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