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FM 1

Inflammatory role of ASC in antigen-induced arthritis is independent of caspase-1, NALP-3 and IPAF

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Introduction: As IL-1b plays an important role in inflammation in human and murine arthritis, we investigated the contribution of the inflammasome components ASC, NALP-3, IPAF and caspase-1 to inflammatory arthritis.
Methods: We first studied the phenotype of ASC-deficient mice (–/–), (+/–), and wild-type (+/+) mice during Antigen-Induced Arthritis (AIA).
Results: ASC–/– mice showed reduced severity of AIA, decreased levels of synovial IL-1b and diminished SAA levels. In contrast, mice deficient in NALP-3, IPAF or caspase-1 did not show any alteration of joint inflammation, thus indicating that ASC's effects on AIA are independent of the classical NALP-3 or IPAF inflammasomes. Because ASC is an ubiquitous cytoplasmic protein that has been implicated in multiple cellular processes, we explored other pathways through which ASC may modulate inflammation. Antigen-specific proliferation of lymph node and spleen cells from ASC-deficient mice was significantly decreased in vitro, as was the production of IFN-g, while IL-10 production was enhanced. TCR-CD3 ligation by anti CD3 antibodies induced a reduction in T cell proliferation in ASC–/– T cells compared to wild-type ones. In vivo lymph node cell proliferation was also significantly decreased in ASC–/– mice, but no effects on apoptosis were observed either in vitro or in vivo in these mice.
Conclusion: These results strongly suggest that ASC modulates joint inflammation in AIA through its effects on cell-mediated immune responses but not via its implication in inflammasome formation.

FM 2

The long-term impact of early treatment of rheumatoid arthritis

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Introduction: Treatment of rheumatoid arthritis (RA) has evolved towards a more aggressive therapeutic approach with early initiation of disease-modifying antirheumatic drugs (DMARD). While early initiation of DMARDs is effective in controlling progressive short-term joint damage, the long-term effect on disease progression is still debated.
Objective: To examine the long-term benefit of early initiation of DMARD therapy on the rate of radiographic damage progression in early RA.
Methods: We performed a cohort study within the Swiss RA registry (SCQM-RA). The SCQM-RA monitors disease activity, radiographic damage, patient characteristics and various symptom questionnaires at regular intervals. Joint erosions (ERO) were assessed in 38 joints of hands and feet with a validated scoring method (Ratingen score) by a single experienced reader, blinded to clinical history and are expressed in % of the maximum damage score. Inclusion criteria were enrollment in the SCQM-RA at the time of first DMARD initiation (baseline) and therapy with conventional, synthetic DMARDs. Exclusion criteria were incomplete data on RA symptom onset or absence of sequential X-rays. Patients were dichotomized according to RA symptom duration at DMARD initiation: "EARLY DMARD" if antirheumatic drugs were initiated within ≤1 year of symptom onset versus "LATE DMARD" if antirheumatic drugs were initiated after 1–5 years of symptom onset. The rate of ERO progression was analysed using a multivariate longitudinal regression model. We adjusted for differences in estimated baseline rates of radiographic damage progression, baseline disease activity (DAS28), baseline functional disability (HAQ), type of DMARDs, use of concomitant glucocorticoids, presence of rheumatoid factor, sex, age, and education level.
Results: 970 RA patients, with an average of 3 sequential X-rays and 4 years of follow-up were included. 368 patients in the EARLY DMARD group initiated their first DMARD after median symptom duration of 6 months, while 602 patients in the LATE DMARD group started their first DMARD only after 2.5 years. As expected, patients in the EARLY DMARD group had less radiographic damage at baseline, but with higher estimated baseline rates of radiographic damage progression than patients in the LATE DMARD group. Other important risk factors of disease progression such as rheumatoid factor seropositivity or methotrexate use did not differ between groups. After adjusting for differences in prognostic factors, we found a significant increase in long-term rates of ERO progression in patients initiating DMARDs later compared to earlier (p = 0.029). The ERO progressed at an annual rate of 0.59% (95% CI: 0.47–0.72) in the LATE DMARD group versus 0.41% (95% CI: 0.30–0.53) in the EARLY DMARD group.
Conclusion: These results support the notion of a therapeutic window of opportunity early in the course of RA with a sustained benefit on radiographic progression, and suggest that prompt initiation of DMARD therapy in RA has the potential to change the long-term course of the disease.

FM 3

Bone Micro-Architecture Assessed by TBS Predicts Hip, Clinical Spine and All Osteoporotic Fractures Independently of BMD in 22,234 Women aged 50 and Older: The Manitoba Prospective Study

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Introduction: BMD as assessed by DXA constitutes the gold standard for osteoporosis diagnosis. However, it does not take into account deterioration in bone micro-architecture. Trabecular Bone Score (TBS), a new grey-level texture measurement that can be extracted from the DXA image, correlates with 3D parameters of bone micro-architecture. Previous cross-sectional studies reported the ability of spine TBS to discriminate fractured women from age- and BMD-matched controls. The aim of our study was to prospectively evaluate the ability of lumbar spine TBS to predict osteoporotic fractures.
Methods: 22,234 women age 50 years and older at the time of baseline hip and spine DXA were identified in a database containing all clinical results for the Province of Manitoba, Canada. Health service records were assessed for the presence of non-trauma osteoporotic fracture codes subsequent to BMD testing. Lumbar spine TBS was derived by the Bone Disease Unit, University of Lausanne, for each spine DXA examination using anonymized files (blinded from clinical parameters and outcomes). We used Cox proportional hazard regression to model the hazard of first hip, spine or any osteoporotic fracture (hip, clinical spine, humerus, forearm). Age-adjusted HRs for fracture per SD decrease in TBS and/or BMD are reported. Incremental gain in prediction information when TBS was added to age and BMD was assessed using the log-likelihood ratio test (LLR).
Results: The mean age of the population was 65.0 ± 9.5 y and the numbers of fractures during mean 4.6 y of follow up were: all osteoporotic 946 (4.3%), hip 194 (0.9%) and clinical spine 297 (1.3%). Significantly lower spine BMD, total hip BMD and spine TBS parameters were found in fracture than non fracture women for all fracture definitions (all p <.0001). Correlation between spine BMD and spine TBS was modest (r = .32) and less than correlation between spine and hip BMD (r = .72), consistent with a skeletal parameter largely unrelated to BMD. Spine BMD and TBS predicted fractures equally well and independently. Total hip BMD was the best predictor of hip fracture but addition of spine TBS significantly improved hip fracture prediction.
Conclusion: We have demonstrated that spine TBS predicts fractures (hip, clinical spine and all osteoporotic). Furthermore, TBS provided information that was independent of spine and hip BMD. Combining the TBS micro-architecture index with BMD from conventional DXA incrementally improved fracture prediction in postmenopausal women.

		Clinical Spine Fractures HR / SD (95% CI)	P	Hip Fractures HR / SD (95% CI)	P	All Osteoporotic Fractures HR / SD (95%CI)	P
Univariate	DXA Hip	1.70 (1.48–1.95)		2.98 (2.53–3.51)		1.79 (1.67–1.93)	
	DXA Spine	1.49 (1.31–1.70)	N/A	1.53 (1.31–1.78)	N/A	1.53 (1.43–1.64)	N/A
	TBS Spine	1.42 (1.26–1.60)		1.50 (1.31–1.72)		1.34 (1.26–1.43)	
Combined	DXA Hip	1.59 (1.39–1.83)	<.0001	2.78 (2.35–3.29)	.0060	1.70 (1.58–1.83)	<.0001
	TBS Spine	1.33 (1.18–1.51)		1.24 (1.07–1.43)		1.23 (1.15–1.31)	
Combined	DXA Spine	1.37 (1.20–1.58)	<.0001	1.38 (1.18–1.62)	<.0001	1.44 (1.34–1.55)	<.0001
	TBS Spine	1.32 (1.17–1.50)		1.39 (1.21–1.61)		1.23 (1.15–1.31)	

All models are age-adjusted. P value is for improvement in model fit when TBS added to BMD and age.

P 1

Rituximab in Rheumatoid Arthritis: Evidence for a Learning Curve by Rheumatologists

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Introduction: The very long duration of response makes Rituximab (RTX) an attractive therapeutic option for rheumatoid arthritis (RA), but the timing of RTX re-treatment is not yet well established. Most rheumatologists currently use a flexible re-treatment approach as opposed to fixed interval re-treatment. Because the therapeutic management of RTX is unique among DMARDs, rheumatologists need to gain some experience in order to become effective at handling patients treated with this agent.
Objective: To describe patterns of RTX re-treatment in current practice and examine potential trends.
Methods: All patients in the Swiss RA cohort receiving RTX were included. RTX could subsequently be repeated, according to the rheumatologist's opinion. Time to RTX re-treatment was analysed using survival analysis. The evolution of DAS28 was analysed using longitudinal regression models. RA disease flare was operationally defined as an increase of >0.6 DAS28 units or an absolute DAS28 level above 5.2, four months (Mo) after RTX infusion.
Results: A total of 265 retreatment courses in 278 RA patients were analysed. The median time to re-treatment after the 1st RTX cycle was 10.9 months (IQR: 6.4–12.6), and the duration of the following RTX cycles was similar. We observed a significant trend for shorter time to re-treatment in more recent calendar years ($p < 0.001$): 11.9 Mo (IQR: 6.7–19.1) before 2006, 9.4 Mo (IQR: 6.3–11.3) in 2007 and 7.8 Mo (IQR: 5.6–9.0) in 2008. A similar trend was apparent for DAS28 levels at RTX re-treatment, which decreased over time and with successive re-treatments. Overall, at time of re-treatments 57% of patients had evidence of an RA flare. The delay between first evidence of flare and re-treatment was 3 months (IQR 0.2–9.4).
Conclusion: Time to RTX re-treatment has shortened in recent years, suggesting that rheumatologists have fine-tuned their treatment practice. Yet, a majority of patients still present evidence of disease flares at time of re-treatment, which is probably suboptimal for patients. These results suggest that DAS28 levels should be monitored carefully in order to optimize the timing of RTX retreatment.

P 2

Progression of radiographic joint damage in alcohol drinkers versus non-drinkers: should patients with Rheumatoid Arthritis cease drinking?

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Background: Alcohol consumption has recently been found to have a protective effect on the development of rheumatoid arthritis (RA) [1]. However, it remains unknown whether RA patients who drink alcohol have less severe disease progression over time than non-drinkers.
Objective: To compare the rates of radiographic progression in alcohol drinkers (D) and in non-drinkers (ND) in a large prospective RA cohort.
Methods: All patients in the Swiss Clinical Quality Management in Rheumatic Diseases RA registry database with sequential X-rays were included. Joint erosions were assessed in 38 joints of hands and feet with a validated scoring method (Ratingen score) by a single experienced reader, blinded to clinical history and expressed as a percentage of the maximum damage score. The rate of erosive progression was analysed using a multivariate longitudinal regression model.
Results: 2908 RA patients with a median of 4 sequential X-rays and 4 years of follow-up were included. The 1824 D (62.7%) were more often male, younger, smokers, had shorter disease durations, lower DAS28 and HAQ scores, and consequently had less joint erosions at baseline than the ND. After adjusting for differences in baseline prognostic factors, we found a trend towards a reduced rate of radiographic progression in D compared to ND (0.99 v 1.13, $p = 0.058$). In sub-group analyses, a trend for a more favorable evolution existed in the "occasional" consumers (0.99 v 1.13, $p = 0.096$) and the "daily" consumers (0.92 v 1.13, $p = 0.087$), whereas there was no benefit in the "heavy consumers" (1.29 v 1.13, $p = 0.511$). Male D had significantly reduced progression when compared to male ND (0.86 v 1.35, $p < 0.01$).
Conclusion: A trend towards reduced radiographic progression was observed in D compared to ND, particularly in occasional and daily alcohol consumers. There was a significant protective effect of alcohol on radiographic progression in male RA patients. The clinical significance of these effects is unknown given the relatively small effect size. While a dose-dependent effect was not observed, it may be that low to moderate alcohol consumption is of benefit, as in cardiovascular disease.
Reference: 1 Källberg H, et al. Ann Rheum Dis. 2009;68:222–7.

P 3

Tender papulo-nodular skin eruption in a patient with rheumatoid arthritis

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A 47-year-old patient with a two-year history of erosive rheumatoid arthritis was referred to hospital for evaluation of a non tender papulo-nodular skin eruption with dozens of lesions on the face and trunk of three months duration, rapidly progressive in the last month. Some of the nodules were ulcerated and covered by crusts. From the beginning, RA had been treated with methotrexate weekly 15 mg s.c. Due to inadequate response, etanercept 50 mg weekly s.c. was added after five months. Seven months later etanercept was replaced by infliximab, 3 mg/kg every 8 weeks because of new radiographic erosions. After 4 months infliximab was increased to 5 mg/kg because of persisting joint pain and synovitis. At admission RA was mildly active with four swollen joints and tenosynovitis of the right extensor carpi ulnaris. Cardiovascular, pulmonary, gastrointestinal and neurological examinations revealed no pathologic findings. ESR was 19 mm, full blood count, serum chemistry, urine examination and repeated blood cultures were normal. IFN-^{3} stimulation test (Quantiferon®) was positive. High resolution CT of the chest showed a lesion in the right posterior upper lobe, which was unchanged compared to 6 months previously. A bronchoscopy with lavage showed no evidence of a mycobacterial infection. Cultures of a skin biopsy were negative for mycobacteria, actinomyces, nocardia and fungi. Conventional histology of a skin nodule showed granulomatous inflammation with histiocytes containing small intracellular bodies. The diagnosis was confirmed by PCR, which showed the subspecies Leishmania infantum. Treatment was with meglumine antimoniate intramuscularly for 28 days. The skin lesions resolved, and the IFN-^{3} stimulation test became negative. The travel history included trips to Mexico, Tuscany and Egypt. Since L. infantum does not occur in Mexico and is endemic in Tuscany and Egypt our patient was most likely infected in either of the latter places. The time point of the infection cannot be precisely determined, though was probably years ago. The cutaneous eruption is likely due to reactivation of the latent infection after infliximab was increased to 5 mg/kg. Our case is the first to be described with disseminated cutaneous leishmaniasis due to L. infantum.

P 4

Induction of IL-1β maturation by basic calcium phosphate crystals in macrophages

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Introduction: Inflammatory crystals such as monosodium urate (MSU) and calcium pyrophosphate dihydrate (CPPD) have been associated to gout and chondrocalcinosis respectively and have been previously reported to induce Il-1β activation via a caspase-1 dependent mechanism, involving the inflammasome. Basic calcium phosphate (BCP) crystals, including hydroxyapatite (HA), octacalcium phosphate (OCP) and carbonate-apatite (CA), have been associated with severe osteoarthritis and several degenerative arthropathies, but their role in Il-1β activation is still unknown.
Methods: To investigate whether BCP crystals induced Il-1β activation, differentiated THP1 cells were cultured in the presence or absence of OCP, HA, and CA crystals at various concentrations (10–750 µg/ml).
Results: All three crystal types stimulated secretion of Il-1β in a dose-dependent fashion (at 100 µg/ml: OCP: 987.37 ± 33.93 pg/ml, HA: 1114.06 ± 80.88 pg/ml, CA: 954.03 ± 50.30 pg/ml). Moreover, BCP crystal stimulation was more efficient compared to MSU and CPPD (at 100 µg/ml OCP: 987.37 ± 33.93 pg/ml, MSU: 323.03 ± 12.90 pg/ml, CPPD: 399.73 ± 22.82 pg/ml). In THP-1 cells deficient for caspase-1, OCP, HA and CA induction of Il-1β secretion were decreased, compared to THP-1 mock cells (mock cells at 100 µg/ml: OCP: 1838.42 ± 40.7 pg/ml, HA: 636.32 ± 56.14 pg/ml, CA: 378.07 ± 31.35 pg/ml, Caspase-1 deficient cells at 100 µg/ml OCP: 1096.32 ± 56.84 pg/ml, HA: 39.82 ± 13.57 pg/ml, CA: 30.70 ± 10.29 pg/ml), demonstrating that inflammasome is involved in BCP induced-Il-1β maturation.
Conclusion: These results indicate that BCP crystals strongly induce Il-1β maturation. Therapeutical strategies based on Il-1β blockade may represent future avenues in the management of severe arthropathies associated with BCP crystals.

P 5

Role of ASC in T cell Activation and Effector Function

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Background: Apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) is an adaptor protein that is essential for the recruitment of pro-capase-1 into inflammasomes and thus plays a key role in regulating capase-1-dependent IL-1β and IL-18 production. Although the proinflammatory role of ASC-dependent inflammasomes is now widely acknowledged, the requirement for ASC inflammasomes in the generation of adaptive immune responses is less clear. Despite recent evidence implicating ASC in adaptive immunity against certain viral infections 1, hyperresponsiveness 2 and vaccination 3, the cellular and molecular basis for the involvement of ASC in adaptive immune responses remains largely unexplored.
Aim: To investigate the impact of ASC on T cell activation and subsequent effector function.
Methods: ASC+/+ and ASC–/– T cells or purified CD4+ and CD8+ T cells were activated in vitro through anti-CD3 stimulation and their proliferative potential and cytokine profiles characterized.
Results: Proliferative responses by ASC–/– T cells were significantly inhibited following TCR-CD3 ligation when compared to ASC+/+ T cells. Furthermore, cytokine analysis revealed that anti-CD3 activated ASC–/– T cells predominantly displayed a more Th2 phenotype, producing more IL-10 and less IFN-γ. When ASC+/+ and ASC–/– T cells were purified into CD4+ and CD8+ T cell fractions and activated individually using anti-CD3, no inhibition in proliferation was observed amongst activated ASC–/– CD4+ and CD8+ T cells. Interestingly, the activated ASC–/– CD4+ T cell fraction produced significantly more IL-10 (and less IFN-γ) when compared to activated ASC–/– CD8+ T cells and ASC+/+ CD4+ and CD8+ T cells. CD4+ and CD8+ T cell mixing experiments revealed that ASC–/– CD4+ T cells are able to inhibit the proliferative ability of ASC–/– CD8+ T cells and ASC+/+ CD4+ and CD8+ T cells in vitro and that this suppression appears to be mediated by a soluble factor secreted by activated ASC–/– CD4+ T cells.
Conclusion: Collectively, these results demonstrate that the absence of ASC drives CD4+ T cells towards a suppressor cell phenotype, suggesting that ASC might play an important role in determining the fate of CD4+ T cells.

P 6

Analysis of inflammasome expression in arthritic synovium

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Introduction: The inflammasome regulates the processing of pro-inflammatory cytokines, including IL-1b, IL-18 and IL-33 and has been shown to play a role in the pathophysiology of acute inflammatory disorders. Little information is available concerning its expression in the synovium and its activity in chronic inflammatory diseases such as RA.
Methods: The synovial distribution of NALP3 and ASC, components of the inflammasome, was studied by immunostaining. The expression of other members of the NLR family of proteins, ASC, caspase-1 and -5 was studied in synoviocyte cell lines (N = 8) established from biopsies obtained from RA and OA patients using RT-PCR and immunohistochemistry. Synovial cell lines were tested for their ability to produce active IL-1b when stimulated by LPS and MSU. The expression of different components of the inflammasome in RA and OA synovia was compared by western blotting and the levels of synovial caspase-1 and IL-1b measured by ELISA.
Results: In human synovium, both NALP3 and ASC were widely expressed, with the exception of CD3 cells that lacked NALP3 expression. Synovial fibroblast lines generated from RA and OA patients lacked NALP3 and could not be induced to produce mature IL-1b when stimulated with known activators of the NALP3-inflammasome. Comparison of expression of NLRs by RT-PCR failed to show any difference between RA and OA samples, and this was confirmed by western blotting of NALP1, -3, -12 and ASC proteins. However, RA synovia contained significantly higher concentrations of caspase-1.
Conclusions: The expression of NALP3 and ASC is generalized within the synovium and does not show disease specificity between OA and RA. As synovial fibroblasts do not express NALP3, the major source of this protein is likely to be leukocytes and endothelial cells. The higher levels of caspase-1 in RA synovia suggests that other (non-NALP3) inflammasomes may be active and contribute to synovial production of IL-1b in RA.

P 7

Do circulating γδ T cells play a role in pregnant patients with rheumatic diseases?

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Objective: γδ T cells are known to expand at the fetomaternal interface during pregnancy where they induce a tolerogenic milieu. In a prospective study we investigated whether numerical and functional changes of circulating γδ T cells were associated with changes of disease activity observed during pregnancy and post partum in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS).
Methods: Numerical and functional alterations of circulating γδ T cells were investigated in 14 RA patients, 11 AS patients and 14 healthy women once in each trimester and 8 weeks post-partum. The frequency and the intracellular cytokine profile of freshly isolated γδ T cells were analysed by FACS. The phosphoantigen-specific cytokine response of isolated γδ T cells was measured by multiplex cytokine assay.
Results: We demonstrate that the proportion of circulating Vγ9Vδ2 T cells was significantly reduced during pregnancy as compared to the number found 8 weeks post-partum. By contrast, circulating Vδ1 T cells tended to increase in the third trimester and decreased after delivery. These effects were more pronounced in patients than in healthy controls. Moreover, the intracellular cytokine staining revealed a reduced proportion of IFNγ positive Vδ2 T cells in the third trimester compared to 8 weeks post-partum. Upon IPP stimulation γδ T cells isolated during pregnancy produced significantly less IFNγ compared to those isolated in the post-partum period. The percentages of Vγ9Vδ2 T cells correlated with disease activity during and after pregnancy.
Conclusion: The amelioration of disease activity in the third trimester corresponded to the decrease of IFNγ producing Vδ2 T cells. As an epiphenomenona, pregnancy is able to partly suppress cytotoxic Vδ2 T cells and thereby contribute to the mitigation of symptoms in a Th1-biased disease.

P 8

One-year results of canakinumab (ACZ885), a fully human anti-IL-1beta monoclonal antibody in patients with cryopyrin-associated periodic fever syndrome (CAPS)

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Background: CAPS is driven by dysregulated production of IL-1beta, resulting in systemic inflammation with a risk of AA amyloidosis and end stage renal failure as well as progressive disability. Canakinumab offers potent, selective and sustained blockade of IL-1beta.
Objectives: To evaluate the efficacy and safety of canakinumab in CAPS patients over a one year period.
Methods: In this 3-part, multicenter study, CAPS patients with *NLRP3* mutations received one initial dose of canakinumab 150 mg sc or 2 mg/kg (patients ≤40 kg) [Part 1]; after 8 weeks complete and sustained responders were randomized to canakinumab 150 mg or placebo every 8 weeks for 24 weeks [Part 2]. After completion or disease relapse in Part II, patients received open-label canakinumab every 8 weeks [Part 3]. The primary efficacy objective was to compare the proportion of patients with flares (disease relapse/discontinuation) on canakinumab *vs* placebo in Part II. Secondary efficacy variables included proportion of patients without disease relapse in Part 3 and change in CRP, SAA levels, safety and tolerability. Response and relapse were defined as composites of clinical (physician's global and skin disease) and serologic (CRP/SAA) markers.
Results: In part 1 34/35 (97%) patients achieved a complete response after a single dose of canakinumab. Most patients responded rapidly, 25/35 (71%) achieved complete remission by day 8. Thirty-one patients entered part 2 of whom the 15 receiving canakinumab remained in remission; disease flares occurred in 13/16 (81%) patients receiving placebo (P <0.001). Mean CRP and SAA values at the end of part 2 were normal (both <10 mg/L) in patients receiving canakinumab but were elevated in those receiving placebo (P ≤0.002). All 31 patients proceeded to study part 3 and 29 (94%) completed the study. Clinical and biochemical remission was sustained in 28 of 29 patients (97%) who completed the study. Two serious adverse events occurred: one case of uorsepsis and an episode of vertigo.
Conclusion: Canakinumab every 8 weeks induced rapid and sustained clinical and serological remission in CAPS patients with a good safety and tolerability profile during one year treatment.

P 9

Parenteral nutrition in severe gastrointestinal manifestation of scleroderma

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Introduction: We report the case of a 64-year-old female with an 8 year history of systemic sclerosis consecutively involving skin, heart, lungs, kidneys and intestine. After 2 years of intensive episodes of diarrhoea, cyclic antibiotics and prolonged weight loss, she presents with malnutrition, severe dehydration, vomiting, dizziness and abdominal pain due to acute pseudoobstruction of the large intestine in March 2008.
Methods: After acute management a Hickman catheter is inserted into the right subclavian vein. The patient is started on continuous parenteral nutrition. Diarrhoea is reduced, she starts a slow oral refeeding. After acute recovery she continues on home parenteral nutrition with 1.5 liter infusions containing 1600 kcal each during 15 hours overnight on 5 of 7 days a week allowing for additional oral food. Infusion service is rendered by home care service. Controls of laboratory parameters including infection status are established weekly.
Results: Weight gain and rehabilitation are sufficient, there is no volume overload, no catheter infection or obstruction (please see table). Parenteral volume is reduced to 1 liter on 4 of 7 days a week due to sufficient nutrition and slight elevation of liver enzymes. Trace elements have to be adjusted.

		March 2008	April 2009
BMI	[kg/m²]	18.6	23.5
diarrhoea	[frequency/day]	25	15
serum-albumin	[g/l]	28	42
hemoglobin	[g/l]	85	103
creatinine-clearance	[ml/min]	<30	44

Conclusions: Home parenteral nutrition is a safe and successful option in rehabilitation of severe scleroderma-associated gastrointestinal manifestation indicating prolonged survival and increased quality of life despite otherwise poor prognosis.
References: 1 Steen VD, et al. Ann Rheum Dis. 2007;66(7):940–4. 2 Brown M, et al. Rheumatology. 2008;47(2):176–9. 3 Sallam H, et al. Aliment Pharmacol Ther. 2006;23(6):691–712.

P 10

Low-dose radiotherapy of sacroiliac joint arthritis: a case report

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Introduction: Successful treatment with low dose fractionated ionizing radiation of a patient with refractory rheumatoid arthritis of the sacro-iliacal joint.
Methods: The 41-year-old female patient suffers from an undifferenciated rheumatoid arthritis since 06/05. Symptom control including pain reduction of the peripheral arthritis with sustained treatment of Methotrexat (MTX), Remicade and Aredia. Persistent symptoms of the axial SI-joint. Patient stopped working due to the persistent lower back pain. Therefore symptomatic low dose fractionated ionizing radiotherapy was indicated using our standardised RT-regimen of 6 × 0.3 Gy = 1.8 Gy, twice a week with 6 MeV photons and CT-based 3-D planning. Treatment response was documented with a standardised pain score and repeated MRI scans.
Results: Radiation was applied as planned. A two level response pattern was observed with initial pain increase for 3 months followed by steady pain decrease over the next 2 month without changes in the basic antirheumatoid medication and a steady reduction of the pain medication. MRI documented the treatment success. By 04/09 the patient was almost symptom free and able to work.
Conclusion: The low dose radiotherapy regimen was an effective and longlasting treatment for the affected SI-joint. Concurrent MTX might be one reason for the acute and prolonged reaction of the infield connective tissue to low doses RT.

P 11

Functional Capacity Evaluation in chronic low back pain associated to pain evaluation after rehabilitation

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In situations with chronic low back pain, lifting is said to be on of the major risk factors associated with the work conditions. Several programs have been proposed to treat this problem, but the outcome is difficult to predict without an evaluation of work capacity, associated to the pain progression. We have already presented a simplified functional capacity measuring that we use daily in practise, but how does it fit to the prediction of work ability, and the return to work after rehabilitation.
Method: 340 patients have been evaluated on this base. The majority was referred to multidisciplinary rehabilitation treatment. The patients had recurrent back problems. Inclusion criteria were between 18 and 64 years, currently of work – but for less than 8 months – no work compensation. Exclusion criteria were chronic low back pain with a specific cause. They followed an outpatient rehabilitation program associated with a one-hour evaluation test as a functional capacity evaluation at the end, it was compared to the pain evaluation.
Results: We included 340 subjects: 180 men and 160 women. We studied the caring foot-hip, hip-shoulder, 5 meter carrying, pushing and tiring and the global weight carried during the test. The increase of the global weight had a clear incidence on a greater work ability, as had a decrease. In association the pain evaluation decreased.
Conclusions: We were able to confirm that the our easy lifting capacity program gave an idea on how to reorient the patients according to their work place and their capacities. We also have an information on the pain evaluation. It should be more tested and compared to standard capacity in the healthy population.

P 12

An examination chair to measure internal rotation of the hip in routing settings: a validation study

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Introduction: A limited range of motion (ROM) is a standard criterion of the American College of Rheumatology in the assessment of hip osteoarthritis, with internal rotation of <15° considered pathological. For clinical and epidemiological studies, exact measurement of internal rotation is important. We developed a new examination chair to measure internal rotation and compared it to clinical examination.
Methods: The examination chair allows measurement of ROM of internal rotation in a sitting position, with the hips and knees flexed 90° and the lower legs unsupported over the edge of the bed. A constant load of 5 kg was applied to both ankles and internal rotation of the two hips was measured by a goniometer. Clinical examination of ROM was measured in the supine position using a goniometer, the hip and the knee flexed to 90°. Inter-observer reliability was assessed using intra-class correlation coefficients (ICC) in a first sample of 84 consecutive participants of a large population-based inception cohort of young male individuals. A second sample of 64 participants was evaluated for the comparison of the two examinations, using Pearson correlation coefficients.
Results: Inter-observer reliability of the examination chair was excellent for both hips with ICC = 0.92 (95% CI 0.89 to 0.95) for the right hip and 0.90 (95% CI 0.86 to 0.94) for the left, and significantly higher when compared to the clinical examination (ICC's of 0.65 [95% CI 0.49 to 0.77], p <0.001 for the right hip and 0.69 [95% CI 0.54 to 0.80], p = 0.001 for the left). ROM of internal rotation was similar between methods, with differences of 0.9° (95% CI –1.6 to 3.3) for the right and 1.2° (95% CI –1.2 to 3.6) for the left hip. The correlation between the two methods was 0.75 for both hips.
Conclusion: A newly developed examination chair is a reliable and accurate tool to measure ROM of internal rotation. This can be useful for preclinical and clinical screening and also for epidemiological studies.

P 13

Have all the men and women with a fragility fracture a low bone mineral density? A Nationwide Swiss Survey

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Background: The prevalence of a low bone mineral density (T-score ≤–1 SD) in postmenopausal women with a fragility fracture may vary from 70% to less than 50%. In one study (Siris ES. Arch Intern Med 2004;164:1108–12), the prevalence of osteoporosis was very low at 6.4%. The corresponding values in men are rarely reported.
Methods: In a nationwide Swiss survey, all consecutive patients aged 50+ presenting with one or more fractures to the emergency ward, were recruited by 8 participating hospitals (University Hospitals: Basel, Bern, and Lausanne; cantonal hospitals: Fribourg, Luzern, and St Gallen; two regional hospitals: Estavayer and Riaz) between 2004 and 2006. Diagnostic workup was collected for descriptive analysis.

Results: 3667 consecutive patients with a fragility fracture, 2797 women (73.8 ± 11.6 years) and 870 men (70.0 ± 12.1 years), were included. DXA measurement was performed in 1152 (44%) patients. The mean of the lowest T-score values was –2.34 SD in women and –2.16 SD in men. In the 908 women, the prevalence of osteoporosis and osteopenia according to the fracture type was: sacrum (100%, 0%), rib (100%, 0%), thoracic vertebral (78%, 22%), femur trochanter (67%, 26%), pelvis (66%, 32%), lumbar vertebral (63%, 28%), femoral neck (53%, 34%), femur shaft (50%, 50%), proximal humerus (50%, 34%), distal forearm (41%, 45%), tibia proximal (41%, 31%), malleolar lateral (28%, 46%), malleolar median (13%, 47%). The corresponding percentages in the 244 men were: distal forearm (70%, 19%), rib (63%, 11%), pelvis (60%, 20%), malleolar median (60%, 32%), femur trochanter (48%, 31%), thoracic vertebral (47%, 53%), lumbar vertebral (43%, 36%), proximal humerus (40%, 43%), femoral neck (28%, 55%), tibia proximal (26%, 36%), malleolar lateral (18%, 56%).
Conclusion: The probability of underlying osteoporosis or osteopenia in men and women aged 50+ who experienced a fragility fracture was beyond 75% in fractures of the sacrum, pelvis, spine, femur, proximal humerus and distal forearm. The medial and lateral malleolar fractures had the lowest predictive value in women, not in men.

P 14

Clinical effectiveness of an interdisciplinary pain management program as compared with standard inpatient rehabilitation in chronic pain. A naturalistic, prospective controlled cohort study

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Introduction: It is often difficult for primary care providers to justify their decision to allocate patients to specific inpatient therapies after unsuccessful outpatient pain management. The aim of this study was to compare the effects of an interdisciplinary pain management program with those of standard inpatient rehabilitation.
Methods: In this naturalistic prospective controlled cohort study, 164 chronic pain patients who participated in the interdisciplinary pain program and 143 who underwent standard rehabilitation were assessed by standardized self-assessment instruments. Effect sizes (ES) were bivariately compared and analyzed by multivariate logistic regression to control for baseline differences in the outcome variables and confounders.
Results: On entry into the clinic, the interdisciplinary pain program patients were younger and showed significantly worse somatic, mental and psychosocial health than the standard rehabilitation patients. At discharge, the interdisciplinary treated patients reported greater improvement on pain (ES: 0.76 versus 0.61, multivariate p = 0.034), social functioning (ES: 0.52 vs 0.20, bivariate p = 0.009), and in trend in catastrophizing and ability to decrease pain. At the 6 month follow-up, the effects in pain (e.g., ES: 0.44 vs 0.36), catastrophizing, and decrease pain were still but not significantly higher in the interdisciplinary group while the standard rehabilitation group experienced higher effects on physical functioning (e.g., ES: 0.48 vs 0.32), social functioning , anxiety, and life control (multivariate p = 0.013 to 0.050).
Conclusion: Intensive interdisciplinary rehabilitation with more intense behavioral therapies was accompanied by greater improvement in severely affected pain patients compared with standard rehabilitation by the end of the stay but not in the mid-term. The highly resource-consuming patients may benefit from subsequent, individually tailored outpatient care.
Reference: Angst F, et al. J Rehabil Med. 2009;41:569–75.

P 15

Glycemic profile before and after epidural versus intra-articular infiltration of methylprednisolone in diabetic patients

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Background: Several studies have shown that in diabetic patients, the glycemic profile was disturbed after intra-articular infiltration of methylprednisolone. Little is known about the impact of epidural infiltration in such patients. Diabetic patients frequently reject the procedure for fear of a hyperglycemic decompensation.
Objectives: The goal of the study was to compare the glycemic profile of 10 diabetic patients after an epidural or intra-articular infiltration of 80 mg methylprednisolone.
Methods: Diabetes had to be stabile for more than ten days before the procedure. No change in the diabetic treatment was allowed during the study period. Blood glucose was measured with a continuous glucose monitoring system (CGMS by Medtronic) the day before and the 2 days following the infiltration. Epidural infiltration was performed via the sacral route under fluoroscopic control in order to ensure that the steroid was injected into the epidural space along the lumbar vertebral canal. Intra-articular infiltration was done according to standard procedure.
Results: In the 5 patients with peridural infiltrations we observed no significant change in glycemic profile (mean enhancement of: 0.2 mmol at day 1 and –0.5 mmol at day 2). However, the glycemic profile of patients who underwent intra-articular steroid injection was significantly modified (mean enhancement of: 1.8 mmol at day 1 and 2.9 mmol at day 2).
Conclusion: The absence of glycemic elevation after epidural infiltration suggests that contrary to intra-articular injections, methylprednisolone mostly remains locally in the epidural space and does not diffuse to the rest of the body. The procedure is therefore not contraindicated in diabetic patients.

P 16

Cost-effectiveness analysis of a 3-month exercise program vs. routine follow-up in patients who have completed functional multidisciplinary rehabilitation for low back pain

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Background: Chronic low back pain (CLBP) is a major health and socioeconomic problem in Western countries. Among the many treatment modalities, functional multidisciplinary rehabilitation (FMR) seems to be the best strategy [1]. Post-FMR, the patient traditionally manages the problem himself with his general practitioner.
Objective: The aim of this study was to evaluate the cost effectiveness of an exercise program vs. routine follow-up in CLBP patients who have completed FMR.
Methods: A cost effectiveness analysis was conducted alongside a randomized controlled trial. 105 CLBP patients who had completed a 3-week FMR were randomly assigned to a 3-month exercise program (EP) or routine follow-up (RF). EP consisted of 24 exercise sessions over 12 weeks. Quality of life was measured by the 36-item short-form health survey (SF-36). Direct and indirect costs were measured by means of cost diaries. Costs were assessed from a societal perspective. Significance was declared when P <0.05.
Results: The physical summary score of the SF-36 significantly improved over time for both groups. The improvement in the mental summary score was significant only for the EP group. However, no between group difference was found. From the start of FMR to 1-year follow-up, total costs were divided by 2–2.5 by both groups. The decreases in direct and indirect costs were significant for both groups.
Conclusion: The present results did not show superiority of PE over RF in CLBP patients who had completed a 3-week FMR in terms of quality of life improvement or cost saving. Both groups showed increased health outcomes together with decreased costs at 1-year follow-up. This underscores the good long term results of FMR alone, together with the need of better individualising exercises and identifying which patients need exercise supervision after FMR.
References: 1 Guzman J, et al. BMJ. 2001;322(7301):1511–6.

P 17

Osteoporotic fracture: a new collaboration with surgeons

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Introduction: Osteoporotic fractures represent a considerable and growing burden to patients, society and health-care financing. Although several initiatives in hospital setting (clinical pathway, guidelines, dedicated personnel for consulting) have been reported to improve clinical osteoporosis management, recent data from different countries, including Switzerland [1], have shown that after a low trauma fracture, osteoporosis remains frequently undiagnosed and untreated. In the best cases, only 10 to 25% of patients have an adequate diagnosis workup and are adequately treated. The creation of the DAL (Département de l'Appareil Locomoteur) at the CHUV in Lausanne was a good opportunity to create a specific bone disease unit and to implement a new concept based on a systematic handle of all patients during and after the hospitalization for osteoporotic fracture.
Methods: Thanks to the close collaboration with the traumatologic surgeons, medical doctors from the bone disease unit have a direct access to patients with suspected osteoporosis related fracture. Subsequently, patients admitted for a fragility fracture in the trauma unit are identified by a nurse according to a predefined questionnaire and are then clinically evaluated by the doctor. Upon the results of the clinical examination, a systematic adequate management is proposed to the patients (laboratory tests, DXA, calcium, vitamin D, specific antiosteoporotic drugs) and this, during the acute hospital stay. This management also included a follow-up proposition witch could be done by either the bone disease unit in the outpatient clinic of the DAL or by the usual practitioner of the patient. During the follow-up, clinical and biological parameters and adherence to the treatment are

evaluated. The impact on quality of medical care of these measures will be prospectively assessed.
Results: After 5 months, 250 consecutive inpatients (women 70%, men 30%, mean age 72 years, hip fractures 33%) were evaluated by our team (specific bone unit). Primilary results showed that the great majority of the patients have adhered to the diagnosis workup, the treatment and the follow up in the outpatient clinic. In addition, the level of satisfaction of patients was excellent. More detailed results will be presented (type of fracture, evaluation of biologic parameters during the hospital stay and after 3 months and one year, adherence to the treatment and the follow up). However, as today, we have already identified 2% of all inpatients with secondary cause of osteoporosis (multiple myeloma, metastasis, primary hyperparathyroidism), indicating the importance of clinical evaluation by a bone specialist.
Conclusion: This new approach based on direct and systematic management of patients likely suffering of osteoporotic related fracture, improved considerably the detection of patients at high risk. This approach is about to be extended to the ambulatory patients.
References: 1 ECCEO 2007 Osteoporosis is largely underdiagnosed and undertreated The 2-YEAR Lausanne Survey. O. Lamy[1], N. Simard[1], MA. Krieg[1], PF. O. Borens[2], Leyvraz[2]
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P 18

Allergic vs. non-allergic infusion reactions to infliximab – lessons from 3 instructional cases

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Introduction: Acute reactions during or immediately after infusion of infliximab are a common complication in about 3% of treated patients. Some reactions are highly suggestive of an IgE-mediated allergy. Because of the high risk of subsequent anaphylactic reactions in these patients despite premedication, infliximab should be strictly omited. A consistent differentiation between allergic and non-allergic complications is still lacking in current literature.
Cases: 3 consecutive female patients aged 28, 33 and 46 years with different underlying diseases (psoriasis-associated arthritis, spondarthritis, Still's disease) developed acute reaction during infusion of infliximab with pruritic erythema, rhinoconjunctivitis and dyspnea with significant peak flow drop but uncompromised hemodynamics. All responded well to standard treatment with adrenalin, steroids and antihistamines and infliximab therapy was discontinued. Tryptase is a specific marker for mast cell activation. During the acute phase all patients showed an up to fourfold increase of serum tryptase compared to baseline levels (notably maximal levels were still within the normal range). Immune complex and complement analysis were normal. A thorough allergological workup (intradermal skin test, basophile activation test and measurement of IgE specific for infliximab) could not reveal an IgE dependent mechanism.
Conclusion: Despite typical clinical presentation for an IgE mediated allergy and proven mast cell activation (elevation in tryptase levels), we could not demonstrate an IgE dependent mechanism in our three cases. We hypothesize an IgE independent mast cell activation, most probably via the complement system as C5a is a potent mast cell activator.

P 19

Pediatric Rheumatology in Switzerland: data from the Swiss Pediatric Rheumatology Registry

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Background: The frequency of inflammatory diseases and chronic musculoskeletal pain is probably underestimated among children and adolescents, and has not been yet described in Switzerland. For this purpose and to evaluate the outcome of these patients, we created the Swiss Pediatric Rheumatology Registry.
Objectives: To evaluate the prevalence of inflammatory and non-inflammatory rheumatisms in the Swiss pediatric population, and describe their characteristics.
Methods: All children seen between 2004 and 2007 in the 9 main pediatric rheumatology clinics in Switzerland have been included. Data collected comprised diagnosis, treatment and demographic data.
Results: 2269 patients were included: mean age 10 years, male/female sex ratio 1/1.2, 1582 (69.7%) with an inflammatory disease, 687 (30.3%) with a non-inflammatory disease. In the inflammatory group of patients, 916 (59.7%) had juvenile idiopathic arthritis, 141 (8.9%) connective tissue diseases, 53 (3.4%) vasculitis, 202 (12.8%) infectious or post infectious arthritis, 70 (4.4%) periodic fever syndromes, 54 (3.4%) ocular disease, and 146 (9.2%) different other conditions. Patients with non-inflammatory disease, 314 (40.4%) had orthopedic problems, 322 (41.4%) chronic musculoskeletal pain, 51 (6.6%) different of other conditions. The majority of the patients 1181 (52%) had good functional abilities with a Steinbrocker score at I, and only 38 (1.6%) had a score of III and IV, 571 (25%) patients were not scored.
Conclusions: Among the patients seen in the pediatric rheumatology clinics in Switzerland more than 2/3 presented an inflammatory disease (more than 1 case per 1000 children). The majority of these patients had good functional abilities at the time of diagnosis. These data show that a substantial number of children are suffering from chronic rheumatologic conditions. Therefore an early identification and adequate care are crucial to prevent long-term disabilities, and enough medical facilities should be provided in Switzerland to achieve this goal.

P 20

Calcium pyrophosphate dihydrate tophus in a finger

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Calcium pyrophosphate dihydrate (CPPD) deposits are frequently observed in elderly people. They usually occur in the joints but can also be observed in other tissues. Contrarily to monosodium urate deposits, CPPD crystals rarely present as a tophus.
This presentation concerns an 81-year-old man who developed during a period of several years a huge tumor-like tophus of CPPD crystals on the antero-lateral side of his 3d right finger, impairing the mobility of the joints and reducing the superficial sensibility of the lateral aspect of the finger. Laboratory tests were normal. X-rays showed a cloudy calcified mass, eroding the proximal phalanx associated with intra-tendinous deposits. Surgery consisted in a nearly total resection of the mass. Analysis of the removed tissues showed typical CPPD crystals. There were no other crystals, metaplasia or abnormal cells. Similarly to the majority of the previous cases, there was no associated chondrocalcinosis. Further evolution was good without recurrence after 3½ years. A little more than one hundred cases of CPPD tophi have been reported in the literature. In the finger, a CPPD tophus has only been reported in ± 10 cases. All the fingers may be involved and the tophus, usually single, can be proximal or distal. Initially, the nodule may be transparent on the plain X-rays. Thereafter, the calcification may appear punctuated or as an amorphous mass. The CT scan delineates the calcification and the MRI may show inflammation and extension to the surrounding soft tissues. Mild trauma could be involved in the pathophysiology. Total resection usually prevents recurrence. Better knowledge of this entity could avoid enlarged surgery as it has been done on some occasion.

P 21

Successful treatment of macrophage activation syndrome as initial presentation of systemic onset juvenile idiopathic arthritis with interleukin-1-antagonist anakinra in a 3-year-old girl

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Introduction: Macrophage activation syndrom (MAS) is a potentially life-threatening complication of systemic childhood inflammatory disorders, such as systemic onset juvenile idiopathic arthritis. The immunopathogenesis of MAS is characterized by excessive activation and proliferation of T lymphocytes and macrophages resulting in hemophagocytosis. Immunosuppressive medication such as corticosteroids and ciclosporin are currently used, but can fail in severe cases. This is the first report of successful treatment of MAS with anakinra, an interleukin-1-receptor antagonist.
Methods/Results: A 3-year-old girl presented with a 3 days history of refusal to walk with fever up to 40 °C. Due to remarkably elevated inflammation markers the girl was started on antibiotic treatment for suspected osteomyelitis. However, bone scintigraphy could not reveal any osseous focus. Infectious causes (cultures in blood, urine, cerebrospinal fluid and extensive serologies) could be excluded. The girl developed macular exanthema, hepatosplenomegaly, generalized lymphadenopathy, tenosynovitis on hands and feets, anemia, hyperferritinemia and finally presented encephalopathy with status epilepticus. Presence of phagocytosis by macrophages in cerebrospinal fluid and bone marrow confirmed our suspicion of macrophage activation syndrome. High dose corticosteroids, ciclosporin and intravenous immunoglobulins were uneffective. Anakinra 50 mg (3.5 mg/kg/dose) s.c. daily, later increased to 75 mg (5.4 mg/kg/dose) per day over a week's period, led to prompt response with resolution of fever and clinical improvement.
Conclusion: Anakinra was an effective treatment in this severe course

of MAS, indicating that IL-1 is a major mediator in the underlying inflammatory disease. Further studies have to be established to confirm this first report.

P 22

CRMO in children: a case study

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Background: Chronic recurrent multifocal osteomyelitis (CRMO) is a clinical entity wich occurs mainly in children. It is characterized by a prolonged, fluctuating course with recurrent episodes of pain and swelling occurring over several years. CRMO is often multifocal and most often seen in tubular bones, the clavicle, and less frequently the spine and pelvic bones; other locations are rare. The radiographic appearance suggests subacute or chronic osteomyelitis. Histopathological and laboratory findings are nonspecific and bacterial culture is negative. CRMO is often diagnosed by exclusion of the two main differential diagnoses – bacterial infections and tumor – by assessing for a characteristic course and the findings by conventional radiography, if necessary supplemented by scintigraphy and/or MRI. CRMO is discussed to be an entity of the SAPHO-Syndrome in adults.
Methods: We report 6 patients (9, 11, 15, 16 and 17-year-old females and 15-year-old male), each with distinct disease onset, time of diagnosis, evolution, therapy and outcome.
Results: In our patients symptoms began between the age of 4 to 13, definive diagnosis was made after 2 month up to 2 years after first symptoms. 4/6 showed typical multifocal location. Two girls had just one focus. In all patients laboratory findings were unspecific with elevated ESR. A histology was done in 5/6 Patients, which showed unspecific chronic inflammation, bacterias could not be found. HLAB 27 was negative in all patients, ANA in 3/6 positive. 4/6 patients got at the beginning of symptoms a therapy with antibiotics. 4/6 patients had a good improvement with antirheumatic therapy but 2 girls had a prolonged course of disease with several relapses and a reduced quality of life: with anti- TNF-α they were free of symptoms. None of our patients fulfilled the criterias for the SAPHO-Syndrome.
Conclusion: CRMO is important to consider in the differential diagnosis of septic osteomyelitis and bone tumors. Children whose disease is still active under NSAR drugs can benefit from anti TNF-α.

P 23

Recruitment approaches for a novel screening strategy for rheumatoid arthritis

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Introduction: Rheumatoid arthritis (RA) was once viewed as an inexorably progressive disease, but has become a potentially curable disease with very early use of disease-modifying antirheumatic therapy. Therefore, diagnosing RA early and identifying pre-clinical RA as accurately as possible has become a high-stakes undertaking. The contemporary view of its pathophysiology is a process that starts with a pathologic activation of the adaptive immune system (or *"immune onset of the disease"*), followed by an asymptomatic period (or *"preclinical phase"*), which eventually leads to the *"clinical onset of the disease"*. During the preclinical phase of RA, auto-antibodies are often already present and synovitis can be demonstrated on histology in clinically uninflamed joints. Biomarkers and clinical risk factors of pre-symptomatic disease exist and suggest that screening at risk populations for early detection of RA and treatment are not out of the realm of the possible.
Objective: To develop and evaluate a screening strategy for the development of RA in first degree relatives of patients with RA.
Methods: We are assembling a cohort of individuals at increased risk of RA, namely first-degree relatives of patients with RA. Participants will have risk factors for RA determined and be tested for biomarkers of RA susceptibility and followed prospectively until they develop RA.
Results: Recruitments strategies of healthy first-degree relatives for this cohort will be achieved via their diseased parent. Patients with RA will be informed of the possibility of a free screening test of RA susceptibility for their unaffected family members via regional RA patient associations, at patient conferences, through advertisement in patient journals, via their treating rheumatologists and on patient websites. We also plan to create internet links to our screening program using sponsored links to "Google.ch" key-words searches. In addition, we will also contact patients from the Swiss RA cohort (SCQM-RA) that have expressed willingness to participate in additional studies and ask them to inform their relatives.
Conclusion: The screening study will establish the diagnostic accuracy of clinical risk factors and biomarkers of RA susceptibility in family members of RA patients. Ultimately this study aims at testing whether an early detection of pre-clinical RA is feasible and whether a screening strategy can be implemented in a high risk population for RA.

P 24

Communication Strategy on Rheumatism

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Rheumaliga Schweiz

Background: Hardly anybody knows that osteoarthritis or osteoporosis are rheumatic diseases. This has been identified as one of the reasons why fundraising for rheumatism is a big challenge for the Swiss League against rheumatism. This fact is also a challenge for the Swiss society of rheumatologists, because patients often do not know when to make an appointment with a rheumatologist. Therefore both associations decided to work together on a new communication strategy.
Objective: The goal of the new communication strategy is to make rheumatism understandable to a large public and the media. This communication strategy is annually reinforced through specific marketing and communication activities, promoting specific services for patients suffering from rhumatism. An additional objective for the Swiss League against rheumatism is to gain more funds.
Method: A working group of the Swiss League against rheumatism and the Swiss society of rheumatologists have defined five common objectives related to communication and activities, to accessibility to optimal treatment and services for patients and to the positioning of rheumatology. Common target groups have been identified, the most important being the patients, followed by the physicians, the media and other players in the field of health care, such as insurances and government. The key element of this new communication strategy is the division of the whole field of rheumatology into five major indications: osteoarthritis, arthritis, low back pain, osteoporosis and soft tissue rheumatism. Each year one of these five topics will be highlighted through all communication channels and services. The 4 other topics will also be presented and kept up to date, but less prominently. Key activities were: the implementation of interactive public conferences nationwide (annual "action-week"); specific internet modules, continuing education programs for health professionals, conferences, specific information material and intense media work.
Results: Results can be evaluated on several levels:
– Patient perspective: Thanks to the new communication channels a larger population has been informed about the disease and related treatment and services and was able to take direct advantage from it. – Rheumatologist perspective: For the first time, more visibility in a large public audience was experienced. – Management perspective: On a management level of the Swiss league against rheumatism, services were developed in a systematic and targeted way along the strategic lines. The limited financial resources could be invested in an optimal way. Thanks to this communication strategy, our goals regarding media coverage could be achieved. – Fundraising perspective: Thanks to the public activities and specific services new sponsoring models and partners could be achieved and new addresses could be gathered which will be used for fundraising purposes in the future.
Conclusion: The first experiences regarding all defined goals of the new strategy were very encouraging. The decision was made to pursue this strategy for the upcoming years. For 2009 the topic chosen is arthritis. The defined services and measures to establish this communication strategy will be reinforced nationwide. New specific services will be developed each year following the main topics.

HP 1

6 and 12 months' effects of resource-oriented joint protection education in people with rheumatoid arthritis. A randomized controlled trial

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Introduction: Group joint protection (JP) education in people with rheumatoid arthritis (RA) applying psycho-educational teaching methods is more effective compared to JP using traditional teaching methods. It is unclear if this applies also for a one-to-one approach. The Pictorial Representation of Illness and Self Measure (PRISM) was used to guide an individualized JP education and support motivation. This study aimed to compare the effects of individual PRISM-based JP education (PRISM-JP) with conventional JP education (C-JP) in people with RA.
Methods: An assessor-blinded randomized controlled trial was conducted in 4 rheumatology centers. Patients were randomized to PRISM-JP or C-JP, consisting of 5 sessions over 3 months. Primary outcome was joint protection behaviour at 6 and 12 months.
Results: A total of 53 patients with RA participated. At 6 and 12 months, C-JP (n = 27) and PRISM-JP (n = 26) improved their JP behaviour ($p < 0.001$), the PRISM-JP group did significantly better at 6 months ($p = 0.02$) and 12 months ($p = 0.04$). No further differences between the groups occurred. Within group analysis showed that the PRISM-JP group had better JP self-efficacy ($p = 0.02$), grip strength ($p = 0.04$) and self-perceived disease activity ($p = 0.04$) at 12 months, whereas the C-JP group had less depression ($p = 0.05$), decreased disease activity ($p = 0.05$), and better quality of life ($p = 0.04$).
Conclusion: In contrast to group JP education, a one-to-one setting improved JP behaviour irrespective of the teaching methods. PRISM-JP may successfully support benefits related to increased use of JP methods, whereas the benefits of the C-JP group seemed to be independent from JP behaviour.

HP 2

Effectiveness of exercise on work disability in patients with non-acute non-specific low back pain: systematic review and meta-analysis of randomised controlled trials

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Objectives: To determine whether exercise is more efficient than usual care to reduce work disability in patients with non acute, non-specific non-acute low back pain, and to explore which type of exercise is most effective.
Methods: A Systematic Review and Meta Analysis of randomised controlled trials investigating the effectiveness of exercise in non acute non-specific low back pain, and reports on work disability was performed. Data sources were MEDLINE, EMBASE, PEDro, Cochrane Library databases, NIOSHTIC-2, PsycINFO to August 2008. Work disability data were converted to odds ratios. Random effects meta-analyses were conducted.
Results: 23 trials met the inclusion criteria. 21 were included in the Meta analysis, allowing 18 comparisons of exercise interventions with usual care and 15 comparisons of two different exercise interventions. Overall treatment effect of exercise interventions in comparison with usual care with a total of 3275 patients was in favour of exercise (OR = 0.67, 95% CI 0.53–0.86). Meta regression showed no significant effect of specific exercise characteristics but there was a trend ($p = 0.109$) favouring home exercises (OR = 0.38, 95% CI 0.17–0.84) compared to supervised exercises (OR = 0.70, 95% CI 0.58–0.85).
Conclusion: Exercise interventions have a significant effect on work disability in patients with non acute non-specific non-acute low back pain. Interestingly, home exercises seem to be at least as effective as supervised programs.

HP 3

The psychometric properties of the German version of the Worker Role Interview (10.0) by clients with musculoskeletal disorders

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Introduction: Occupational therapists play an important role in work rehabilitation in getting people with chronic disabilities back to work. The Worker Role Interview (WRI) is intended to detect psychosocial and environmental factors influencing the ability to return to work for injured or disabled workers. This study examined the psychometric properties of the recently modified German version (WRI-G, 10.0) in a population with work-related musculoskeletal disorders (MSD) in Switzerland.
Methods: Data was gathered from 20 participants with work-related MSD. The interviews were conducted face-to-face and videotaped. Five occupational therapists, trained in the use of the WRI-G, independently rated all twenty interview recordings following the official manual. Thus, 100 ratings were analysed by use of Rasch analysis to test construct validity and transform ordinal raw data into linear data for interrater-reliability calculations.
Results: All items fit the Rasch model, except the item *"perception of boss"*. Four items displayed differential item functioning (DIF) for different groups, which was remedied by item split. The final WRI-G, consisting of 15 items, showed good overall model fit ($X^2 = 54.66$, $p = 0.04$); excellent person-separation reliability (PSI 0.91) and high interrater reliability (mean ICC 0.90).
Conclusions: Based on this sample, the WRI-G (10.0) indicates to be a valid and reliable instrument for assessing psychosocial ability for return to work in a work-related MSD population. It allows occupational therapists to plan their work rehabilitation approach.

HP 5

Effect of different aquatic therapies in patients with a hip/knee replacement

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Introduction: Aquatic exercise is reported to be beneficial in the early phase of rehabilitation after hip and knee joint replacement surgery (Giaquinto, 2007, 2009; Weigenfeld-Lahav, 2007). In Switzerland, general aquatic exercise programs (usual care) focusing on improving strength and range of motion are part of standard rehabilitation after hip and knee joint replacement. The rehab clinic Valens, however, offers a specific aquatic therapy that focuses on coordination and balance training. The effects of such specific aquatic therapy programs after joint replacement surgery have been scarcely examined so far.
Aim: The aim of this study was to compare the effects of a 3-week general aquatic therapy with the effects of a 3-week specific aquatic therapy in patients early after hip or knee joint replacement surgery in terms of balance, mobility, risk of falling, range of motion (ROM) and quality of life.
Methods: The participants were randomly assigned to a 3-week general aquatic therapy (usual care) or a 3-week specific aquatic therapy focusing on coordination and balance training. At the beginning and end of rehabilitation, the Iowa Level of Assistance Scale (ILOAS), the Timed Up and Go test (TUG) and the Western Ontario and McMaster Universities (WOMAC) Questionnaire were conducted. In addition, joint range of motion was measured and the Falls Efficacy Scale International (FES-I) and a questionnaire that daily assessed pain and fear of falling by visual analogue scales were completed. The questionnaires were also completed 3 months after the end of rehabilitation. This study was approved by the ethics commission of the canton St. Gallen.
Results: This study was conducted between April and September 2009. This poster is presenting first results and preliminary conclusions.

HP 6

Cervical impairments in patients with unilateral peripheral vestibular hypofunction associated with chronic dizziness – a cross-sectional pilot study

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Background: Patients with vestibular disorders frequently report neck discomfort associated with dizziness. Cervical pain may develop as they stiffen up their neck muscles to avoid head movements.
Objective: This study aims to objectively describe cervical spine findings in patients with unilateral vestibular hypofunction and dizziness using a standardised examination protocol.
Design and Methods: The study was conducted with a cross-sectional design. Twenty-three participants were recruited from patients referred to our Center for Vertigo & Balance Disorders. Cervical impairment testing included history-taking, "static tests" (isometric contraction of neck muscles) and palpation over the facet joints.
Results: Twenty participants complained of current neck discomfort, 15 of these reported a neck complaint history preceding the peripheral vestibular event. Eleven showed positive "static tests" and 17 cervical pain on palpation. Most frequently, the upper cervical spine as well as all cervical muscle groups were affected. Fisher's exact test revealed a significant correlation between the severity of dizziness and neck complaints ($P = 0.03$).
Conclusions: Neck problems are frequently seen in patients with unilateral vestibular hypofunction and dizziness. Surprisingly, the history of neck problems often dates back to period before the beginning of vestibular symptoms. Despite non-coincidental onsets, there was a strong correlation between severities of neck complaints and dizziness.

Free communications

Antisperm antibodies in women with autoimmune disease

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Problem: Various types of auto – and iso – antibodies are found in autoimmune diseases, but what is the prevalence of antisperm antibodies in women with systemic lupus erythematosus (SLE, N = 40), rheumatoid arthritis (RA, N = 7), and Sjögren's syndrome (SS, N = 2) compared with 50 healthy fertile women?
Patients and Methods: Serum and ovulatory cervical mucus in 49 women with autoimmune disease and fertility disorders (9 cases of repeated unsuccessful in vitro fertilization, 5 cases of successful IVF but spontaneous miscarriages, 13 cases of repeated pregnancy loss, 17 patients without pregnancy so far, 5 patients delivered their first healthy child) were examined. Tray agglutination test and indirect mixed antiglobulin reaction test for IgG, IgA, IgM, and IgE were used.
Results: Serum antisperm IgG antibodies in 6 patients (4 with SLE, 2 with RA), antisperm antibodies, IgG and IgA, in ovulatory cervical mucus were found in 4 women with RA, and in 11 with SLE.
No antisperm antibodies were detected in control group.
Conclusion: The presence of antisperm antibodies in women with autoimmune disease is also an important risk factor for early fertilization. Other antibodies as zona pellucida antibodies, panel of antiphospholipid antibodies, or complete immunological profil should also be examined to complete the immunologic diagnosis of the fertility failure and to plan the appropriate treatment.
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Churg-Strauss syndrome and pregnancy

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Background: Churg-Strauss syndrome (CSS) is characterized by asthma, hypereosinophilia and necrotizing vasculitis involving small to medium sized vessels with eosinophil granulomas. The incidence is estimated between 0.9 and 3.3 per million, the disease usually occurs during the fourth and fifth decades. So, CSS is very rare during pregnancy.
Objectives: The aim of the study was to investigate the effects of pregnancy on Churg-Strauss course and the influences of the disease on gestation and fetal development.
Methods: We describe 4 pregnancies in 4 patients, who referred to us from 2000 through 2006, with a previous diagnosis of CSS, fulfilling the American College of Rheumatology (ACR) criteria. The 4 women were in remission without therapy or only with local steroid and beta-agonist therapy.
Results: Three patients experienced mild flares during pregnancy, that were responsible to low dose oral steroids. The other patient had pneumonia of the right lung, treated with antibiotics, at the end of pregnancy, for which she underwent caesarean section. Two pregnancy were complicated by anhydramnios and the babies were small for gestational age. In one of these cases fetal lung maturation was induced at 29 weeks. The characteristics of the patients and pregnancies are summarized.
Conclusions: Pregnancy is very uncommon in CSS and no prospective studies are available. So most information derives from case reports. Flares of the disease have been described. In our small series we observed frequent but mild flares, all responsive to oral prednisone. Two of the delivered babies displayed SGA and similar data are reported by others. In conclusion our experience suggest that pregnancy in CSS patients has to be planned and started during long-term remission. Moreover the pregnant patients have to be monitored carefully and in case of active disease aggressively treated with corticosteroids.
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Complement in aPL-mediated placental damage: Prospective study

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Background: C' activation was reported in murine models of aPL-induced fetal loss [1] but still debated is whether comparable findings can be found in patients [1].
Aims: To investigate C' deposition in PAPS in a prospective study.
Methods: PAPS placentas at delivery or after abortion & controls from normal term pregnancies were collected. C' deposition was evaluated by immunohistochemistry.
Results: 14 pregnancies (1 twin) in 11 PAPS & 5 in controls were evaluated. 9 PAPS placentas after term pregnancy & 4 abortive specimens (3 at 20th and 1 at 25th wg) were collected. LMWH (100 IU/Kg/day s.c.) and low dose ASA (100 mg/day) were used in 11/24 pregnancies, low dose ASA only in 2/14 as first pregnancies, IVIg and low dose corticosteroids were added to LMWH/ASA in 1 patient because of previous failure. Plasma C3 and C4 levels were within the normal ranges in all the women. Decidual vasculopathy was detectable mainly in PAPS, while decidual necrosis & inflammation were found in some cases and controls. Intervillous thrombi were found in PAPS, while villous infarcts and foci of villitis were detected both in PAPS & controls. C' deposits were constantly detected in PAPS but not in controls. Variation in C' deposition was noticeable in PAPS, though it was not gradable. C1q and C3 were detected on decidual vessel endothelium and colocalized with IgG and/or IgM, as well as in the interstitium among decidual stromal cells at sites of inflammation. In the decidual vessels, C9/TCC showed a subendothelial distribution. Similarly to Ig, C1q, C3 and C9/TCC were also detected on the surface of the villous syncytiotrophoblast, with C9/TCC deposits being more conspicuous in infarcted villi.
Conclusion: As previously reported we did not find any specific histological pattern & widespread inflammation [2]. C' activation was reported for the first time in APS placentas in a prospective study. C' deposition was found both in abortive specimens & in placentas at term, and there was no relationship with therapy.
References: 1 Pierangeli SS, et al. Semin Thromb Hemost. 2008;34:236–50. 2 Park AL. Hughes' Syndrome, MA Khamashta editor, Springer-Verlag London, pp. 362, 2006.

Do the levels of pregnancy hormones affect the natal outcome in Anti-phospholipid syndrome affected women?

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Introduction: Pregnancy has consequences on the maternal immune system. For women who have an autoimmune disease and subsequently become pregnant, pregnancy can induce a significant modification of the natural history of disease. The most studied autoimmune condition during pregnancy is the the anti-phospholipid syndrome (APLS) [1]. In pregnancy, APLS is recognized after recurrent fetal losses (RFL). Human chorionic gonadotropin beta (β-hCG) and LH are two hormones produced during pregnancy that stimulate the placental maturation.
Objectives: We assessed the relationship between APLS (in pregnancy) and circulating β-hCG and LH levels based on the hypothesis that recurrent second-trimester miscarriages are associated with low circulating hormone levels.
Methods: We designed a case-control study nested within in a cohort of women. Peripheral blood was drawn at the end of the10th week of gestation. Cases were women with APLS. Controls were women free of APS, individually matched to a case by age at pregnancy and gestational age. The hormone levels were assessed by immune-ELISA kits. Exclusion criteria included the coexistence of any other auto-immune and severe chronic condition. In the set based on the first 35 cases and 105 controls we performed the analyses by a t-test for paired sets and a Spearman R correlation for non-parametric values.
Results: Total number of cohort was 140 women. Mean serum β-hCG (IU/L) was 102,190 among the cases and 151,410 among the controls ($p < 0.005$). Mean LH (mIU/ml) was 0.1 among the APLS affected women and 1.4 among the healthy controls ($p < 0.005$). The statistics (Spearman R) reveals a strong correlation between low circulating serum levels of both hormones and the likelihood of fetal loss ($r = 0.89$).
Conclusion: Our data show that there is a strong relationship between the presence of APLS and low circulating level of both β-hCG and LH, crucial in pregnant patients. Our experience enforce the belief that low β-hCG secretion from placenta is more common in APLS affected women then in healthy subjects. Further investigations will include pregnancy hormone measurement in the others autoimmune conditions.
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IgG anti-β2glycoprotein I antibodies from one-year-old children born to mothers with systemic autoimmune diseases preferentially target domain 4/5

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Introduction: Anti-β2glycoprotein I antibodies (a-β2GPI) can be detected in healthy children, possibly as a consequence of infections and nutritional exposure to β2GPI. These children do not usually develop any thrombosis, suggesting that their a-β2GPI may not be as pathogenic as those found in patients with the Antiphospholipid Syndrome (APS). Recently, it has been suggested that a-β2GPI against domain 1 (D1) associate with thrombosis, while those recognizing domain 4/5 (D4/5) have been identified in subjects with cardiovascular disease. Aim of this study was to evaluate the specificity of a-β2GPI in one-year-old children.
Methods: Thirty-eight one-year-old children born to mothers with systemic autoimmune diseases (11 Primary APS, 8 SLE, 9 UCTD, 6 Sjögren, 3 MCTD, 1 RA; globally 34% with positive [pos] a-β2GPI) were IgG a-β2GPI pos at our routinely performed home-made assay. Their sera were studied for IgG a-β2GPI D1 and D4/5 using research ELISAs containing recombinant β2GPI domain antigens (QUANTA Lite ELISA, INOVA). Cut-off values were calculated as the 95th percentile on 50 NHS.
Results: IgG a-β2GPI were high pos in 10 children (26%), medium in 14 (37%), low in 14 (37%). No correlation between children's titre and maternal anti-β2GPI was found. Sixteen (42%) children were pos for D4/5, while no isolated pos for D1 was observed. Only 3 children showed low pos D1 in association with pos D4/5. A correlation between values of a-β2GPI and D4/5 was present ($r = 0.85$, $p < 0.01$). No thrombotic events nor systemic autoimmune diseases were detectable in these children.
Conclusion: A-β2GPI detected in children born to mothers with systemic autoimmune diseases do not associated with thrombotic events and do not seem to be correlated to the mothers' disease. The preferential recognition of D4/5 could account for the "innocent" profile of such a-β2GPI.

Induction of CD4+CD25+Foxp3+ T_{reg} cells during Pregnancy

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Introduction: Regulatory T cells (Treg) play an important role in the prevention of autoimmunity as well as in fetomaternal tolerance. A numerical increase in CD4+C25+ T_{reg} during pregnancy has been found in previous studies. One study found a correlation between the expansion of Treg, the induction of an anti-inflammatory cytokine profile and reduction of disease activity in pregnant patients with rheumatoid arthritis (RA). The objective of the present study was to investigate pregnancy related factors that can induce expansion of CD4+CD25+ Foxp3 T_{reg} during pregnancy.
Materials and Methods: Peripheral blood mononuclear cells (PBMC) were isolated by density gradient centrifugation from peripheral venous blood of healthy women of reproductive age. Early placenta explants obtained from elective abortions were cultured and supernatants were collected every 3–4 days. CD4+CD25- T cells were sorted by FACS (purity >99%) and cultured with either human serum, pooled 3rd trimester pregnancy serum, estrogens and progesterone or supernatant from placental explants. Anti-CD3 (1 ug/ml), anti-CD28 (5 ug/ml) and IL-2 (10 U) were added to each condition. CD25 and Foxp3 expression were analysed after 3 days of culture by FACS.
Results: There was an increase in the percentage of Foxp3+CD25+CD4+ expressing T cells in FACS sorted CD4+CD25- T cells cultured with either human AB serum, pooled 3rd trimester pregnancy serum or supernatant from placental explants, but not with estradiol, estriol and progesterone added at pregnancy levels. The increase was most marked in CD4+CD25- T cells cultured with supernatant from placental explants (15.44%; *$p < 0.05$*) as compared to the pooled 3rd trimester pregnancy serum (6.75%) and human AB serum (6.51%). Analysis of placental supernatant and pregnancy serum revealed several cytokines as inducers of Foxp3 expression.
Conclusion: The results suggest that the increase in the percentage of Foxp3 expression was due to the conversion of CD4+CD25-Foxp3- T cells by factors present in placental supernatant and pregnancy serum. An analysis of possible factors showed no effect of pregnancy hormones, but of different cytokines on induction of Foxp3 in CD4+CD25- T cells.
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Lifetime fertility rates in women with chronic inflammatory arthritides: results from a patient register linked to a medical birth registry

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Introduction: Inflammatory arthritides may influence fertility rates.
Objective: To compare fertility rates in women with juvenile idiopatic arthritis (JIA), rheumatoid arthritis (RA), other chronic arthritides (OCA) and controls.
Methods: Data of premenopausal women from the Norwegian Disease Modifying Antirheumatic Drug (NOR-DMARD) register were linked with data from the Medical Birth Registry of Norway (MBRN) to provide information about age at first delivery. Pairwise comparisons with log rank (Mantel-Cox) analysis with event at age of first delivery and latest sensoring at 45 years of age were applied to compare fertility rates in JIA, RA, OCA and controls from MBRN without inflammatory arthritides. The patients and the controls (n = 10,000) were matched for time periods of delivery. Infertility rate in the controls was estimated to 10% according to Statistics Norway.
Results: Data from 71 JIA, 156 RA and 107 OCA patients, all with diagnosis before the first delivery, were linked with MBRN. In the JIA group 43 (60.5%) of the patients were nulliparous. The corresponding numbers for RA and OCA were 96 (61.5%) and 67 (62.6%). JIA women were significantly more nulliparous than the controls ($p < 0.001$). RA women were significantly more nulliparous than JIA women ($p = 0.04$) and controls ($p < 0.001$), but not compared to OCA women ($p = 0.9$), and OCA women were significantly more nulliparous than JIA women ($p = 0.04$) and controls ($p < 0.001$).
Conclusion: Fertility rate was reduced in all patient groups compared to the controls and adds to the burden of rheumatic diseases in general.

NSAID inhibit ovulation in women with rheumatic disease

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Introduction: Periovulatory administration of NSAIDs may impair ovulation by leading to the luteinized unruptured follicle (LUF) syndrome. Cox 2 inhibitors are more frequently involved in this process. Women with chronic inflammatory rheumatic diseases are candidates for chronic NSAID exposure and hence for the development of LUF.
Objectives: To identify the incidence of the LUF syndrome in women with rheumatic diseases exposed to NSAIDs and compare the incidence to that in general population.
Methods: Prospective intravaginal ultrasound monitoring of follicular development and detection of ovulation was made in women with rheumatic diseases and healthy subjects. A LUF syndrome was suspicioned at the detection of a persistent unruptured follicle with dimensions over 23 mm after day 25. During each menstrual cycle disease activity and continuous or intermittent administration of NSAIDs was recorded.
Results: In 58 monitored cycles we detected 14 (24.13%) LUF syndromes compared to only 3.38% of LUF in untreated healthy women. LUF occurred in 32.6% of cases in the 43 cycles exposed to continuous NSAIDs regimens. Interestingly the frequency of LUF was 37.5% in patients with inactive disease compared to only 18.2% in patients with active disease. A continuous regimen of etoricoxib generated 11 (78.6%) out of the 14 LUF syndromes, being responsible for 33.3% and 90.9% of LUF in active versus inactive disease. We did not register any LUF syndrome in the 11 cycles representing 25.5% of all cycles in the women exposed to Ibuprofen. Four pregnancies occured in women with documented LUF under NSAID exposure: 3 after total NSAIDs cessation and the 4 th after NSAID was stopped at day 8.
Conclusions: Compared to healthy women, the LUF syndrome occurs more frequently in women with rheumatic disease exposed to NSAID, particularly in those with inactive disease. Etoricoxib seems to be a more potent inductor of delayed ovulation because of strong COX 2 inhibition and a long half life. Discontinuing or replacing NSAIDs with analgesic drugs starting with day 8 of the menstrual cycle may represent a feasible alternative for women with rheumatic disease who want to become pregnant.
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Regulatory T cells and NK cells are correlated with hormonal status during pregnancy

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Introduction: During pregnancy the maternal immune system obtains tolerance to the fetal semiallograft. This is partially mediated by T cells, regulatory T cells (Treg) and NK cells/activating and inhibitor receptors. Nevertheless, the influence of hormones on these cells during pregnancy has not been sufficiently studied.
Methods: We included 13 pregnant women (20–35 years old) followed-up through the first, second and third trimester. T cells, Treg, NK cells and their receptors were determined by flow cytometry in peripheral blood. The hormone levels were determined by the chemiluminescence method.
Results: We did not observe significant changes in the number of T and NK cells in the trimesters of pregnancy. However, the number of $CD4^+CD25^+$ Treg was reduced in the second and third trimester compared to first trimester of pregnancy ($p < 0.01$). We correlated the hormone levels with $CD4^+C25^+$ Treg finding a negative correlation with progesterone in the second trimester ($r = –0.7331$, $p < 0.01$).
A positive correlation between prolactin or cortisol and $CD56^+CD16^+$ NK cells ($r = 0.7373$, $p < 0.01$; $r = 0.5612$, $p < 0.05$, respectively) during the first trimester of pregnancy was noticed. A positive correlation between prolactin or cortisol and $CD56^{dim}CD16^+$ ($r = 0.6319$, $p < 0.05$, $r = 0.5934$, $p < 0.05$) during the first trimester of pregnancy. Moreover, we observed a negative correlation between the hormones and $CD56^{bright}CD16^-$. On the other hand we observed a negative correlation between oestradiol and NKp46 (second trimester) and ILT2 (first trimester) expressed in $CD3–C56^+$ cells ($r = –0.6538$, $p < 0.05$; $r = –0.5604$, $p < 0.05$, respectively) in the first trimester of pregnancy.
Conclusions: These results suggest a role of Treg and NK cells as well as their receptors for tolerance during pregnancy.

TNF alpha antagonists do not impair sperm quality in men with spondylarthritis

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Introduction: TNF antagonists are an established therapy in spondylarthritis. Most of the young male patients may still wish for children. It is not known whether TNF inhibitors are gonadotoxic or impair fertility in men. The aim of the study was to investigate the influence of TNF antagonists on spermatogenesis in men with spondylarthritis.
Methods: 26 men suffering from spondylarthritis who were under therapy with infliximab, etanercept or adalimumab or in whom such treatment was planned. A sperm analysis was done before start of therapy and once or twice times during treatment.
Results: Twelve patients had a sperm analysis before start of therapy. Teratozoospermia was detected in 11 of these patients, one had a normal sperm analysis. At retesting after at least three months of therapy, the sperm analysis had improved in six patients. Fourteen patients were studied during therapy with an TNFα inhibitor. In six of these patients, a normal sperm analysis was found. In eight patients teratozoospermia (of moderate degree in five cases) was detected and in three of the latter additional oligospermia. In the five patients who repeated the sperm analysis because of pathology, only one turned from pathology to normal, the others had unchanged findings. Hormonal status in men with repeated testing was normal.
Conclusion: The majority of patients tested before the start of TNFα antagonists had abnormal sperm morphology with a moderate to severe degree of teratozoospermia. In patients tested before and after treatment with TNF antagonists, therapy did not deteriorate sperm quality. On the contrary, spermatogenesis improved in 40% of the patients under therapy.
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Posters

P 1

Outcome and Growth of Infants Fetally Exposed to Heart Block-Associated Maternal Anti-Ro52/SSA Autoantibodies

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Objective: The purpose of this work was to analyze outcome with focus on growth in infants fetally exposed to heart block-associated maternal anti-Ro52/SSA autoantibodies and identify maternal factors other than the autoantibodies increasing the risk of fetal heart block.
Patients and Methods: 32 pregnancies in 30 anti-Ro52-positive mothers were included. Seven fetuses developed second-degree or third-degree atrioventricular block, 8 developed first-degree atrioventricular block, and 17 had normal atrioventricular conduction, as diagnosed by using Doppler echocardiography. Maternal and longitudinal infant data were collected from planned neonatal follow-up and childhood health records from birth to 12 months of age in 31 survivors.
Results: Women giving birth to infants with prenatal second-degree or third-degree atrioventricular block were older and with higher parity than those with first-degree atrioventricular block or normal atrioventricular conduction. Second-degree or third-degree atrioventricular block pregnancies were <40 completed weeks, whereas pregnancies with first-degree atrioventricular block or normal atrioventricular conduction had a normal duration. Fetuses with second-degree or third-degree atrioventricular block were retarded by –0.98 ± 0.77 SD in weight at birth and did not show any catch-up during infancy. In contrast, fetuses with first-degree atrioventricular block or normal atrioventricular conduction had a weight reduction of –0.51 ± 1.01 SD with a catch-up during the first months after birth.
Conclusions: This report documents that newborns with

autoantibody-mediated second-degree or third-degree atrioventricular block are retarded in growth, with no catch-up during infancy, whereas fetuses with first-degree atrioventricular block or normal atrioventricular conduction have a normal growth soon after birth. Increased maternal age and/or parity seem to carry an increased risk for fetal heart block.

P 2

A decision aid for women with systemic lupus erythematosus

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Introduction: In a randomized controlled trial Martine Prunty et al. [1] documented the importance of a decision aid tool for women with multiple sclerosis deciding whether to start or enlarge their families. No data are available for women with systemic lupus erythematosus (SLE).
Methods: We created a decision aid material to help women with SLE make motherhood choice by providing information about the different aspects of the pregnancy in SLE. In this first phase of the study the booklet was examined by a group of women with SLE who recently had a pregnancy.
Results: The booklet contains evidence-based information on the disease (symptoms, course, and prognosis) and on the treatment (therapeutic options, efficacy and safety) and the community resources for the patients. The major part of the booklet was specifically related to the effects of the pregnancy on the disease (risk of relapse). The impact of the disease on the pregnancy was also illustrated (including the risk for the newborn, the labor and delivery; the safety of the commonly employed drugs). A distinct section was devoted to the psychosocial impact of SLE on the quality of life and in the family of a woman suffering of SLE. Ten women with SLE who had a pregnancy in the last 18 month received the booklet. They reported great interest, higher self-efficacy and they had a positive judgement about the reliability of the DA. Women's satisfaction was related to the information received and to the opportunity of discussing many concerns about family-planning with health professionals.
Conclusion: Even if a larger group is needed to verify the effectiveness of our decision aid tool, we could demonstrate its importance in helping women with SLE facing the decision of motherhood.
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P 3

Women with anti-Ro/SSA autoantibodies: Experiences during pregnancy and after childbirth

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Introduction: Pregnant women with anti-Ro/SSA autoantibodies, foremost patients with Sjögrens syndrome and systemic lupus erythematosus (SLE) but also women without symptoms, have a higher risk to give birth to a child with fetal heart block (CHB). The purpose of this study was to explore how the women experience this risk and how the women's life during pregancy and the postpartum period was influenced.
Method: Women with anti-Ro/SSA antibodies were interviewed. None of their children were born with a heart block. The women were individually interviewed using a semi structural interview guide, the interviews were recorded by a digital recorder, transcribed verbatim and analysed with content analysis.
Result: Three main themes where identified from the interviews: Information, Concern and Support. Between pregnancy week 18–24 the women were followed with multiple Doppler echocardiography to assess the fetal heart rate [1]. During that period the women felt secure and well supported by the medical team. However, during the pregnancy other complications occurred related to their autoimmune disorder, and these situations caused concern, anxiety and unmet need for information and support for the women in this study.
Conclusion: Information and support given to women diagnosed with anti-Ro/SSA antibodies in this study were focused in week 18–24 of the pregnancy. There was a lack of coherent care adapted to the special pregnancy situation for this group of women, and it is thus of great importance to increase the knowledge about anti-SSA/Ro-positive womens experiences during pregnancy and postpartum period. Using this knowledge it would be possible to meet the need of coherent information and support, and to develop guidelines for a more patientcentered care throughout this vulnerable period.
References: Sonesson SE, et al. Arthritis & Reumatism. 2004;4:1253–61.

P 4

Autoimmune diseases with oncological complications in identical female twins – case report

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Introduction: We report a special case on the history of identical female twins born in 1977 suffered from autoimmune diseases (twin A – Sjogren's syndrome, and twin B – systemic lupus erythematosus).
Patients: Twins – A – LR (2250 g/45 cm). At the age of 17 years, her menarche commenced, at 18 years of age the diagnosis of autoimmune disease, manifested as Sjogren's syndrome was found. On June 2006, in her 37th week of pregnancy, she spontaneously delivered a daughter, 2670 g/48 cm, Apgar 9-10-10 with cheilognathopalatoschis. At the age of 31 years, loop electrosurgical excision procedure (LEEP) proved precancerosis of cervix uteri. Twins –B – LI (2260 g/45 cm). Her menarche commenced at the age of 15 years. At the age of 23 years, systemic lupus erythematosus and chronic rheumatism were diagnosed. At the age of 28 years, carcinoma vaginae, with invasive proliferation (T2 NX Mx G2) appeared.
Results: Both sisters suffered from autoimmune and gynecological diseases at the same time. Relationships between disease activities and severities in the female twins were similar and the treatments were directed according to clinical symptoms and laboratory results.
Conclusion: Dramatic change, unfortunately, occurred with twin B. The reason may be the association between SLE activity (lupus nephritis), hematological complication (leukopenia) and oncological fatal vaginal recidivation.

P 5

Cytokine serum level variations during pregnancy in SLE

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Introduction: Our aim was to evaluate the serum level variations of some cytokines involved in the Th1-Th2 shift during pregnancy in SLE patients and healthy women [1].
Methods: 47 consecutive successful pregnancies in 46 SLE patients (mean age 30.5) and 56 pregnancies in 56 matched healthy subjects, as controls, were prospectively studied. All patients were regularly monitored during pregnancy for laboratory and clinical parameters, including treatment. Sera obtained at 1st trimester (9–11 weeks) and 3rd trimester (29–31 weeks) of pregnancy were stored at –80 °C until analysis. Serum IL-1α, IL-1β, IL-2, IL-6, IL-8, IL-10, IL-12p70, INFγ and TNFα were detected by a highly sensitive, multiplexed sandwich ELISA (SearchLight Human Inflammatory Cytokine Array by Pierce Biotechnology, Rockford, IL). Statistics were performed by the SPSS package using the Wilcoxon test for paired data and the Mann-Whitney U-test.
Results: In healthy women, the serum levels of the most Th1-type cytokines were significantly lower in the 3rd trimester compared with those observed in the 1st trimester: IL-1α p = 0.003; IL-1β p = 0.018; IL-2 p = 0.018; IL-12p70 p = 0.018; INFγ p = 0.001; and TNFα p = 0.001. In SLE patients only the IL-1α serum levels were reduced in the 3rd trimester compared with the 1st trimester (p = 0.006). We observed a decrease in INFγ/IL-6 and INFγ/IL-10 ratios from the 1st to the 3rd trimester of pregnancy in healthy subjects (p = 0.033 and 0.067, respectively) but not in SLE patients. We did not observe any significant differences in the 1st and 3rd trimester cytokine serum levels between patients and controls apart from the IL-10 serum levels which were higher in SLE patients compared to controls in the 1st trimester (p = 0.028) as well as in the 3rd trimester (p = 0.001) of pregnancy. The difference in IL-10 serum levels between patients and controls in the 3rd trimester of pregnancy was more significant in patients with active disease (p = 0.004) than in those with inactive disease (p = 0.015).
Conclusion: In SLE patients a lower than expected decrease of Th1 cytokine serum levels was observed in the 3rd trimester of gestation. This could contribute to a lower Th2 cytokine polarization during pregnancy in SLE patients.
References: 1 Doria A, et al. Arthritis Rheum. 2004;51:989–95.

P 6

Lupus Anticoagulants and Pregnancy: clinical relevance of different assay tests

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Background: APS is diagnosed when arterial/venous thrombosis or pregnancy morbidity occur in patients in whom laboratory tests for antiphospholipid antibodies (lupus anticoagulants, LA, anticardiolipin

antibodies, aCL, and anti beta-2-glycoprotein I, anti-β2GPI) are repeatedly positive. LAs were thought to be consistently associated with pregnancy morbidity, which implies that measuring them is helpful to define the patients' risk. Nonetheless, with respect to LAs, many "screening" and "confirmatory" assays have been proposed, recommending the use of two assay tests, without specific indication of which tests should be used.
Aim of the study: To compare the sensitivity for APS diagnosis of four different LA assay tests (DRVVT, KCT, SCT and STACLOT-LA), aCL and anti-β2GPI levels in a series of patients with suspected APS for pregnancy morbidity.
Methods: LA with 4 assay tests, aCL IgG/IgM isotype and anti β2GPI IgG/IgM isotype were performed in a series of 157 consecutive patients (aged 17–43 years, mean 36.2 years), referred to our Centre from January 2004–December 2006 for pregnancy morbidity not explained by common risk factors.
Results: 19 out 157 (12.1%) received the diagnosis of APS 10 (52.63%) for three or more unexplained consecutive spontaneous abortions, 2 (10.52%) for one or more premature births of a morphologically normal neonate before the 34th week, 6 (31.57%) for one or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation). LA being positive in 18 (94.73%), aCL IgG/IgM isotype in 13 and 14 (68.44% and 73.68%) and anti-β2GPI IgG/IgM isotype in 8 and 9 patients (42.1% and 47.36% respectively). The sensitivity for APS diagnosis was 95% for LA testing, 63% and 79% for aCL IgG/IgM isotype, and 53 and 58% for anti-β 2GPI IgG/IgM respectively. The sensitivity, calculated for each couple of LA assay tests, was 58% for STACLOT + dRVVT, 89% for SCT + KCT, dRVVT + SCT and STACLOT + SCT, 95% for STACLOT + KCT and dRVVT + KCT (the less expensive).
Conclusion: All available tests for antiphospholipid antibodies need to be performed when APS is suspected, as there is no single test with 100% sensitivity. LAs assay tests have the highest sensitivity for APS diagnosis, when compared to aCL and anti-β2GPI antibodies.

P 7

Pregnancy in Systemic Sclerosis

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In the past, pregnant SSc patients were thought to be at high risk for poor fetal and maternal outcome. Today, a careful planning, close monitoring and appropriate therapy allows a successful pregnancy in SSc patients. Retrospective studies clearly show an increased frequency of pre-term births and small full-term infants but the frequency of miscarriage and neonatal survival rate did not differ from healthy controls. Raynaud's ph. usually improves during pregnancy as well as the increased cardiac output in the second half of pregnancy while gastro-oesophageal reflux worsens particularly during third trimester. The worst life-threatening complication of a pregnancy is scleroderma renal crisis: despite the fact that ACE inhibitors are associated with congenital abnormalities and are relatively contraindicated in pregnancy, in this case their use is recommended. In diffuse SSc, skin thickening may worsen in post-partum but sometimes it may be accelerated during pregnancy along the rapid deterioration of the function of internal organs. In this case, the physician – depending on the week of pregnancy and after a thorough consultation with the mother – may consider during the first trimester an elective termination to allow an aggressive treatment to slow disease progression. During the third trimester, an induced pre-term birth is recommended in order to start promptly aggressive treatment. This scenario is the worst one and every decision must be shared with the mother and the choice of the procedure always remain hers. In order to avoid complications, pregnancies in SSc should be planned when the disease is stable, and should be avoided in rapidly progressing diffuse SSc that are at a greater risk for developing serious cardiopulmonary and renal problems. Hydrossichlorquine, intravenous immunoglobulins (if blood pressure is not high and renal function is normal) and low doses of steroids may be safely used. In order to minimize risks, a multidisciplinary team should assist SSc patients to suggest the best timing for a pregnancy and to tailor adequate supportive treatment during the pregnancy.

P 8

Efficacy and safety of bemiparin in high risk pregnancy

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Introduction: Low molecular weight heparin (LMWH) is widely regarded as the anticoagulant treatment of choice for the prevention and treatment of thrombophilia during pregnancy. The safety and efficacy of bemiparin has been demonstrated in several studies and it is currently licensed for treatment and prophylaxis of venous thromboembolism (VTE) [1]. However, previous studies have demonstrated that the pharmacokinetic profiles of LMWH vary significantly with increasing gestation [2]. Consequently, it remains unclear whether LMWH regimens recommended for use in nonpregnant individuals can be safely extrapolated to pregnant women. The aims of this study were to assess the safety and the efficacy of bemiparin administered only once daily during pregnancy.
Methods: We have evaluated retrospectively all the pregnant women affected by thrompholia who were treated with bemiparin in our Hospital from January 2004 to April 2009. We describe the pregnancy and perinatal outcomes.
Results: Fifteen pregnancy women (2 of them twice) were treated with bemiparin. The mean age was 31.57 ± 14. The pathologies were: four with factor V Leiden mutation (one of them with heterozygosity for MTHFR), seven with antiphospholipid syndrome (three of them with heterozigosity for MTHFR), 1 with protein S deficiency, one with positive anticardiolipin antibodies, one with APC resistance and deficit de factor XII, and one with homozygosity for MTHFR [1]. Nine of them with previous abortions. Six patients received 5000 IU/daily, one 2500 IU/daily and 8 were treated with 3500 IU/daily. Ten patients received also 100 mg of aspirin. Three patients developed oligoamnios and one had previa placenta. Perinatal outcomes were: 1 abortion at eight week and 14 newborns at full term with adecuated weight and Apgar test. There were no cases of heparin-induced thrombocytopaenia, symptomatic osteoporosis, or foetal malformations.
Conclusion: Once daily bemiparine was well tolerated, safe and effective in pregnant women with thrombophilia.
References: 1 Martínez-González J, et al. Expert Rev Cardiovasc Ther. 2008;6:793–802. 2 Ensom MH, et al. J Soc Gynecol Investig. 2004;11:377–83.

P 9

Mother and perinatal outcomes in pregnancies with autoimmune systemic diseases

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Introduction: The pregnancy in women with autoimmune systemic diseases has been associated to a higher obstetric risk [1–3], both maternal and fetal-neonatal risk.
Material and methods: Descriptive Study of 60 gestations, in 53 women affected with autoimmune systemic diseases.
Results: The most consulted pathologies by the pregnant women have been: lupus (31), antiphospholipid syndrome (28), Sjögren syndrome (4), vasculitis (4), Bechet's disease (2). Many of these women have several diseases. There were nine abortions (all of them in women with recurrent miscarriages and with several pathologies). The most frequent maternal complication has been the arterial hypertension (3 cases). Two women had flare lupus: one of them affected by cutaneous-articular symptoms; and another flare was in a woman dead by massive pulmonary haemorrhage. Nine women had positive anti-Ro. There were four pregnancies affected by placental pathology. The perinatal outcomes have been: 46 newborns at full term, two of them were small-for-gestational-age with healthy live birth. There were five preterm delivery (in women with complicated pregnancies): one of them was a intrauterine growth restriction with good neonatal and infant development. Another preterm delivery took place in the case of the dead mother, and it was a dead fetus at 26th week of gestation.
Conclusions: A careful exhaustive multidisciplinary care during pregnancy in women with autoimmune systemic diseases improves perinatal and mother outcomes; nevertheless, they can appear serious unforeseen complications in these pregnancies.
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P 10

Preconceptional counselling in systemic autoimmunity diseases and/or hypercoagulability states

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Introduction: Some diseases, like systemic autoimmunity diseases and/or hypercoagulability states, may increased risk of maternal-newborn during pregnancy, so it is advisable that women realize a preconceptional counselling [1] where they receive information about these risks, the best clinical conditions for pregnancy [2, 3], the safety of the medications (drugs contraindicated) [3] and to assess their clinical status (disease activity and other associated pathologies) [1, 3].

Methods: Descriptive study of 29 women (6 of them twice) affected by systemic autoimmunity diseases and/or hypercoagulability states who want preconceptional counselling. We describe maternal decision and perinatal outcome.
Results: The most consulted pathologies are lupus (16), antiphospholipid syndrome (13) and inherited thrombophilia (11). Many of these women have several diseases. After preconceptional counselling: 8 women decided not to attempt pregnancy, 3 are planning it and 24 achieved pregnancy gestation. There were 5 abortions (3 of them in women with recurrent miscarriages), usually in women with several diseases. Perinatal outcomes were: 17 newborns at full term with adequate weight and Apgar test; 2 preterm delivery, one of them by intrauterine growth restriction with live birth and posterior good neonatal and infant development; in the other preterm delivery occurred by fetal death. This stillbirth happened in a woman that dead by massive pulmonary hemorrhage at 26th weeks' gestation.
Conclusion: Adequate preconceptional counselling and an exhaustive multidisciplinary care during pregnancy improve perinatal outcomes.
References: 1 Hillemeier MM, et al. Women's preconceptional health and use of health services: implications for preconception care. Health Serv Res. 2008;43:54–75. 2 de Weerd S, et al. Preconception counseling improves folate status of women planning pregnancy. Obstet Gynecol. 2002;99:45–50. 3 Petri M. The Hopkins Lupus Pregnancy Center: Ten key issues in management. Rheum Dis Clin N Am. 2007;33:227–35.

P 11

Congenital heart block (CHB) after ovodonation

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Introduction: Anti-Ro/SSA antibodies are insufficient to cause CHB.
Patients and methods: The recipient of a fertilized egg (oocytes' donor was anonymous) was a 36 years old woman anti-Ro/SSA positive. At 23 wks gestation 3rd CHB was detected (ventricular rate 52 bpm). The infant developed a dilated cardiomyopathy which necessitated heart transplant at the age of 17 months.
Results: DNA were interrogated for polymorphism of candidate genes including HLA (typing), TNFα (TNFα –308A polymorphism-TNF2 allele, proinflammatory-) and TGFβ1 (rs1982073; T allele, profibrosing).

	DQB1	DRB1	Cw	TNF	TGF
Surrogate Mother	2/3	3/11	7/1	½	T/C
Father	3/6	4/13	4/16	1/1	C/C
CHB (ovodonation)	2/6	7/13	4/16	1/1	T/C

The surrogate anti-Ro/SSA positive mother had HLA alleles consistent with published values. The child (product of ovodonation) shared on HLA allele (DQB1) and carried a profibrosing T allele for TGFβ.
Conclusions: This case report shows for the first time that a genetically unrelated fetus exposed *in utero* to anti-Ro/SSA antibodies can develop CHB. Accordingly, a genetic relationship may not be necessary. However, there was sharing of DQ2 and the presence of a profibrosing TGFβ allele; the foetal genetics may be an added risk factor and paternal genes may also be relevant. Testing for anti-Ro/SSA antibodies would be a useful screen for women undergoing techniques of artificial fertilization.

P 12

Systemic Lupus Erythematosus and Pregnancy: follow-up results

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Introduction: Systemic lupus erythematosus (SLE) is one of the most common autoimmune disorders that affect women during their childbearing years. Some authors report exacerbation of SLE during pregnancy [Urowitz MB et al. 1993], still others do not describe increased flares at said period [Ruiz-Irastorza G et al. 1996].
Aim: Based on the data obtained, to study the outcomes of pregnancy, and their influence on the course of the disease in patients with SLE.
Methods: Retrospective observation of pregnant women with SLE was conducted during 5 years. The outcome of pregnancy, exacerbation of SLE, presence of lupus-nephritis and secondary antiphospholipid syndrome (APS) in 11 patients with significant SLE (ARA, 1982) was assessed. The average age of the patients was 24.82 years (range: 19–29), and the average duration of the disease was 6.72 years (range: 3–14).
Results: 11 patients under study developed 28 pregnancies. In 10 cases (35.7%) foetal loss was observed, 8 of which, including 7 cases of foetal mortality and 1 case of spontaneous abortion, happened prior to diagnosing SLE (despite the patients' specific complaints). 2 spontaneous abortions developed in SLE diagnosed patients under treatment (7.1%). 18 pregnancies (64.3%) ended successfully, with 11 cases of natural childbirth (39.3%) and 7 cases of caesarean section (25%). 7 of 11 patients had had nephritis in history (including 3 with nephrotic syndrome). In 5 patients, concomitant secondary APS was observed. In 2 cases (11.2%) the pregnancies developed at severe exacerbation of the disease. One patient received 32 mg/day of methypred and intravenous immunoglobulin, and the other patient – 24 mg/day of methypred. Other pregnancies (16, or 88.9%) developed in 9 patients, who before the pregnancy had been in remission for at least 1 year. They did not need any immunosuppressive drugs or hydroxychloroquine. They received maintenance doses of methypred (4–12 mg/day, depending on the clinical and laboratory indices), and low-dose aspirin, when necessary.
Conclusion: The follow-up during at least 1 year of persistent remission makes successful outcomes of pregnancies possible in patients with SLE receiving maintenance therapy, even in cases they had such severe manifestations of SLE, as renal involvement or secondary APS in their past history.

P 13

Pilot testing of a Database with the purpose of research on women with rheumatic disease before, during and after pregnancy

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Background: Rheumatic diseases frequently affect women of fertile age. Adverse pregnancy outcome and recurrent pregnancy complications are increased in women with rheumatic disease. To increase the quality of care given to the rheumatic women and their families, and to improve the empirical basis for the interventions designed for these patients, systematic collection of data on pregnancy and pregnancy outcome in women with rheumatic diseases is needed.
Methods: The objective of this project is the development and pilot testing of a database for the purpose of collection of clinical data on women with a rheumatic disease before, during and after pregnancy. In collaboration with a multidisciplinary team consisting of rheumatologists, rheumatology nurses, nephrologist, gynaecologist, dermatologist, occupational therapist and computer program developer we conducted the content of a database software tool. Patients were included for pilot testing for 15 months to identify strengths, weaknesses and opportunities of the database.
Results: We performed the pilot testing at the Centre for mothers with rheumatic disease, dept. of Rheumatology, St. Olavs Hospital. 60 patients were included. Eight registrations were made for each patient (before pregnancy, in each trimester, at birth, six weeks postpartum, six months posts partum and twelve months postpartum). Due to the complexity of the different rheumatic diseases we developed different disease profiles for each diagnosis. Topical variables were related to demographic data, characteristics of the disease (diagnosis, damage, disease activity, complications, severity, laboratory, etc.), pregnancy related variables, medical profile, outcome measurements on disease activity, mode of delivery, fetal outcome and lactation. The major challenge was to find and adjust good outcome measures to be used in rheumatic diseases during pregnancy. Another major challenge was to include the patients before they got pregnant. The different elements and contents of the database were changed at the end of the pilot testing to fit the needs of the principal aims for future research. The database is now ready for national use and the implementation at different hospitals across Norway has started.
Conclusion: The database gives a unique opportunity for systematic collection of data. We experienced that the database as a tool made a good system to ensure appropriate follow-up of the patients. The collected data will be used to perform prospective longitudinal research studies that aim to increase the quality of care given.

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Anti-Fibrillin-1 autoantibodies in normal pregnancy and recurrent pregnancy loss

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Background: Fibrillin-1 is an extracellular matrix glycoprotein, a main component of microfibrils as free bundles or in association with elastin-containing elastic fibrils. It is present in the structures

undergoing intensive remodeling during menstrual cycle and pregnancy, hence endometrium and decidua.
Problem: The aim of this study was to investigate anti-fibrillin-1 autoantibodies in patients with a history of recurrent pregnancy loss (RPL) and during normal pregnancy.
Method of study: Anti-fibrillin-1 IgG and IgM autoantibodies were measured by a home-made ELISA in serum samples of 48 medically and obstetrically normal pregnant women, classified to two groups, according to the number of the undergoing pregnancies (Group 1–27 primigravida, Group 2–21 multigravida), 15 non-pregnant female patients with a history of RPL, and two control groups of non-pregnant healthy women (11 with a history of successful pregnancies and 15 nulligravida). One way analyses of variance and Least Significant Difference method were used for a statistical analysis.
Results: The levels of anti-fibrillin-1 IgM autoantibodies were significantly decreased in the primigravida group compared to the nulligravida controls ($p = 0.018$). Comparing RPL patients with the healthy non-pregnant controls established significantly increased anti-fibrillin-1 antibody IgM levels in RPL compared to the group with a history of successful pregnancies ($p = 0.005$). There were no significant differences in the levels of anti-fibrillin-1 IgG autoantibodies between the studied groups.
Conclusion: Variations in the serum levels of anti-fibrillin-1 IgM autoantibodies were established in normal pregnancy as well as in the RPL patients compared with the healthy non-pregnant women. Increased anti-fibrillin-1 autoantibodies may contribute to the pathogenesis of immune-mediated pregnancy losses.

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Parenting disability postpartum of RA women is strongly correlated with disease activity and erosive disease: results from a nationwide prospective study

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Background: Rheumatoid arthritis (RA) may affect women's ability to fulfill parenting tasks postpartum.
Objective: To describe parenting disability (PD) of women with RA postpartum and its correlations with disease activity and HAQ scores, define factors influencing PD postpartum, and examine responsiveness of PD scores.
Patients and methods: This study is embedded in the nationwide prospective study on pregnancy and RA, the PARA-study. At 6, 12 and 26 weeks postpartum HAQ-scores and Parenting Disability Index scores (PDI and modified-PDI) were calculated, medication use was registered and disease activity was scored with DAS28-CRP-3. Correlations between PDIs, HAQ, and DAS28 were calculated. GEE was performed with PDIs as dependent variables and covariates DAS28, medication use, duration of RA, and family size. Responsiveness of the PDI to RA flare defined with "reversed" EULAR response criteria was assessed.
Results: Data from 100 women with RA, were available. Sixty-eight percent was erosive. Mean (SD) PDI scores at three visits postpartum were stable: PDI 0.51 (0.42), mPDI 0.64 (0.56). PDI scores were significantly correlated with both HAQ and DAS28. Higher disease activity and erosive disease were associated with higher PDI scores postpartum. Activities in which women most frequently encountered difficulty were carrying and bathing the baby and household chores. PDI scores rose significantly in women with a flare postpartum, suggesting responsiveness of PDI scores.
Conclusion: PDI scores postpartum are significantly influenced by disease activity and erosive disease. Therefore the treatment goal postpartum should be focussed on the modifiable factors as lowering disease activity and giving joint protective advices before delivery, to preserve the parental tasks of RA patients.

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Common and distinct gene expression profiles in inflammation

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Introduction: Rheumatoid Arthritis (RA) is a systemic autoimmune disease presenting with inflammatory joint disease, but can also affect multiple organ systems. A causative role of Infectious agents like bacteria or viruses has been intensively studied, but so far their participation in the pathogenesis of RA could not be proven.
Methods: In order to find unique gene expression patterns for this disease whole blood sample of healthy donors and RA patients were analyzed. As a first step several microarray experiments were perfomed. The results were then compared with those for infectious diseases, caused by Influenza virus, E. coli, Staphylococcus aureus, and Streptococcus pneumoniae – derived from the GEO [1] and the Bioretis [2] databases.
Results: The TOP 100 genes of all pairwise comparisons (infected to uninfected donors with a >1.5 fold difference) were selected. The hierarchical clustering performed with this genelist indicated that RA clearly shows a different pattern than all the infectious diseases.
Conclusion: These preliminary results however are only a first, as they need further verification and statistical testimony. But more inference can be made in the near future after the analyses of further microarray and real-time PCR data.
References: 1 http://www.ncbi.nlm.nih.gov/geo/. 2 http://www.bioretis-analysis.de

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