Annual meeting of the
Swiss Society of Rheumatology SGR
Symposium Health Professionals in Rheumatology
combined with the VI\textsuperscript{th} Conference on
Sex Hormones, Pregnancy and Rheumatic Diseases

Lausanne (Switzerland), September 10/11, 2009
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Inflammatory role of ASC in antigen-induced arthritis is independent of caspase-1, NALP-3 and IPAF

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Introduction: ASC plays an important role in inflammation in human and murine arthritis, and 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. Asc-specific proliferation of lymph node and spleen cells from ASC-deficient mice was significantly decreased in vitro, as was the production of IFN-γ, while IL-10 production was enhanced. In vivo, ASC−/− mice showed decreased arthritis severity and joint swelling 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.

The long-term impact of early treatment of rheumatoid arthritis A. Finck1, C. Gabay2, D. Kiyburz3, on behalf of the SCQM physicians4

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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.

Objectives: 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 erosion (ERO) were assessed in 38 joints of hands and feet with a validated scoring method (Ratcliffe 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 dichotomised 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 were baseline disability, the long-term effect on disease progression is still debated.

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.

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 of osteoporosis were 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 = −0.32) 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.

<table>
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<th>Clinical Spine Fractures</th>
<th>Hip Fractures</th>
<th>All Osteoporotic Fractures</th>
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<tr>
<td>HR / SD (95% CI)</td>
<td>P</td>
<td>HR / SD (95% CI)</td>
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<td>DEXA Hip</td>
<td>1.70 (1.48–1.95)</td>
<td>2.98 (2.53–3.51)</td>
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<tr>
<td>DEXA Spine</td>
<td>1.49 (1.17–1.70)</td>
<td>1.53 (1.17–1.87)</td>
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<tr>
<td>TBS Spine</td>
<td>1.24 (1.26–1.60)</td>
<td>1.34 (1.26–1.43)</td>
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<tr>
<td>Combined</td>
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<tr>
<td>DEXA Hip</td>
<td>1.59 (1.39–1.83)</td>
<td>&lt;.0001</td>
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<tr>
<td>TBS Spine</td>
<td>1.33 (1.18–1.51)</td>
<td>1.24 (1.07–1.43)</td>
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<tr>
<td>DEXA Spine</td>
<td>1.37 (1.20–1.58)</td>
<td>&lt;.0001</td>
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<tr>
<td>TBS Spine</td>
<td>1.32 (1.17–1.50)</td>
<td>1.39 (1.12–1.61)</td>
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All models are age-adjusted. P value is for improvement in model fit when TBS added to BMD and age.
Rituximab in Rheumatoid Arthritis: Evidence for a Learning Curve by Rheumatologists

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on behalf of the pharmacons of the SCoM-RA

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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 intervals. 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 evaluation of the 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 re-treatment 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 similarly defined. A trend was observed for shorter interval 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: 5.8–9.0) in 2008. A similar trend was apparent for DAS28 levels at RTX re-treatment, with decreasing 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 Mo (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 re-treatment.

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 a less severe disease progression over time than non-drinkers.

Objective: To compare the rates of progression of joint damage 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 (Rattingen score) by a single experienced reader, blinded to clinical history and expressed as a percentage of the maximum 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).

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 (0.97 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.


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 artropathies, 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: 1114.06 ± 80.88 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: 393.73 ± 22.82 pg/ml). In THP-1 cells deficient for caspase-1, OCP, HA and CA induced 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).

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.
Do circulating γT cells play a role in pregnant patients with rheumatic diseases?
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Objective: γT 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 γT 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 γT 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 γT cells were analysed by FACS. The phosphoanion-specific cytokine response of isolated γT 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 Vγ6 Vδ2 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 Vγ9+γδ+ γ T cells positive Vδ2 T cells in the third trimester compared to 8 weeks post-partum. Upon IPP stimulation γT cells isolated during pregnancy produced significantly less IFN-γ compared to those isolated in the post-partum period. The percentages of Vγ9Vδ2 γ T cells correlated with disease activity during and after pregnancy.

Conclusion: The amelioration of disease activity in the third trimester contributed to the decrease of IFN-γ producing Vδ2 T cells. As an explanation, a pregnancy is able to partly suppress cytoktic Vδ2 T cells and thereby contribute to the mitigation of symptoms in a Th1-biased disease.

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: Canakinumab 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 cryopyrin-associated periodic fever syndrome (CAPS) were enrolled. Patients were randomized to receive canakinumab 150 mg subcutaneous (sc) every 8 weeks [Part 1], a fixed dosing every 8 weeks (Part 2) or placebo every 8 weeks [Part 3]. Part 1 began approximately 12 months after patients had entered Part 2. Multiple assessments were performed every 8 weeks in Part 1 and every 4 weeks in Part 2. Primary endpoints included proportion of patients with complete clinical and serological remission in CAPS patients with active disease over a one year period.

Results: 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 ≤10 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 protein levels, safety and tolerability. Response and relapse were defined as depression 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 (<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. Sustained clinical and serological remission was maintained in 28 of 29 patients (97%) who completed the study. Two serious adverse events occurred: one case of urosepsis 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.
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 pronounced symptoms, severe dehydration, dyspnoea 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 to April 2009

BMI [kg/m²]

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Low-dose radiotherapy of sacroiliac joint arthritis: a case report
I. Takacs, S. Bodis
Institut Radio-Onkologie, Kantonssspital Aarau

Introduction: Successful treatment with low dose fractionated ionizing radiation of a patient with refractory rheumatoid arthritis of the sacro-iliac joint.

Methods: The 41-year-old female patient suffers from an undifferentiated rheumatoid arthritis since 06/05. Symptom control including pain reduction of the peripheral arthritis with sustained treatment of Methotrexat (MTX), Remicade and Aredia. Persistent problems, especially of the right 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 x 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 months without changes in the baseline antirheumatic 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 long-lasting treatment for the affected SI-joint. Concurrent MTX might be one reason for the acute and prolonged reaction of theinfeld connective tissue to low doses RT.

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 incurred 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 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 tugging 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.

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 –0.3 to 3.6) for the left. 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.

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 ≤–2.5) 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 patients were screened for preclinical and clinical screening and also for epidemiological studies.
Clinical effectiveness of an interdisciplinary pain management program as compared with standard inpatient rehabilitation in chronic pain. A naturalistic, prospective controlled cohort study

**Introduction:** It is often difficult for primary care providers to justify their decision to allocate patients to specific inpatient therapies after unsuccessful outpatient 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 = 0.009), and in trend catastrophizing and ability to decrease pain. At the 6 month follow-up, the effects in pain (ES: 0.44 vs 0.36), catastrophizing, and social functioning (ES: 0.52 vs 0.20, bivariate p = 0.009), and in trend improvement on pain (ES: 0.76 versus 0.61, multivariate p = 0.034), were still but not significantly higher in the experienced higher effects on physical functioning (e.g., ES: 0.48 vs 0.32), health-related quality of life (e.g., ES: 0.37 vs 0.32), and confounders.

**Conclusion:** The probability of undertreatment 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.

Osteoporotic fracture: a new collaboration with surgeons

**Introduction:** Osteoporotic fractures represent 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 fragility 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’Anatomie and L’Orthopédie) 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 which 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 monitored. When it was necessary, the patient was directly referred to the DAL for a more appropriate management.

**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.
Evaluating 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 (supporting information). Primary results showed that the great majority of the patients had 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 in due course, evaluating other 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 osteoporotic fracture, improved considerably the detection of patients at high risk. This approach is about to be extended to the ambulatory patients.

**Conclusions:** 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. More detailed results will be presented in due course, evaluating other 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 osteoporotic fracture, improved considerably the detection of patients at high risk. This approach is about to be extended to the ambulatory patients.

**References:**
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**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 suspicious of an IgE-mediated allergy. Because of the high risk of subsequent anaphylactic reactions in these patients despite premedication, infliximab should be strictly omitted. A consistent differentiation between allergic and non-allergic complications is still lacking in current literature.

**Cases:** 3 consecutive patients aged 28, 33 and 46 years with different underlying diseases (psoriasis-associated arthritis, spondarthritidae, 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 adrenaline, 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, basophil 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 likely via the complement system as C5a is a potent mast cell inflammatory mediator, indicating the importance of clinical evaluation by a bone specialist.

**Allergen 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 suspicious of an IgE-mediated allergy. Because of the high risk of subsequent anaphylactic reactions in these patients despite premedication, infliximab should be strictly omitted. A consistent differentiation between allergic and non-allergic complications is still lacking in current literature.

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CRMO in children: a case study
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Background: Chronic recurrent multifocal osteomyelitis (CRMO) is a clinical entity which 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, definitive diagnosis was made after 2 months up to 2 years after first symptoms. 4/6 showed typical multifocal location. Two girls had just one focus. In every patient laboratory findings were unspecific with elevated ESR. A histology was done in 5/6 patients, which showed unspecific chronic inflammation, bacteria 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 criteria for the SAPHO-Syndrome.

Conclusion: CRMO is a differential diagnosis of septic osteomyelitis and bone tumors. Children whose disease is still active under NSA drugs can benefit from anti-TNF-α.

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 uninfamed 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: Recruitment 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.

Communication Strategy on Rheumatism
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Background: Hardly anybody knows that osteoarthritis or osteoporosis are also 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 and available 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 rheumatism. 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 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 an active 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.
6 and 12 months' effects of resource-oriented joint protection education in patients with rheumatoid arthritis. A randomised 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 identify 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 were observed. 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 conventional JP education, 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.

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.

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.

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; Weigendfahrt-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 (ILLOS), 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.
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 observed 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-coincident 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 disease, but the antigens involved are not always known. The presence 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 analyzed.

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 profile 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 vessels (e.g., vessels of the skin and lungs). The natural history of CSS is characterized by recurrent and remitting infarcts, often with severe long-term sequelae.

Aims: To evaluate the presence and the role of antisperm antibodies in women with autoimmune disease, comparing their frequency with that of a control group.

Methods: Women with autoimmune disease (SS, N = 2) compared with 50 healthy fertile women.

Results: No antisperm antibodies were detected in control group. Serology work-up was negative in 10/11 women with autoimmune disease. The prevalence of anti-SSA/Ro, anti-SSB/La, and anti-RNP antibodies was 10/11 in women with autoimmune disease and 5/50 in controls.

Conclusion: Antisperm antibodies were not detected in women with autoimmune disease, but react with spermatozoa in controls. The role of these antibodies in the pathogenesis of infertility and pregnancy is still under investigation.

References:

Complement in aPL-mediated placental damage: A 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: 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].

Conclusion: Although the role of C’ in aPL-mediated placental damage is still debated, this study provides evidence for C’ activation in human PAPS, which may contribute to the understanding of the pathogenesis of aPL-mediated fetal loss.

References:
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 anti-phospholipid syndrome (APS). APS is recognized after recurrent fetal losses (RFL). Human chonic 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 the 10th 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 autoimmune 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. β-hCG serum [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 in APPLS affected women then in healthy subjects. Further investigations will include pregnancy hormone measurement in the other autoimmune conditions.


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 nutritional 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 Anti-phospholipid 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 Sjogren, 3 MCTD, 1 RA; globally 34% with positive [pos] a-β2GPI) were included. 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 β2GPI, 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 did not correlate 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+ Treg 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 fetalmaternal tolerance. A numerical increase in CD4+CD25+ Treg cells during pregnancy has been found in previous studies. One study found a correlation between the expansion of Treg and the induction of anabolic 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+ Treg cells 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, estrogen and progesterone or supernatant from placental explants. Anti-CD3 (1 μg/ml), anti-CD28 (5 μg/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 (15.4±4.8%) 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. Analysis of an possible factors showed no effect of pregnancy hormones, but of different cytokines on induction of Foxp3 in CD4+CD25+ T-cells.


Lifetime fertility rates in women with chronic inflammatory arthritis: results from a patient register linked to a medical birth registry

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Introduction: Inflammatory arthritis may influence fertility rates.

Objective: To compare fertility rates in women with juvenile idiopathic 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 of event at age of first delivery and log rank (Mantel-Cox) analysis with event at age of first delivery. Pairwise comparisons with log rank (Mantel-Cox) analysis with event at age of first delivery. Pairwise comparisons with log rank (Mantel-Cox) analysis with event at age of first delivery. Pairwise comparisons with log rank (Mantel-Cox) analysis with event at age of first delivery. Pairwise comparisons with log rank (Mantel-Cox) analysis with event at age of first delivery. Pairwise comparisons with log rank (Mantel-Cox) analysis with event at age of first delivery. Pairwise comparisons with log rank (Mantel-Cox) analysis with event at age of first delivery.

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 (60.8%) 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 RA women (p = 0.9), and OCA women were significantly more nulliparous than RA women (p = 0.04) and controls (p <0.001). RA women were significantly more nulliparous than 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 unperturbed 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.

Objective: 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 periovulatory ovulation was made in women with rheumatic diseases and healthy subjects. A LUF syndrome was suspected at the detection of a persistent unperturbed follicle with dimensions over 23 mm after day 25. During each menstrual cycle 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 90.0% 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 occurred in women with documented LUF under NSAID exposure: 3 after total NSAIDs cessation and the 4th 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 inducer of delayed ovulation because of strong COX 2 inhibition and a long half life. Discontinuing or replacing NSAIDs with analgesics starting with day 8 of the menstrual cycle may represent a feasible alternative for women with rheumatic disease who want to become pregnant.

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 (SLE)).

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, Agapar 9-10-10 with chelognathopitatosich. At the age of 31 years, loop electrosurgical excision procedure (LEEP) proved precanceris 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 vaginiae, 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 accordingly to different 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 recidivation.
antibodies, aCL, and anti beta-2-glycoprotein I, anti-j2GPI) 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-j2GPI levels in a series of patients with suspected APS for pregnancy morbidity.

**Methods:** LA with 4 assay tests, aCL IgG/IgM isotype and anti j2GPI IgG/IgM isotype were performed in a series of 157 pregnant women with clinical criteria of SSc. The pregnancy was planned after consultation with the mother – maybe considered during the first trimester in order to avoid complications, pregnancies in SSc should be planned 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.

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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 have already commenced pregnancy according to their decision. 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 died by massive pulmonary hemorrhage at 26th weeks’ gestation.


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-α) and TGFβ1 (rs1980207; T allele, proinflaming).

Surrogate Mother

<table>
<thead>
<tr>
<th>DQB1</th>
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<th>Cw</th>
<th>TNF</th>
<th>TGF</th>
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<tr>
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<td>3/11</td>
<td>7/1</td>
<td>1/1</td>
<td>1/1</td>
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<tr>
<td>Father</td>
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<tr>
<td>3/6</td>
<td>4/13</td>
<td>4/16</td>
<td>1/1</td>
<td>C/C</td>
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<td>CHB (ovodonation)</td>
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<td>2/6</td>
<td>7/13</td>
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<td>T/C</td>
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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 proinflaming T allele for TGFβ1.

Conclusions: This case report shows for the first time that a genetically unlinked donor, who is negative for 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 proinflaming TGFβ1 allele; the foetal genetics may be an added risk factor against antinatal outcome of pregnancy.

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 diagnosed in SLE diagnosed in SLE diagnosed in SLE following 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 the rheumatologists’ and gynaecologists’ communication, and 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, at 6 weeks postpartum, months post 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.