spend a substantial amount of their time and able to travel frequently, is another obstacle to overcome.

This presentation provides some examples of the involvement in Health Technology Assessments of the German Rheumatism League, Germany's largest patient organisation with about 3 00 000 members, and the essential prerequisites for the participation of patient organisations in that process.

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EULAR Projects in investigative rheumatology_____

SP0110 AUTOANTIBODY STANDARDISATION IN RHEUMATIC DISEASES. THE ROLE OF THE EUROPEAN CONSENSUS FINDING STUDY GROUP ON AUTOANTIBODIES IN RHEUMATIC DISEASES (ECFSG)

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The aim of the European Consensus Finding Study Group on autoantibodies in rheumatic diseases (ECFSG), a.k.a the EULAR autoantibody study group, is to achieve a common consensus in autoantibody diagnostics: a laboratory result should be the same, independent of the country or laboratory where the result is obtained. Since 1988, the ECFSG has yearly distributed unknown sera to European laboratories (presently 43) for evaluation in a clinical context. These sera are chosen to reveal differences between different laboratories. The results are discussed in conjunction to the European Workshop for Rheumatology Research (EWRR) every year. Use of reference materials helps to align test results by adopting internationally used measurement units, but reference materials are missing for many autoantibody specificities. Since 2014 an ECFSG focus has been on evaluating samples that might constitute new reference materials for companies producing autoantibody measurement assays, as well as for clinical laboratories. Hitherto investigated autoantibody specificities are provided in the table 1. In my talk I will present the work of ECFSG, including the characterisation of the samples that have constituted raw material for currently available reference materials. I will also tell about our first characterisation of a tentative new reagent sample, that thereafter was produced as reference material by the National Institute of Biological Standards and Control (NIBSC) in the UK. In November 2017 that reagent was endorsed by the World Health Organisation (WHO) to become the new international reference reagent for anti-double stranded DNA (anti-dsDNA) antibodies.

Abstract SP0110 – Table 1. Hitherto tested tentative or now existing reference reagents

2014	anti-dsDNA (now publicly available WHO standard, NIBSC 15/174)
2015	ACPA
2016	anti-PR3 (standard available from the EU Science Hub, ERM-DA483/IFCC)
2016	anti-MPO (standard available from the EU Science Hub, ERM-DA476/IFCC)
2016	IgG anti-b2GP1
2017	anti-GBM
2018	anti-DFS70

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SP0111 HOW NEURO ENDOCRINE IMMUNOLOGY IMPACT RHEUMATIC DISEASES?

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The Neuro Endocrine Immune Network (NEI) is the most important communication-system in human body to maintain the health status. NEIRD evaluate the relationships between NEI and Rheumatic and Musculoskeletal Diseases (RMDs). The altered interaction between the nervous system, the immune/inflammatory cells and the endocrine system plays an important role in the pathophysiology of autoimmunity and chronic inflammation. The involvement of the adrenal steroid

hormones in the immune response is fundamental and follow a circadian rhythm (circadian rhythm studies obtained the Nobel Prize for Medicine in 2017). As Matter of fact, the nocturnal ability of the NEI system to mount an efficient immune and inflammatory response, with related clinical consequences, is matter of important chronotherapeutic approaches with exogenous steroids, in particular with glucocorticoids (GCs) (their discovery obtained the Nobel Prize in 1950 and still a pillar in the treatment of RMDs and not only). Other important steroid hormones involved in the NEI are the sex hormones (estrogens. E2 OH-metabolites are potent enhancers of cell proliferation) and the d-hormone (steroidal hormone structure of the final metabolite of Vitamin D). Clinical observations indicate a strong influence of the neuroendocrine system on immune function and *vice versa* in chronic inflammatory rheumatic diseases. The influence of hormones and neuronal pathways happens before and after the outbreak of the disease. Very recent data demonstrate the modulatory role of estrogens on epigenetic mechanisms (ie DNA methylation and gene upregulation). For example differentially expressed miRNA pathways linked to E2 in human endothelial cells through ER have been shown, and provide new insights by which oestrogen can modulate endothelial function. This point might be crucial in autoimmune diseases like systemic sclerosis (SSc) a disease prevalent in females and that start from damaged endothelium. We have started a large study on epigenetic and pregnancy on patients with RMDs such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). On the other hand, the disease process with an activated immune system influences several hormonal and neuronal pathways. In addition, the energy bottleneck leads to important disease sequelae such as sickness behaviour/fatigue/depressive symptoms, sleep disturbances, anorexia and malnutrition, bone loss, muscle wasting and cachectic obesity, insulin resistance with hyperinsulinemia (insulin-like growth factor-1 resistance), dyslipidemia, alterations of steroid hormone axes, disturbances of the hypothalamic-pituitary-gonadal (HPG) axis, elevated sympathetic tone, hypertension and volume overload, decreased parasympathetic tone, inflammation-related anaemia, and finally circadian (circannual) rhythms of symptoms. New therapeutic strategies should respect these findings because rheumatic patients die earlier due to the mentioned disease sequelae. It is suggested that disease sequelae must be treated more consequently because they are inherent to chronic inflammatory systemic diseases (possible evolution for some of them in cancer). Therapeutic strategies in this field of NEIRD are slowly developing. Low-dose glucocorticoid therapy as supplementation of the "small adrenal engine", chronotherapy with glucocorticoids (night release) and vitamin D supplementation are the best examples of the successful utilisation of demonstrated concepts.

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SP0112 MICROCIRCULATION IN RHEUMATIC DISEASES

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Background: The EULAR Study Group on Microcirculation in Rheumatic Diseases (SG MC/RD) aims to build an international network of expert centres to facilitate and exchange knowledge. It is a non-profit group and has no financial support. Both altered microvascular morphology and peripheral flow are the main focus of research.

Objectives: 1) To integrate different expertises to study the pathophysiology of disease processes. 2) To exchange knowledge and to facilitate standardisation concerning different techniques to assess the (micro)circulation such as nailfold capillaroscopy, laser doppler and laser speckle contrast analysis (LASCA). 3) To elaborate predictive indexes for disease progression and follow-up based on the integration of different tools and biomarkers. 4) To develop intervention protocols based upon an understanding of and targeting disease mechanisms (i.e. microvascular damage progression to fibrosis).

Methods: The EULAR SG MC/RD was accepted by the EULAR Executive committee in March 2014 and is being supervised by the EULAR Committee on Investigative Rheumatology, currently chaired by Prof. X. Mariette. Anno 2018 the number of members has risen to 79 (out of which 26 from 14 non-European countries). The EULAR study group meets half yearly (every EULAR/ACR) and

organises training courses every two years at Genova and supplies continuous training through the EULAR imaging library.

Results: The following projects resulted in publications: As standardisation of techniques to evaluate the microcirculation is one of the aims of the study group, a first activity was a multi-centre study to assess the reliability of simple capillaroscopic definitions to evaluate morphologies of single capillaries.¹ Optimisation of reliability of initial definitions has been obtained at the 7th EULAR course on capillaroscopy.² Secondly, the evaluation of interrater reliability of microcirculatory flow evaluation by LASCA was piloted by 2 of the founding members and has been published.³ Thirdly, a cross-sectional, international SURvey on non-invasive techniques to assess which tools are being used to evaluate the microcirculation in patients with Raynaud's phenomenon has been performed in between 471 eligible physicians.⁴ A 4th publication resulted from a systematic review, analysing the role of capillaroscopy in systemic lupus erythematosus, based on standard interpretation of capillaroscopy according to the EULAR SG MC/RD.⁵

Conclusions: The relatively young EULAR SG MC/RD is thriving well, based on multi-centre joint forces to achieve standardisation of microcirculatory evaluation of rheumatic diseases as well as in achieving clinical as well as basic science research.⁶

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Laboratory course – from the clinic to the lab and back

SP0113 NEW TRENDS IN BIOMARKERS IN INFLAMMATORY JOINT DISEASE

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This lecture provides an overview on new developments in biomarker research and standardisation in inflammatory joint diseases. The presentation includes an introduction of established and new biomarkers in serum and synovial fluid as well as methods for their detection. Furthermore, an overview on different modifications of auto-antigens (including citrullinated and carbamylated isoforms) and their role in immune response and pathogenesis of disease will be given. The diagnostic performance of new and established biomarkers will be discussed including antibodies against modified antigens also illustrated by difficult to diagnose cases. In this context, special attention will be attributed to the predictive value of biomarkers for diagnosis of disease and treatment response.

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New assessments in clinical practice

SP0114 HOW TO PERFORM A QUICK AND RELIABLE PHYSICAL EXAMINATION IN RHEUMATOLOGY

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The GALs (Gait, Arms, Legs, Spine) screen is a quick, reasonably sensitive way to detect common musculoskeletal (MSK) abnormalities as part of a wider medical assessment.¹ However, for someone with MSK complaints a detailed assessment is required to determine the diagnosis and impact of the condition on that person. The history is the key starting point. This needs to be holistic and individualised as the enquiry proceeds, since the impact of any condition is person-specific and influenced by many factors (e.g. psychosocial, illness perceptions, sleep, comorbidity etc.). A thorough history usually suggests the single most likely cause for the patient's problem(s) and should then guide the examination – an efficient

targeted “rapier” approach where the practitioner selects appropriate skills from a range of competencies according to specific history elements. This contrasts with a longer hypothesis-free “screen” where an identical set of procedures is undertaken in each patient.

This presentation covers key principles and considerations of assessment and illustrates how the history guides the subsequent “rapier” examination.² Examples include:

(1) in the *history*: determination of pain localisation and features associated with radiated pain; pain and stiffness characteristics that differentiate mechanical usage-related pain, inflammatory pain, acute crystal synovitis, destructive bone pain and neurogenic pain; non-specific symptoms of inflammation.

(2) in the *examination*: usual order of inspection at rest, inspection during movement, then palpation at rest and during movement of symptomatic regions; contrasting clinical findings that quickly differentiate joint and peri-articular problems; initial selection of the movement(s) that is affected first and most severely by arthritis – the tight pack position(s); detection of “stress pain” (pain worse in tight-pack but reduced/absent in loose-pack positions – the most sensitive sign of inflammation); examination for effusion, soft-tissue and firm swelling; use of resisted active movements and stress tests for peri-articular lesions; a targeted screen for asymptomatic disease prompted by the main diagnosis.

EULAR learning resources available at http://www.eular.org/edu_training_dvd.cfm include: ¹ The “GALS” screen and ² Principles of the musculoskeletal history and examination.

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SP0115 VALUE OF INFLAMMATORY BIOMARKERS IN CLINICAL DECISION MAKING

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Inflammation is known to play a major role in rheumatologic disorders. Inflammatory biomarkers can help clinicians diagnose rheumatic diseases and assess disease activity more accurately. These markers have been incorporated into classification criteria of several diseases to enable early diagnosis and timely initiation of treatment. Quantification of inflammation has become essential to tailor the treatment strategy, especially in patients with rheumatoid arthritis, polymyalgia rheumatica and vasculitides. Inflammation can be measured from different perspectives – the measures that quantify biomarkers participating in inflammation, surrogate markers of inflammation, and the by-products of the inflammation process.

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels are among the most commonly used acute phase reactants in the detection and follow-up of rheumatologic disorders. These markers are not specific to trigger factors of inflammation, limiting their capacity to discriminate the cause for stimuli as well as the organs involved.

In the current presentation the advantages and limitations of new and established inflammatory biomarkers in clinical decision making will be discussed illustrated by case reports.

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SP0116 VALUE OF ULTRASOUND IN CLINICAL DECISION MAKING

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The use of ultrasound (US) has increased over the past 20 years for clinical decision making and for optimised patient care. The utility of US for correctly diagnosing the cause of musculoskeletal symptoms is known by many clinicians but little published data exist in this area. However, the value of US for diagnosing and handling treatment decisions especially in patients with rheumatoid arthritis (RA) has been well documented. US has been proven to be more sensitive than clinical joint evaluation.^{1 2} This has resulted in the acknowledgement of US as an addition to the clinical joint evaluation in suspected RA patients for assessing a more elaborate joint involvement helping the clinician to correctly classify the patients according to the new RA classification criteria.³ Likewise, in early undifferentiated inflammatory arthritis the use of US may assist in pinpointing those patients who will develop persistent inflammatory arthritis over time.⁴ US may also impact diagnosis and treatment decisions. This has been shown both in situations with regional pain such as the painful foot in chronic inflammatory diseases and the possible need for corticosteroid injections but also in global disease activity assessment in RA patients where US provides additional disease activity information leading to altered treatment decisions as compared to regularly DAS28 assessment.^{5 6} Also, in remission US may – by assessing subclinical inflammation