The transplacental passage of maternal aPL does not generally produce any thrombotic complication in the neonate. The registry of infants born to mothers with APS, started by the European Forum on aPL in 2003, is collecting precious information for the assessment of neonatal outcome and subsequent development. The exposure to maternal aPL was linked to learning disabilities (LD) in children born to both mothers with SLE and with APS, based on the experimental observation that aPL can affect neural cells functioning. A recent study on the long-term neurodevelopment of children exposed in utero to aPL was reassuring for a normal neurological functioning and intelligence level, but found a higher rate of LD as compared to the general population (19% vs 3%) (Nalli, Lupus 2017). These affected children were all born at term to triple aPL positive mothers.

Although systemic autoimmune diseases are not hereditary, newborns may receive from the mother a genetic background that may predispose to the emergence of autoimmunity and, possibly, of related symptoms. However, the incidence of autoimmune diseases in the offspring was rather low (1%) among 269 children with a mean age of 15 years collected in the previously cited survey of Italian Rheumatology Centers.

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Neuronal and hormonal alterations in arthritis

SP0115 NEUROTRANSMITTERS AND INNERVATION IN SYNOVIUM

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The synovial tissue is innervated by nociceptive sensory nerve fibers and sympathetic postganglionic nerve fibers. While sensory nerve fibers have afferent (by transmitting pain to the CNS) and efferent functions (by local release of neuropeptides), sympathetic nerve fibers exert mainly efferent vasoregulatory, energy-regulating and immunomodulating roles. In synovial tissue of patients with rheumatoid arthritis (RA), the major proinflammatory neuropeptide of sensory nerve fibers is substance P, which is upregulated relative to anti-inflammatory calcitonin gene-regulated peptide (CGRP). In addition, sensory nerve fibers undergo a sprouting response leading to sensory hyperinnervation of RA synovial tissue. Removal of sensory nerve fibers exerts anti-inflammatory effects, and it is thought that this elimination is beneficial during hemiplegia, which can spare the paralytic limb from developing RA. Therapeutic neutralization of substance P was not successful, most probably due to vast receptor redundancy. Furthermore, the sensory nervous system undergoes a sensitization response (aggravation of pain and inflammation) in the synovial tissue, the dorsal root ganglion, the spinal cord, and more central in the brain. Chemical sympathectomy or suppression of adrenergic signaling significantly reduce inflammatory processes in the initial acute state of inflammation whereas the same procedures may increase inflammation at later stages. These findings indicate that the sympathetic nervous system supports the development of inflammation but can reduce inflammation at more chronic stages. During chronic inflammation, the density of sympathetic nerve fibers in synovial tissue is reduced but other tyrosine hydroxylase-positive cells secreting noradrenaline appear in the inflamed joint. In addition to local vascular effects in the joint, the sympathetic nervous system influences numerous immune processes in the joint and in lymphoid organs. Hence the net effect of the sympathetic nervous system on inflamed tissue results from local sympathetic effects in the joint as well as from sympathetic influences on major systemic immune processes and energy regulation. This lecture summarize the central aspects of the two nervous systems.

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SP0116 HOW TO TARGET NEURONAL AND HORMONAL ALTERATIONS IN ARTHRITIS

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Neuroendocrine pathways link the central nervous system (CNS) with the periphery by means of hormones and nerve fibres. Neuroendocrine connections are important for integrating signals throughout the body. Hormones are soluble factors circulating in the blood and lymph, while nerve fibres are solid cables connecting brain centres with distinct anatomical sites in the periphery.

Several network connecting the NeuroEndocrine Immune (NEI) system are target for the treatment of chronic immune inflammatory diseases, including arthritis in RMD (1).

The hypothalamic–pituitary–adrenal (HPA) axis is the best studied connection between the CNS and peripheral sites of inflammation. The HPA axis hormones comprise CRH, adrenocorticotropic hormone (ACTH) and several steroid hormones of the adrenal gland, including cortisol and adrenal androgens such as dehydroepiandrosterone (DHEA), its biologically inactive degradation product DHEA sulfate (DHEAS), and androstenedione (ASD). The adrenal gland synthesises glucocorticoids (GCs) following a circadian rhythm and the exogenous administration of GCs in chronic arthritis should be regarded as a replacement therapy for adrenal gland hypofuntion (2).

The hypothalamic–pituitary–gonadal (HPG) axis has been linked to rheumatic diseases because we observe a female preponderance in the prevalence and incidence of rheumatic diseases, which is most probably linked to sex hormones. Hormones of the HPG axis comprise gonadotropin-releasing hormone, luteinising hormone/follicle-stimulating hormone and the two major bioactive steroid hormones of the gonadal glands, testosterone and oestrogens. Increased peripheral metabolism of sex hormones is seen in chronic arthritis (ie. synovial tissue).

The hypothalamic–pituitary–prolactin axis is important since Prolactin is thought to have proinflammatory effects in RMD. Blood levels rise sharply at the beginning of sleep so this hormone can be a regulatory element in the circadian rhythms of the immune system (1).

Similar condition for the melatonin pathway, that in addition is increased I rheumatoid arthritis patients. Blood levels rise sharply at the beginning of sleep and melatonin might, thus, be a regulatory element in the circadian rhythms of the immune system. Melatonin at normal concentrations has proinflammatory effects. Finally, the vitamin D endocrine system, which is one of the most complex and diffuse systems controlling bone mass and also the immune response in autoimmune rheumatic diseases. Vitamnin D deficiancy is common in chronic RMD and decreased in winter with related flares of RMD.

Finally, vitamin D, via its active hormonal metabolite 1,25(OH)2D3 (D hormone), regulates both innate and adaptive immunity, potentiating the innate response (monocytes/macrophages with antimicrobial activity and antigen presentation) but suppressing adaptive immunity (T and B lymphocyte functions). D hormone deficiency is a risk factor for autoimmunity and for infections and cancer.

By considering that all steroid hormones before mentioned, are also produced *via* intracrine synthesis by the inflammatory cells (ie. macrophages) at the site of arthritis, it is increasing in presence of localized inflammatory conditions the local treatment (ie injection of GCs in joints). On the other hands, the immune stimulating action of estrogens should noy suggest their use in pathological conditions. Same caution with the use of melatonin in presence of arthritis, whereas 1,25(OH)2D3 is considered an adhiuvant in immune system suppression at dosages over 2,000 IU/day.

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Fighting osteoporosis fragilities

SP0117 OSTEOPOROTIC FRACTURES IN EUROPE: ARE WE DOING ENOUGH

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The past 30 years has seen significant milestones in assessment and management of osteoporosis. These include the development of DXA and FRAX to identify individuals at high risk of fragility fracture and the development of interventions that have been shown to significantly decrease the risk of fracture in well-designed clinical trials. A major challenge has been how to apply these treatments. Measurements of bone mineral density (BMD) are used for diagnosis and for fracture risk prediction. Facilities for BMD testing are patchy and many European countries have inadequate resources to service the societal needs. In addition, BMD has poor sensitivity for the prediction of fracture so that the majority of fractures occur in individuals with T-scores >-2.5 SD. The development of FRAX has improved the sensitivity of fracture risk prediction and is now adopted in many assessment guidelins.

Despite these advances, there are a number of challenges to be faced. Of paramount importance is that few patients with a prior fracture and even less with osteoporosis alone actually receive treatment. In Europe, there is wide inter-country variation in the treatment of women at high risk for osteoporotic fractures. The treatment gap varies from 25% in Spain to 95% in Bulgaria. Large treatment gaps were identified in countries with populations at both high and low risk of fracture. In total in the EU, it is estimated that, out of the 18.4 million women that exceed the risk level in 2010, 10.6 million were untreated. These figures are conservative since an undetermined proportion of low-risk women will have received treatment. Moreover, the treatment gap is increasing in many countries. Thus the disease is under-recognised by the medical community.

Urgent action is required to address the under-recognition of osteoporosis and fragility fracture. Simple measures include:

- The development of country-specific guidelines,
- Piloting screening strategies in the elderly,
- Identifying the determinants of imminent risk,
- The development of fracture liaison services.

Whereas osteoporosis is recognized, worldwide, as a major Public Health issue, with one in two women and one in five men over the age of 50 years presenting

a fragility fracture, a vast proportion of women at high risk remain untreated. Case-finding strategies prioritizing assessment of men and women with prior fracture are required to alleviate this problem.
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SP0118 ESTABLISHING AND IMPLEMENTING A FRACTURE LIAISON SERVICE

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Objectives: The objective of the National Osteoporosis Society (NOS) is to establish a Fracture Liaison Service (FLS) in every NHS Trust in the United Kingdom (UK). The Service Delivery Manager supports sites to establish, implement and develop a new FLS, as well as to improve the quality of existing services. The FLS model enables secondary fracture prevention through identification of fragility fractures in every person who breaks a bone aged over 50 using dedicated case-finding, with assessment and appropriate management of osteoporosis where necessary. The object of FLS is to prevent secondary fractures, in particular expensive hip and vertebral fractures, thereby providing both clinical and cost effectiveness for patients and payers. The NOS has developed a unique service to support FLS across the UK.
Developments: A team of specialist development managers with clinical and commissioning experience support providers and payers in the process of establishing new FLS's by offering consultation and guidance at every step of the process from pathway development to successful funding of services. This model has been replicated across the UK since April 2015 with the support and expertise of the NOS. Once an FLS is established the NOS provides support with service improvement, whether through additional commissioning of funds, Peer review or Gap analysis.
Results: Results from a range of analyses show that FLS has a positive impact on fracture rate and in particular hip fractures.
At the time of writing, the NOS is currently supporting 166 sites across the UK. 83 sites are improving the quality of their service; 58 sites are developing new services. 13 new services have been commissioned since commencement of the work programme, delivering new FLS provision to an additional 1.6 million people over 50, preventing 1,482 hip fractures over a 5-year period. Figures have been calculated from the NOS FLS Benefits Calculator https://benefits.nos.org.uk
Challenges: The primary challenge in establishing an FLS is identifying a clinical champion - this maybe a nurse, an allied health professional, rheumatologist or ortho-geriatrician in the hospital, or a representative from Public Health or from a Clinical Commissioning Group (CCG). The champion can lead and take the FLS from an idea to implementation.
To support the establishment and implementation of FLS the NOS has developed the FLS Implementation Toolkit as well as the Clinical Standards for FLS. The Clinical Standards will shortly be supported with a supplementation - New Clinical Guidance on the identification of Vertebral Fractures.
Furthermore, the Charity has developed the Fracture Prevention Practitioner (FPP) training for those wishing to implement an FLS. This is backed by the Competency Framework for Nurses, allied health professional and doctors to ensure best practice in fracture prevention.
Conclusion: The NOS service development model of support is successful in driving the establishment, implementation and improvement of FLS across the UK. This is tough in an economic climate where health budgets are constrained. However, there is strong evidence that investment in FLS improves the quality of care as well as illustrating financial savings in health and social care. NHS England recommends that every patient with/or at risk of osteoporosis and fragility fractures should have access to a commissioned service.
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SP0119 PREDICTING FRACTURE RISK: ACCURACY AND FEASIBILITY OF TOOLS

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Several therapeutic options and screening strategies are available to effectively decrease fracture risk. However the main clinical challenge still consists in accurately identifying and selecting individuals for bone densitometry and for pharmacological treatment, in order to increase efficiency and minimize individual and societal costs.
The World Health Organization provided an operational definition of osteoporosis as a bone mineral density (BMD) that lies 2.5 or more standard deviations below the average value for young healthy women of the same gender and ethnical background [T-score $\leq$-2.5]. However, BMD has limited sensitivity and specificity in the prediction of fracture. In fact, a large number of conditions have been firmly established as risk factors for the occurrence of fragility fractures, independently from BMD. These have been combined into prediction algorithms to estimate fracture probability and are currently available for calculate the risk of fractures. However, the existing tools differ in many relevant aspects: from their own feasibility, to the number and availability of clinical risk factors included, the accessibility of BMD measurements and, finally, their performance in different settings.
With this session we aim to identify and synthesize the best available evidence on the accuracy and feasibility of the currently available tools designed to predict fracture risk.
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SP0120 PREDICTING THE RISK OF FALLS AND PROMOTING BALANCE IN OLDER ADULTS

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Falls are the leading cause of injury and death due to injury among the older adult population in the United States. Of those who fall, 24% will sustain serious injuries and 6% will experience fractures. In addition to injury, older adults who fall may experience decreased functional ability, loss of independence, a poorer quality of life, or premature mortality. At a global level, these statistics are similar among developed countries. It is important to first identify the intrinsic and extrinsic risk factors that contribute to falls and then intervene appropriately once the level of fall risk has been identified. It is important to understand that there is no one size suits all fall risk reduction program and that the type of program will vary as a function of the level of risk. Core components of successful fall risk reduction programs include exercise, environmental modifications, and behavior change techniques aimed at fostering long-term adherence to engaging in fall risk reducing behaviors. The purpose of this presentation will be to describe appropriate methods for identifying fall risk, and intervention strategies that have been shown to significantly reduce fall risk and/or fall incidence rates across the continuum of fall risk.
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Biological agents in juvenile idiopathic arthritis: open issues

SP0121 LONG TERM SIDE EFFECTS OF BIOLOGICAL AGENTS IN JIA

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In the last years, the interest in the concept of comorbidity and its societal as well as individual impact has increased. Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease starting in childhood which often persists into adulthood. Clinicians are facing an aging population with multiple morbid conditions occurring in one individual. Long term outcome studies show the high prevalence and the potential interaction of coexisting diseases. For JIA recent studies reported that uveitis, asthma/atopic diseases and diabetes mellitus are prevalent comorbidities in JIA with 11.6–30%, 10.8% and 3.5% respectively, followed by cardiovascular disease, malignancies and inflammatory bowel diseases. Childhood long term outcome studies and Pharmacovigilance registries already revealed associations of co-existing diseases and the role of used medication (especially biologicals). It is important to plan preventive and screening strategies in order to prevent or early detect and treat comorbidities and integrated follow up once comorbidity exists.
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