gent surgery. These may be observed in polyarteritis nodosa, cryoglobulinemic vasculitis, eosinophilic granulomatosis with polyangiitis and other AAV. High-dose glucocorticoids and cyclophosphamide are usually applied.Children with IgA vasculitis may develop bowel intussusception
Deep venous thrombosis and pulmonary embolisms are significantly more frequent in AAV and Behçet disease than in the general population, especially during active disease. Anti-coagulation may be needed in AAV, although this approach is controversial in Behçet's disease. By contrast, aneurysm formation is typical in polyarteritis nodosa and Behçet's disease and may be occasionally seen in AAV. Massive bleeding derived form aneurysm rupture usually requires arterial embolization.
It is important to keep in mind that during the early course of diagnosed vasculitis, intense immunosuppressive therapy may favour life-threatening infections including opportunistic infections such as pneumocystis jiroveci pneumonia or disseminated CMV.
In summary, systemic vasculitis may present with a variety of severe complications and other may develop during follow-up. These complications are heterogeneous, vary according to the size of vessels involved, and usually require specific procedures or treatments in addition to immunosuppressive therapy. Due to the life-threatening nature of these complications their immediate recognition and management are crucial to patient survival.
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AxSpA: From bug to gut and to disease phenotype –

SP0111 INHIBITING BONE FORMATION IN THE CLINIC. ARE WE THERE YET?

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One of the most characteristic features of axial spondyloarthritis (axSpA) is bone formation in the spine (syndesmophytes). Syndesmophytes may occur at any time during the course of the disease, are more frequent in patients with radiographic axSpA (AS) than in those with non-radiographic axSpA, and are best seen on conventional X-rays of the spine. Currently, it is suggested that (low-radiation) CT-scanning of the spine provides a better (more sensitive) picture of developing syndesmophytes than conventional X-rays.
Syndesmophytes matter in that they interfere with spinal mobility and physical function independent of inflammation. As such, it makes sens to try and prevent their occurrence or to inhibit their progression.
It is a matter of debate whether current available treatments are able to inhibit syndesmophyte growth or occurrence. Part of the debate is the methodological challenges related to measuring syndesmophyte progression properly.
In this lecture I will address current issues related to inhibition of syndesmophyte formation in patients with axial SpA.
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Pregnancy meets rheumatic patients

SP0112 WHICH DRUGS IN PREGNANT PATIENTS?

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Management of rheumatic disease during pregnancy starts with prepregnancy counselling.Assessment of maternal and fetal risks is necessary for adjusting therapy before and during pregnancy. The aim of therapy is to keep the disease in remission or at least at low activity throughout pregnancy.
Immunosuppressive drugs requiring withdrawal before conception are methotrexate, cyclophosphamide,and mycophenolate which are known teratogenic drugs. Other drugs like leflunomide, tofacitinib and several biological should be discontinued because pregnancy experience is at present insufficient and safety for the fetus has not been proven.Flares of rheumatic disease showing be treated immediately and with pregnancy compatible drugs.For patients with inflammatory arthritis like rheumatoid arthritis,spondyloarthritis and juvenile idioipathic arthritis disease activity during pregnancy can be controlled with antimalarials, sulfasalazine and TNF inhibitors. Women with systemic lupus erythematosus should continue basic therapy with hydroxychloroquine, and azathioprine, ciclosporine or tacrolimus added when necessary due to organ manifestations. Severe flares during pregnancy may require biologics like rituximab,abatacept,tocilizumab or Anakonda, in SLE corticoid pulses or, if life threatening, intravenous gamma globulin or cyclophosphamide.
Treatment during pregnancy demands balancing suppression of maternal disease and no harm to the child. Selecting the adequate type, the right dose and the right timing of medications for optimal care of pregnant patients remains a challenge.
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SP0113 PREGNANCY IN SLE: STILL CHALLENGING FETAL AND MATERNAL ISSUES

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Patients with SLE are mostly young women diagnosed during their childbearing years. Several "unmet needs" in the management of reproductive health issues may impact on the decision to have children. Because of earlier recognition of disease and advances in medical treatment, family planning has gained greater importance. Concerns include the effect of pregnancy on maternal disease, the impact of disease activity on fetal health, and the safety of medications during pregnancy and breastfeeding. Preconception counselling and risk stratification (including life style, disease activity, autoantibody profile, previous vascular and pregnancy morbidity, hypertension and the use of drugs with emphasis on benefits from hydroxychloroquine and antiplatelets/anticoagulants) are essential for prevention of unwanted complications during pregnancy. Recommendations for the management of family planning and antirheumatic treatment during pregnancy and lactation have been published recently by EULAR. However, many lupus patients still do not feel that their family planning concerns are adequately addressed in current clinical practice and report that they receive inconsistent advice from the various healthcare professionals. There is a clear need for provision of up-to-date and consistent information/support to our patients.
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SP0114 CHILDREN OF PATIENTS WITH RHEUMATIC DISEASES: ISSUES RELATED TO MATERNAL DISEASE AND TREATMENT

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A major source of anxiety for women with systemic autoimmune diseases (SADs) who wish to become pregnant is the possible impact of maternal disease and medications on the offspring, in terms of physical and mental development. A recent multicenter survey conducted in 24 Italian Rheumatology Centers showed that more than 50% women affected by SADs restricted their family size mainly because they were afraid that children could get an autoimmune disease or could be harmed by intrauterine exposure to maternal autoantibodies and anti-rheumatic drugs (Dall'Ara, ACR abstract, Arthritis Rheumatol 2016; 68, suppl 10). Therefore, the long-term follow-up children born to mothers with SADs is a topic of major relevance for the counselling on family planning.
First of all, it should be emphasized that preterm birth and other foetal complications, such as low birth weight and babies small for gestational age, are more common in patients with systemic autoimmune diseases as compared to the general population. These conditions carry themselves an increased risk for poorer physical and neuropsychiatric development. Therefore, the prevention of foetal complications should be operated by means of close obstetrical monitoring and tight control of maternal disease activity, which would be detrimental for foetal wellbeing. In this context, the use of "safe" anti-rheumatic drugs is of paramount importance for pregnant women with SADs.
Recently, a dedicated EULAR Task Force has released points to consider for the use of anti-rheumatic drugs during pregnancy and lactation (Gotestam Skorpen, Ann Rheum Dis 2016). The work of this Task Force was focused on updating the information about the use of "conventional synthetic" (cs) DMARDs but also to provide for the first time evidence-base indications on the use of "biologic" (b) DMARDs, mainly anti-TNFalfa agents.
No significant impairment in the maturation and functioning of the child's immune system has been observed for several csDMARDs, supporting their safety of use during pregnancy (Andreoli, J Autoimm 2012).
Turning to bDMARDs, a case-control study on the long-term follow-up of children exposed in utero to anti-TNFalfa drugs showed the safety of use either until the positive pregnancy index or during the second and third trimester of gestation (Dall'Ara, EULAR abstract, Ann Rheum Dis 2016; 75, Suppl 2:493). No differences between exposed and non-exposed children were found in terms of congenital defects, developmental milestones, response to vaccinations and major health problems. No particular problems were also observed in children who were breastfed while maternal anti-TNFalfa intake. The use of anti-TNFalfa agents during breastfeeding had been proposed to women who were strongly motivated based on the following considerations: 1) these drugs are poorly or absolutely not excreted into breast milk as recently demonstrated for certolizumab pegol (Clowse, ACR abstract, Arthritis Rheumatol 2016; 68, suppl 10); 2) even this was the case, the drug will be degraded in the baby's gastrointestinal tract and absorption could not be possible.
Regarding maternal disease, major concerns are linked to fetal exposure to maternal autoantibodies, mainly anti-Ro/SSA (for the development of Neonatal Lupus) and antiphospholipid antibodies (aPL). Therefore, the evaluation of these autoantibodies with potential negative impact on pregnancy and neonatal outcome should be part of the preconception work-up of women with SADs in order to provide adequate counselling and preventative strategies (Andreoli, Ann Rheum Dis 2017).

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