .001$). We found a consistent association of higher catastrophizing with greater discordance between subjective and objective physical function. A significant association of higher self-efficacy with lower discordance was only found when subjective physical function was reported on the SF-36 but not on the FIQR.

Conclusions: Although both are markedly impaired, subjective physical function is more impaired than objective physical function in fibromyalgia. Catastrophizing is associated with this discordance. In rehabilitation settings, physical function of fibromyalgia females should be evaluated by both subjective and objective assessments to fully understand their physical function.

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SP0188 THE DRUGS DON'T WORK

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This presentation will depict the journey of Louise, a previous school teacher and a single mother of two, living with Fibromyalgia as well as multiple other diagnoses. Louise will discuss her feelings around being diagnosed with Fibromyalgia, how this was communicated to her and what this meant for her career and family life. Following this, Louise will share her journey through the secondary care as a Fibromyalgia patient, and her own search for answers and cure to Fibromyalgia in an attempt to salvage her life and independence, prior to accepting that this is a long-term condition which will require self-management and perseverance. In addition, Louise will share her thoughts on pain and fatigue in Fibromyalgia, and how the "drugs don't work".

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Interactive cases from the HOT and WIN sessions

SP0189 HOT SESSION: INTERACTIVE CLINICAL ASPECTS AND CASES ON VASCULITIS TREATMENT

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The systemic vasculitides are characterized by inflammation of blood vessels resulting in end organ, or tissue damage or necrosis. They are defined by the Chapel Hill nomenclature according to the calibre of the predominantly affected vessels. Other forms of vasculitis not defined by a predominant vessel size are also recognized (e.g. Behçet's syndrome). Large vessel vasculitides include giant cell arteritis and Takayasu arteritis; medium vessel vasculitides includes Kawasaki disease and PAN; small vessel vasculitides are divided into: immune complex small vessel vasculitis and anti-neutrophil cytoplasm antibody (ANCA) - associated vasculitis (AAV). The immune complex group, with moderate to marked vessel wall deposits of immunoglobulin and/or complement, is represented by anti-glomerular basement membrane disease, cryoglobulinaemic vasculitis, hypocomplementaemic urticarial vasculitis (anti-C1q vasculitis) and IgA vasculitis (Henoch-Schönlein). By contrast, AAV has few or no immune deposits and is associated with (in most cases) the presence of ANCA specific for myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA). Depending on their clinical presentation and ANCA specificity, AAV is divided into three major variants: granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss syndrome). In some cases, vasculitis is relatively trivial and may lead to minor, often asymptomatic clinical features such as splinter haemorrhages. However, in severe forms of ANCA associated vasculitis, the consequences of rapid onset of ischaemia and occlusion of blood vessels can lead to organ failure and death.

The multisystem involvement in most forms of vasculitis can be a real challenge. Patients may present to different specialists resulting in diagnostic delay. The investigation of patients with suspected vasculitis should follow on from a careful history and examination to determine the likely diagnosis. The differential diagnosis is very wide. It is important to correctly identify patients with vasculitis as early as possible, but it is also important to rule out more common causes. In acutely unwell patients, the differential diagnosis depends on the combination of clinical features. Vasculitides tend to involve multiple organ systems. In fact, the more organ systems affected, the more likely it is that the patient has vasculitis.