Epidemiologic studies have shown that not only fracture risk, but also mortality is increased after fracture, and that adequate therapy can not only decrease fracture risk but also increase survival.
Fracture risk is not constant over time. It is highest the years following a fracture, and immediately increases in some instances, such as after starting glucocorticoids or androgen deprivation therapy. This has raised the concept of "imminent" fracture risk, in contrast to long-term fracture risk as included in FRAX. In this context, we present the the EULAR initiative, in collaboration with EFORT, that published recommendations for multidisciplinary acute fracture care, including orthogeriatric care after hip fracture, and subsequent fracture prevention at the Fracture Liaison Service.
The presence, number and severity of vertebral fractures contribute to fracture risk, independent of BMD. Most vertebral fractures are subclinical and can therefore only be diagnosed by imaging of the spine. The role of vertebral fracture assessment (VFA) using DXA will be discussed.
New treatment insights will be reviewed, including for glucocorticoid users, combined and sequential treatments with anti-resorptive and bone forming drugs, real world data and the role of fall prevention.
Prescription of and adherence to treatment are still major issues. In patients adherent to therapy, new insights and recommendations will be reviewed on the need for early treatment, duration of treatment and the clinical approach when considering stopping drug therapy.
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## What is behind vasculitis?

### SP0131 AUTOIMMUNE ATHEROSCLEROSIS

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Arthritides have been associated with accelerated atherosclerosis to increased vascular disease risk. Traditional risk factors, as well as the role of systemic inflammation including cytokines, chamokines, proteases, autoantibodies, adhesion receptors and others have been implicated in the development of these vascular diseases. Accelerated atherosclerosis and increased cardio- and cerebrovascular morbidity and mortality have been observed in rheumatoid arthritis (RA) and spondyloarthropathies (SpA).
Endothelial dysfunction, overt atherosclerosis and vascular stiffness may be indicated by brachial artery flow-mediated vasodilation (FMD), common carotid intima-media thickness (ccIMT) and aortic pulse-wave velocity (PWV), respectively. These abnormalities have been described in most inflammatory rheumatic diseases. While ccIMT and stiffness are relatively stable, FMD may be influenced by many confounding factors.
In addition to traditional vasculoprotection, immunosuppressive agents including corticosteroids, traditional and biologic DMARDs may have significant vascular and metabolic effects. The official EULAR recommendations on the assessment and management of cardiovascular disease in arthritides have been published.
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### SP0132 VIRUSES DRIVING VASCULITIS

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Viruses have long been associated with varying forms of vasculitis in both pre-clinical models and human diseases. Immunopathogenic mechanisms have varied and include direct vascular invasion, immune complex mediated and more recently novel mechanisms which include autoinflammatory like responses. This discussion will review major advances in the field of medical virology as it applies to rheumatic diseases, especially vascular inflammatory disease, including an introduction to the human and more specifically vascular microviromes. Major forms of virally mediated vasculitis will be discussed with an emphasis on new viral vasculitis syndromes largely defined by next generation sequencing and their potential clinical impact.
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### SP0133 ANCA AND THEIR ENVIRONMENT

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The association between antibodies to neutrophil cytoplasm (ANCA) and systemic vasculitis has transformed our understanding of granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). ANCA undoubtedly play a major role in their pathogenesis. There are different forms of ANCA, but only two of direct clinical relevance: cytoplasmic c-ANCA (usually directed against proteinase 3, PR3), and perinuclear p-ANCA (usually directed against myeloperoxidase, MPO). P-ANCA can also be directed against other antigens including bactericidal/permeability-increasing protein, lactoferrin, human neutrophil elastase, cathepsin G and azurocidin, but their clinical significance is not clear.
Transfer of MPO ANCA in humans (maternal-foetal route) and animal models (necrotizing pauci-immune glomerulonephritis after passive transfer of purified antibody or splenocytes from MPO-deficient mice immunized with murine MPO) has resulted in features of MPA. By contrast, the pathogenicity of anti-PR3 antibodies is less well-established. There is a significant genetic predisposition to disease in patients with AAV. Patients with PR3-ANCA have a strong association with HLA-DP and genes encoding alpha-1-antitrypsin and proteinase 3; by contrast, patients with MPO-ANCA have an association with HLA-DQ. Other factors that could interact with ANCA include: loss of B cell and T cell tolerance; direct involvement by neutrophils and their mediators in vascular injury and damage, degranulation and cytokine production; environmental exposure to silica or certain strains of Staphylococcus aureus, coupled with a lack of effective T cell regulation to prevent inflammation. Neutrophils spontaneously release of neutrophil extracellular traps (NETS), which directly cause endothelial cell damage and complement activation. NETS retain proteinase 3 and myeloperoxidase, helping to break immune tolerance and inducing antibody formation. The alternative complement pathway plays a crucial role in the pathogenesis of AAV. Activated neutrophils produce C5a, which in addition to recruitment, primes additional neutrophils for further activation by ANCA. C3a, C5a, soluble C5b-9 are elevated in active disease and plasma levels of complement factor H, a regulator of the alternative complement pathway is significantly lower in patients with active AAV.
Central to the pathogenesis of AAV is a dysregulated immune response to ANCA and aberrant expression of their target autoantigens, MPO and PR3. Environmental exposure to silica may inactivates $\alpha$1-antitrypsin, whilst activating monocytes and macrophages releasing cytokines such as interleukin-1 and TNF-$\alpha$, oxygen radicals and lysosomal enzymes (such as PR3 and MPO). Other environmental interactions include CpG-ODN, a short synthetic DNA containing unmethylated CpG and several drugs, especially propylthiouracil and levamisole-adulterated cocaine. Some of these associations could provide a better insight into the development of ANCA associated disease.
ANCA play a central role in the pathogenesis of systemic vasculitis, supported by a dysregulated immune system, with significant interactions with micro-organisms, environmental toxins and drugs, all of which can contribute to the development and severity of disease.
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## Cytokine taxonomy: reflection in the therapy of arthritides and other IMIDs

### SP0134 INTERLEUKIN-2 THERAPY IN SLE

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There is an unmet need for more effective and selective therapeutics in severe autoimmune diseases such as systemic lupus erythematosus (SLE). A deeper understanding of the pathogenic mechanisms in the past has led to the clinical translation of low-dose interleukin-2 (IL-2) therapy which primarily aims to restore the activity of regulatory T cells. First results from phase I/II studies are promising by proving the selective expansion of regulatory T cells *in vivo* and by providing first evidence for the clinical efficacy of low-dose IL-2 therapy in SLE. Here we will summarize key findings which led to the development of this novel therapeutic concept and will highlight the main rationales for the clinical translation of low-dose IL-2 therapy in SLE.
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## Regulatory molecules in connective tissue

### SP0135 MYOSTATIN, SCLEROSTIN, SYNDECAN AND MORE

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Rheumatoid arthritis (RA) is the prototype of an inflammatory arthritis that is characterized by chronic inflammation, progressive cartilage destruction and bone erosion. Development of RA is marked by the hyperplasia of the synovial membrane as caused by an infiltration and accumulation of inflammatory cells such as macrophages and lymphocytes as well as an increase in the number of resident mesenchymal cells. These fibroblast-like synoviocytes (FLS) are a key part of the local immune system in the joints and integrate signals